

Comprehensive Management Of Prostate Cancer

By Charles E. Myers, M.D.

Since 1987, I have specialized in the treatment of men with prostate cancer. As many of you know, I was diagnosed with this disease in February 1999. At that time, I had a palpable nodule, a PSA of 20.4 ng/ml and a Gleason 3+4 = 7 cancer. I decided that my only chance at survival was to pull out all stops and treat this cancer very aggressively. I received hormonal therapy with Lupron, Casodex, and Proscar for 18 months. Additionally, I received radioactive seed implantation and 3-D conformal external beam radiation therapy to a dose of 80 Gy or more to the prostate, a rim of surrounding tissue, the bottom third of the seminal vesicles, and the lymph nodes that drain the prostate gland.

During this process, I had found that as a prostate cancer patient I had to confront many serious issues that are often not addressed by the medical profession. Cancer is not just a lump in your body that can be cut out or killed by radiation or drugs. It alters every aspect of your life. Time and again, patients would tell me this. Some would even say that, in the end, it was the best thing that ever happened to them.

Statements like this make no sense to a physician who is solely focused on planning the details of surgery, radiation therapy, or androgen ablation. In my own case, prostate cancer led to a dramatic change in the direction of my medical career and altered the lives of all of those close to me. It completely altered what I view as the meaning of my life as well as the role I should play in the treatment of cancer patients. Through this experience, I have come to the conclusion that you, as a patient, simply cannot allow the management of your cancer and your life to be limited by the narrow views of the physicians you encounter.

Young Men with Prostate Cancer

I come from a family in which no one has died before age 80 for several generations. I had come to think of long life as a birthright. When I was diagnosed with prostate cancer at age 55, I remember professional colleagues trying to reassure me with promising five and ten year survival figures. I still remember the shock I felt when I realized they were talking about how nice it was that I might live to age 60-65! I immediately began to look seriously for 15, 20 or 30-year survival numbers. What I found was completely inadequate. The truth is that the long-term survival statistics are largely limited to 10 years, with a few studies reporting 15-year numbers, and only one or two with 20-year information. I had locally advanced prostate cancer with a significant chance of lymph node involvement and the only really relevant study was by the Mayo clinic on the results with radical prostatectomy and hormonal

therapy. Close to three-quarters of those men were dead at 20 years.

If you are under age 60, are otherwise in good health, and take reasonable advantage of the advances in medical care, you are very likely to live to be 80-90 years of age. None of the prostate cancer treatment options available to you can offer much assurance that you will not develop recurrent cancer sometime before your 80th or 90th birthday. Prostatectomy has been heralded as the "gold standard." Yet we know that approximately 90% of men eligible for radical prostatectomy have prostate cancer cells in their bone marrow at the time of surgery! While the number of cancer cells in the marrow decline in the year after surgery and become undetectable in many, there is no assurance that small nests of cancer cells do not remain in a dormant state waiting to be activated at some future date. Certainly, this phenomenon is not uncommon in breast cancer, a disease with many similarities with prostate cancer. Women can appear to be cancer free only to develop metastatic disease twenty or more years after a radical mastectomy.

I think you would be foolish to depend on surgery or radiation therapy as the sole tool to combat prostate cancer. As you will see, a combination of sensible diet and stress management has already been reported to slow the growth of prostate cancer from a median doubling time of 6.5 months to 17.7 months. If this is true, it means that if you were destined to develop recurrent prostate cancer 5 years from now, you can postpone that 12 to 15 years without the use of any drugs. You need to put in place a program that will slow or even prevent late recurrence of this cancer. This becomes even more prudent when you realize that the same program that makes sense for prostate cancer has proven benefits for the prevention and management of hypertension and atherosclerosis.

Naturally, at age 58, this has become an area of intense focus for me. I am also very interested in working with other young men with this disease to help them set up a program of their own, designed to delay or prevent the recurrence of prostate cancer.

Nature of a Comprehensive Program for Prostate Cancer

At the same time, in the scientific literature, there has been an explosion of new information about the many factors that control the growth and spread of prostate cancer. It is apparent that the behavior of this cancer is influenced by many things; it's controlled by your life-style as much as by anything the medical profession typically provides. There are now randomized controlled trials that point to a major impact of vitamin E, selenium, and lycopene on the progression of prostate cancer. Additionally, there is now strong laboratory-based evidence to support the impact of

vitamin E, selenium, and lycopene on prostate cancer. While each of these trials have some weaknesses, I would point out that neither radical prostatectomy nor radiation therapy have ever been properly compared with no treatment and uncertainties remain about the actual impact of these traditional treatments on prostate cancer patient survival. The point being that there is a strong scientific basis for thinking that comprehensive management of prostate cancer needs to include attention to nutrition and other life-style issues.

There are four key elements in the comprehensive management of prostate cancer.

Element 1: Comprehensive Medical Management

The first, and most obvious element is appropriate medical management that should include an overall health inventory as well as surgery, radiation therapy, or hormonal therapy that directly target your cancer.

You also need to know that the medical management of men with prostate cancer must be far more comprehensive than it usually is. We know that men with prostate cancer are nearly as likely to die of cardiovascular disease as they are of this cancer. The same life-style choices associated with a high risk of prostate cancer also foster the development of hypertension and atherosclerosis. In fact, for many men, prostate cancer is like the "canary in the coal mine" providing a warning of danger. It signals that there is a more fundamental problem that will cost you your life even if the radical prostatectomy is successful. It makes little sense to go through the rigors of prostate cancer treatment without addressing these broader health issues. Fortunately, new developments provide physicians with powerful tools to treat hypertension, atherosclerosis, and many of the complications of diabetes in ways that do not compromise the treatment of prostate cancer. Time and again men have entered my office seeking advice on management of their prostate cancer only to hear me tell them that their atherosclerosis, hypertension, or diabetes mellitus represent a far more serious threat to their survival. This is not an accident, the under treatment of these cardiovascular diseases in communities around the United States is a national tragedy.

Element 2: Stress and Its Management

Many patients recall a period of intense stress in the months to a year preceding the diagnosis of prostate and other cancers. Certainly, the diagnosis of cancer with its life-threatening implications represents a significant source of stress for many patients. There seems to be little controversy that increased stress can lead to anxiety and exacerbate depression. Additionally,

stress acts to intensify pain and delay recovery from medical procedures, such as major surgery. Stress of a life-threatening illness can disrupt families and impair job performance. Stress can exacerbate existing addictions to alcohol, drugs, and tobacco. Some cancer patients who are under prolonged stress from their disease and its treatment, can develop what is called posttraumatic stress disorder or "battle fatigue" from which they never recover, spending their remaining days "shell shocked." As I go around the country talking to patient-support groups, I repeatedly meet men who have been cured of their prostate cancer, but are now unable to function normally because of the devastation caused by the stress associated with their treatment. All of these facts make stress reduction an important part of comprehensive cancer care.

More recently, I have become intrigued by the possibility that stress may be directly linked to the progression of prostate cancer. The major stress hormones in your body are epinephrine and the closely related compound, norepinephrine. You can feel the effects of these chemicals if you are ever startled and sense your heart pounding in your chest.

The stress hormones, epinephrine and norepinephrine, foster the growth and survival of human prostate cancer cells. They do this by increasing the effectiveness of epidermal growth factor, one of the most important compounds supporting growth of hormone resistant cancer cells.

Stress impairs the function of the immune system. Natural killer cells have the capacity to kill cancer cells and this may be important for cancer patients. Following stress the function of natural killer cells is consistently decreased. Natural killer cells have adrenoreceptors on their surface, and activation of these receptors by norepinephrine or epinephrine blocks the effectiveness of these immune cells. The adrenoreceptor in this case is a beta-receptor rather than the alpha-receptor involved in prostate biology. In the laboratory and in tissue culture, drugs that block the beta-2 receptor protect natural killer cells during a period of stress.

In summary, stress causes an increase in the release of epinephrine and norepinephrine from sympathetic nerve endings and from the adrenal medulla. These hormones stimulate the response of prostate cells, normal or malignant, to epidermal growth factor. Additionally, these catecholamines suppress the function of the immune system. If these factors were biologically important, you would predict that prostate cancer cells would spread preferentially to the adrenal gland. This is indeed the case. Recent detailed autopsy studies performed in men showed that the adrenal gland is the fourth most common site involved in metastatic prostate cancer!

The implications of all the evidence supporting a role of epinephrine in the biology of prostate cancer is that stress reduction may improve the quality of your life, reduce your pain, and make for family peace, as well as slow the growth of prostate cancer. The first prospective clinical trial testing this concept has been published. Saxe, et al., combined a low-fat diet with stress reduction techniques in ten patients. The rate at which the PSA was increasing slowed in eight out of ten men with the median PSA doubling time going from 6.5 to 17.7 months! Despite the small numbers, this difference was statistically significant. The limitations of this trial are fairly obvious. The numbers are small and the interventions included stress reduction as well as dietary intervention. A randomized controlled trial testing nutrition and stress reduction is being conducted by Dean Ornish, M.D. and early results suggest that this study will also show a large advantage to stress reduction and a low-fat diet. This trial has a superior design to the Saxe study with a larger numbers of patients, and longer follow-up. However, it still does not directly assess the relative contributions of diet compared with stress reduction.

Element 3: Nutrition

There is a growing body of sound laboratory science that document how various naturally occurring chemicals can either stimulate the growth or, alternatively, cause growth arrest and death of prostate cancer cells.

Table 1. A Few Naturally Occurring Chemicals Able to Suppress Prostate Cancer:

Lycopene
Vitamin E
Calcitriol, the active form of Vitamin D
Fish oil omega 3 fatty acids, DHA and EPA
Green tea polyphenols
Resveratrol, a polyphenol from red wine
Selenium
Quercetin
Silymarin

The story is most complete for the impact of antioxidants on prostate cancer. This area was reviewed in great detail in the May 2001 (published in February 2002) issue of our newsletter, the Prostate Forum. In brief, when prostate cells are exposed to the male sex hormone testosterone, they generate hydrogen peroxide. The peroxide causes oxidative damage to the genetic material in a cell, potentially fostering the emergence of cancer or the progression of cancer already present. In the laboratory, antioxidants like vitamin E and selenium, decrease oxidative damage to prostate cells. Studies done on human prostates show a steady increase in oxidative damage with age. When oxidative damage exceeds a certain threshold, the risk of prostate cancer increases rapidly, approaching 90%.

Two randomized controlled trials have detected an impact of antioxidants on the death rate from prostate cancer. In one trial of more than 1000 people followed for ten years, selenium supplementation caused a greater than 60% decline in the death rate of prostate cancer. In a second trial involving more than 20,000 subjects, vitamin E caused a 40% decline in the death rate from prostate cancer. Both trials have defects and new clinical trials are in progress to see if the results are reproducible. A sizable body of epidemiological studies and limited laboratory work also supports the impact of selenium on prostate cancer deaths. In the case of vitamin E, laboratory studies have shown that vitamin E triggers a suicide program in prostate cancer cells.

Each of these studies focus on a single item in the diet, but fail to give any sense of the overall impact of nutrition on the progress of prostate cancer. As mentioned under stress reduction, the two clinical trials by Saxe and Ornish show impressive effects from the combination of low-fat diets and stress reduction. The all-inclusive nature of these trials means that they do not allow separate assessment of the impact of diet versus stress.

Element 4: Exercise

As with stress reduction, many of the benefits of exercise relate to your general health and overall quality of life. There are a number of specific benefits attributable to exercise. Exercise plays an important role in reducing the risk of osteoporosis. A regular program of exercise will reduce the risk of blood clots and help prevent weight gain associated with hormonal therapy. As we mentioned earlier, cardiovascular disease is a major cause of death in men with prostate cancer and the contribution of exercise to cardiovascular health is well established.

Falls are a serious problem for men and women over the age of 65. Approximately 30% of people in this age group will fall in any given year. For people over 75, falls account for 70% of emergency room visits, 40% of hospital admissions, and represent the leading cause of accidental deaths. The damage is often so severe that 50% of those admitted to the hospital for injuries caused by a fall will be discharged to a nursing home. As you will see, the issues involved in the prevention of falls and the management of prostate cancer overlap in several ways. Exercise that involves endurance, strength, flexibility, and balance, significantly reduces the risk of falls.

Depression and a sense of hopelessness overcome many men after the diagnosis of prostate cancer. This can lead them to neglect their health or even simply give up and wait for death to come. Over the years, I have come to feel that this is the single most important factor limiting our ability to reduce the death rate from prostate cancer. While antidepressants can be very useful,

they are expensive and have troublesome side effects, such as loss of sex drive and weight gain. Exercise has been shown in randomized controlled trials to be effective in lessening depression in the elderly and in those with chronic disease.

Other benefits to exercise are more difficult to quantify. Exercise can decrease fatigue and nausea, as well as improve the ability to conduct daily life and add a sense of well being. These findings are consistent with what I have observed in my patients.

A number of studies indicate a lower risk of prostate cancer in men who exercise. This has remained controversial because men who exercise are also more likely to eat a diet low in fat and rich in fruits and vegetables. They are less likely to be obese and do not smoke. For these reasons, I have not discussed the role of exercise in prostate cancer prevention in the past. I have altered my opinion based on a recently published clinical trial.

The alpha-tocopherol, beta-carotene cancer prevention trial was designed to test the impact of alpha-tocopherol (vitamin E) and beta-carotene on the incidence of lung cancer in tobacco smokers. This is a very large study that has now enrolled more than 20,000 subjects. We discussed this study in our June 1998, issue because it shows a dramatically lower risk of prostate cancer in the men on vitamin E. This study also showed a lower risk of prostate cancer in men who exercised regularly. Furthermore, the largest impact, a 40% reduction, was seen in men who walked at work and exercised moderately for recreation. The mechanism by which exercise might alter the risk of prostate cancer remains uncertain. Exercise has been reported to lower total testosterone and its precursor, androstenedione. Also, mild exercise has been reported to enhance natural killer cell activity.

Assembling Your Own Comprehensive Program

In most communities of any size, you can find people able and willing to help you master techniques of stress reduction and exercise. Since the prostate-healthy diet is very similar to a heart-healthy diet, books or even personal guidance are widely available. If you are proactive and insistent, you can generally find a physician who will treat cardiovascular disease appropriately using the best of the new drugs. However, none of this is likely to happen until you take control of your medical treatment and make it happen.

My own experience has made me want to help other patients put together a program that offers comprehensive management of their prostate cancer. I write a monthly newsletter that permits patients to keep abreast of the advances in prostate cancer treatment. Sara Steck, my wife Rose, and I collaborated to write and publish a book on nutrition, called the Eating Your Way to Better Health. This book reviews the science behind a prostate-healthy diet, includes how to equip your kitchen, menu plans, and a wide range of recipes, based on Italian, Mexican, and Asian cuisine.

Still, many couples I meet have been unable to overcome their inertia to make the life-style changes needed. During the past year, Rose, Sara, and I have been running two-day seminars designed to help patients get over this inertia. We hold them in our home in the foothills of the Blue Ridge Mountains of Virginia limited to 10-11 couples. The small numbers allow us to work closely with couples as they learn how to put these changes into action.

In February, I took the final step and opened the American Institute for Diseases of the Prostate. The goal of this Institute is to provide comprehensive medical management to men with prostate cancer. In the Institute, we carefully evaluate your prostate cancer in the context of your overall health to help create a program specifically tailored to your needs.

Contact Information

Prostate Forum Newsletter and the Nutrition Guide:

**Rivanna Health Publications, Inc.
P.O. Box 6696
Charlottesville, VA 22906-6696**

Telephone: (434) 974-1303 Fax: (434) 974-9597

E-mail: rosemyers@earthlink.net

www.prostateforum.com