

PROSTATE CANCER COMMUNICATION

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VACCINE FOR PROSTATE CANCER

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Shortcomings of current prostate cancer treatment

Roughly 30-40% of patients who initially present with prostate cancer confined to the prostate gland will experience cancer recurrence. Many of these patients will receive drugs that suppress the release of testosterone and other male hormones, since starving prostate cancer cells of circulating male hormones can delay the growth and spread of prostate cancer. Hormonal therapy is often begun when an increase in prostate specific antigen (PSA) is observed after therapy for cancer confined to the prostate. However, hormone suppression therapy does not cure prostate cancer. Prostate cancers become resistant to this therapy within 1-2 years, and there is no effective therapy for patients who have failed hormone suppression therapy following a return of prostate cancer after primary therapy. There is a need for additional therapies that improve the control of prostate cancer that remains confined to the prostate region, and for cancer that metastasizes beyond the prostate.

Background of vaccine therapy for cancer

The immune system is the body's natural defense system against disease. Immune system manipulation as a therapeutic approach for cancerous tumors was first considered when it was observed that some human tumors experience spontaneous regression

All cells have unique proteins or protein components on their surface called antigens. Many cancer cells produce cancer-specific antigens. The goal of using cancer antigens as a vaccine is to teach the immune system to recognize the cancer-specific antigens and to reject any cells with those antigens. The antigens activate white blood cells called B lymphocytes (B cells) and T lymphocytes (T cells). B cells produce antibodies that recognize and bind to a specific antigen to destroy the cancer cell. T cells that recognize a particular antigen can attack and kill cancer cells. Vaccines can also use the patient's own dendritic cells (white blood cells that activate the immune system) to connect antigens to the body's killer cells (T-cells).

Let's Conquer Cancer in OUR Lifetime

Cancer involves uncontrolled abnormal cell growth. The immune system is mostly unable to differentiate between cancer cells and normal cells. The inability to recognize cancer cells as foreign, stems from the fact that cancer cells are cells that were at one time normal. Cancer vaccines facilitate the immune system to overcome its tolerance of cancer cells so that it can recognize them as invading antigens and attack them. This is accomplished by injecting a preparation of inactivated cancer cells, or proteins unique to the given cancer, into the patient.

Prostate cancer vaccine

Background

Therapeutic vaccines, which include prostate cancer vaccines, are used to treat conditions that have already occurred. The premise of prostate cancer vaccine is to induce the immune system to recognize tumor-associated antigens displayed on human malignancies and to direct cytotoxic responses to these targets.

Immunotherapy, or vaccine therapy for prostate can-

cer, is appealing as a therapeutic direction because the prostate gland is not essential for survival, which makes the proteins expressed in normal and cancerous prostate gland cells suitable targets for immune response. Additionally, a large number of genes and proteins with specific or preferential expression in the prostate gland and in prostate cancer have been identified. Agents called promoters that control the expression of these genes have been identified and cloned. Another reason prostate cancer is well-suited as a target for vaccine therapy is the availability of serum PSA as a marker of therapy effectiveness.

PSA is normally present in small amounts in men who are free of prostate cancer, and PSA levels rise when prostate cancer develops. Patients have been shown to mount T-cell responses to PSA. Some prostate cancer vaccines use genetically modified viruses that contain PSA. The patient is injected with the virus, the immune system responds to the virus and becomes sensitized to cancer cells containing PSA, and the sensitized immune system then destroys the cancerous cells.

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Articles authored by other than the editor may not fully reflect the views of the corporation but are printed with the understanding that the patient has the right to make his own interpretation of the efficacy of the information provided.

In an effort to conserve space and be able to insert as much material as possible in the newsletter, references from various articles are intentionally omitted. If you would like to obtain those references, please contact PAACT, we keep all of the original articles and the references used on file.

Types of prostate cancer vaccines

Whole cell vaccines

Whole-cell vaccines potentially use all the antigens found on the tumor cells. The cancer cells come from the patient or from laboratory-derived human tumor cell lines. The cells are inactivated and then re-injected back into the patient. Whole-cell vaccines modify the tumor cells to express an immune-activating agent. GVAX (Cell Genesys) is an example of a whole-cell vaccine.

Antigen-specific vaccines

Invading viruses or bacteria produce protein fragments, or antigens that trigger immune system attacks and antigen-specific vaccines are designed to target tissue-specific proteins such as the antigen. Several prostate-specific proteins have been used as targets for prostate cancer vaccines, including prostate-specific antigen (PSA), prostatic acid phosphatase (PAP), and prostate-specific membrane antigen (PSMA). Other delivery approaches include cancer-associated carbohydrate vaccines, which target carbohydrates preferentially expressed in prostate cancer; viral vaccines, which elicit powerful T cell responses and include the vaccine Prostavac; peptide-based vaccines; and plasmid DNA-based vaccines.

Tumors are skillful at suppressing immune response and evading recognition, but dendritic cells represent a way to bypass a tumor's natural defenses. Dendritic cells activate T cells by locating antigens and directing T cells to them. One strategy used in antigen-specific vaccines is to increase the number of dendritic cells in a vaccine, to trigger a correspondingly robust T-cell response. Dendritic cells can be removed from the patient, and then infused back into the patient to induce a specific antitumor response after being loaded with tumor antigens.

Specific Prostate Cancer Vaccines

Provenge

Provenge (Dendreon) combines a synthetic version of prostatic acid phosphatase (PAP), a protein on the surface of most prostate cancer cells, with dendritic cells removed from the patient. This preparation is designed to break the patient's immune tolerance to PAP.

Provenge is designed to stimulate the immune system to attack the 95% of prostate cancer cells that generate PAP. A patient's own immune cells are collected,

sensitized to the protein, and then reinfused into the patient.

Prostavac

Other prostate cancer vaccines use genetically modified viruses that contain PSA. The patient is injected with the virus, which sensitizes the immune system to cancer cells containing PSA, and then the immune system destroys the cancerous cells. In addition to PSA, PROSTVAC-VF also incorporates TRICOM, Therion Biologics proprietary compound of costimulatory molecules designed to enhance the antigen presentation and activation of immune responses essential for the tumor destruction.

The two components of Prostavac vaccine are the "priming vaccine," made from vaccinia virus, and the "booster," made from fowlpox virus.

GVAX

GVAX® (Cell Genesys) immunotherapy is comprised of two prostate cancer cell lines genetically modified to secrete granulocyte-macrophage colony stimulating factor (GM-CSF), a hormone that stimulates immune response to cancer cells, and then irradiated for safety. The goal of GVAX is to stimulate a systemic immune response against the patient's prostate cancer, destroying prostate cancer cells that persist or recur following surgery, hormone or radiation therapy. GVAX uses inactivated prostate cancer cell lines to express GM-CSF.

What patients are candidates for prostate cancer vaccine?

Most prostate cancer vaccines are currently tested on patients whose cancers are growing or spreading, and are no longer responsive to hormone therapy (sometimes referred to as androgen independent prostate cancer).

Generally speaking, patients with weakened or compromised immune systems are not candidates for prostate cancer vaccine therapy, because they don't have the ability to generate the necessary immune system response. Patients who have the following conditions are not considered suitable candidates for prostate cancer vaccines:

- HIV positive
- Hepatitis B or C
- Current use of topical or systemic steroids such as prednisone

- Autoimmune disorder such as Grave's disease or Addison's disease
- History or current eczema or similar skin condition
- Serious current medical illness
- Cardiac disease

Timing of prostate cancer vaccine:

Vaccine therapy is best administered early in the course of recurrent prostate cancer for maximum likelihood of extending survival and improving quality of life. The ideal time to receive the vaccine is right after hormonal therapy begins to control tumor spread, when immune cells outnumber cancerous ones. It is believed that vaccines stand a better chance of getting T-cells to respond after most of the tumor is destroyed by hormone therapy.

Effectiveness of prostate cancer vaccine:

For the most part, trials of prostate cancer vaccines published to date have not been designed to assess effectiveness in terms of freedom from cancer progression and overall length of patient survival. Instead, many have focused on the number of patients who exhibit a full or partial response to the vaccine therapy, adding to the growing body of evidence that prostate cancer is a feasible target for immunologic manipulation. There are many unknown variables related to prostate cancer vaccine treatment; researchers are still learning about the optimal level of immune response needed to mediate cancerous tumor cell death.

Safety of prostate cancer vaccine:

Prostate cancer vaccines generate a benign side effect profile and are generally well tolerated because they are designed to target only the cancer cells and spare healthy ones. Also, no dose-limiting toxicity has been observed among the many clinical trials conducted.

Availability of prostate cancer vaccine:

Prostate cancer vaccines are experimental; none have been licensed for marketing in the U.S. by the Food and Drug Administration.

At this time, vaccines are only available through enrollment in clinical trials. According to the National Cancer Institute, less than 3 percent of U.S. adults with cancer participate in clinical trials; thus, patients should be encouraged to participate in such trials if they are eligible.

Future outlook for prostate cancer vaccine:

The growing body of evidence strongly supports ongoing and future research and development of prostate cancer vaccine. New discoveries and refinement of current practice will increase the effectiveness of prostate cancer vaccine. An example of this is the discovery that mature dendritic cells are more effective in stimulating T cell response than the immature ones used until recently. There is evidence that radiotherapy can elicit an immune response, and research combining vaccine therapy with radiation therapy is being conducted.

A major limiting factor in the effectiveness of prostate cancer vaccine is the stubborn immune system tolerance displayed by many advanced tumors. Current and future research is expected to make progress in this area.

Another possible application of prostate cancer vaccine is in cancer prevention, which is justified by the large proportion of cancer that is hereditary.

Gale Armstrong 1939-2005

A very dear and special friend of PAACT's, and personally of Rick Profit's, for the past 35 years has passed away from Cancer. This man was very special in many ways and deserves mentioning to our membership.

There are very few people that I can honestly say have held special meaning to me in my life, Gale Armstrong being one of those very special people. I cannot begin to mention the love and affection that Gale and his family have bestowed upon my life without shedding tears. The reason for delaying the eulogy was because Gale's family always includes an update along with their Christmas card.

When I take a moment to stop and think of Gale, there are a few special times that stand out to me. I have been married for twenty nine years come this June and I can still remember what Gale and Carol gave us on our wedding day. There is also a little saying that Gale never let me forget, "You do not need luck, you make your own." It is unfortunate with this job that you become so close to cancer patients and then they eventually move on to their eternal resting place.

If at this time anyone is considering making a donation to PAACT, we would like to encourage you to do so as a memorial on behalf of Mr. Gale Armstrong and those who have passed before him.

Gale Armstrong, 65, passed away on February 16, 2005 after a two year battle with cancer. At his funeral, two statements were read; one written by his son-in-law James Wagenaar, and one by his son, Dean.

Every one needs a Gale Armstrong in their life. A man who was a confidante, advisor, and friend. Gale learned from his humble beginnings, early hardships, and personal struggles how to handle any situation. Gale was one of the wisest men I have had the pleasure to know. He could discuss philosophy, history, religion, politics, or any topic with the command of a college professor. Gale was a man of vision and dreams. Some of us dream, but Gale acted on his dreams. He wasn't afraid of failure or adversities that may arise while chasing your aspirations. Gale lived life and added tobasco sauce!

Gale loved family. As I went through the photographs and memories, I realized that there were few photographs that didn't have five or six of us in them. There were photographs of everyone; in the kitchen, taking hikes, out on a boat, on the beach, playing cards, around the Christmas tree, or somewhere exotic Gale had heard about for families.

Gale worked side by side with his wife and family for many years. There are not many families that can work around each other so much without conflict and strife separating them. Gale kept the peace, made it better, and solved the problems. When we had issues with wives, children, grandchildren or siblings; Gale could counsel us through our differences.

His love for his wife was the kind that great romantic novelists write about. Gale would speak of Carol with misty eyes, like a teenager speaking of his first love. Carol was Gale's everything. She made his life complete. Carol made Gale the caliber of man that he was.

Gale knew nothing of the designation of father-in-law, stepfather, or grandfather. He was a father to us all. He loved us with inspiration from the Heavenly father. The greatness of a man is reflected in the sorrow of those left behind. Our sorrow is immense.

Gale is at peace, the Peace which passes all earthly understanding. We will miss him, but we rejoice in his blessed Eternity. *Dr. James Wagenaar*

My father overcame many obstacles in his life; a birth defect, uncaring parents, and poverty. He was able to overcome them by his intelligence and his drive to succeed, but most importantly by his charm. When he turned it on, he could talk the devil into setting himself on fire. It wasn't charm that could light up a room. Instead it was an easy grace that made the recipient feel both important and respected. While achieving great success in life, he never met anyone he considered superior to him; he also never met anyone he considered inferior. He could talk to kings and convicts; business moguls and busboys with equal magnanimity. He was also generous of his time and money to those causes he saw fit and to those people who needed it the most. I believe he will be remembered the most for his sage wisdom and his advice. Blessed with the ability to view all sides of an issue but with the unerring eye to see the best possible path that a person should take; his council will be sorely missed. *Dean*

Maximum Surveillance with Minimum Intervention: Who to Treat, When to Treat, How to Treat. The Role of Monitoring Tools.

By Dr. Israel Barken
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If all treatment options offered to a patient with prostate cancer were easy, most patients perhaps would have chosen one instead of waiting. Most of us prefer to take action because action cures fear. The diagnosis of cancer instills immediate and overwhelming fear. What will the cancer do if I don't do anything is one of the first thoughts in the patient's mind. Since most treatment options are not palatable to the patient and perhaps not everybody needs to be treated, it's no wonder strategies were developed to avoid treatment if at all possible.

When a patient faces the task of making a decision, the following factors are weighed: the extent of the disease, the aggressiveness of the disease, biological age - as defined by the patient's general health, and

the personal preferences of the patient - defined by his attitude towards uncertainties in relation to gain or loss issues.

There are three historical eras related to watchful waiting as a treatment for prostate cancer. These eras were shaped by the availability of monitoring technology. The newer monitoring tools affected both the use of watchful waiting as a primary treatment and the type of secondary treatment that followed.

The 3 periods can be described as:

1. The pre-PSA era
2. The PSA era
3. The Post PSA era (Tumor markers and sophisticated imaging period).

Pre-PSA Era: Historically, prior to the days of PSA, “Watchful Waiting” was coined to denote avoiding any primary local treatment of the prostate. In reality, however, many patients chose Watchful Waiting because of their fear of making a decision and the desire to avoid distressing side effects. Given the paucity of monitoring tools to follow the patient, Watchful Waiting was a very passive approach. What the follow up consisted of was the reporting of symptoms by the patient, periodic physical examinations and minimal blood testing by the physician. These tools were very limited compared to the new monitoring tools we have today. The treatment of choice when progression of disease became apparent was hormonal blockade. Primary treatment was not available as a choice since the tools of monitoring were not sophisticated enough to catch the disease while it was local only. The Pre-PSA era was typically a “cat is out of the bag” story; by the time we realized the disease was progressing, it was no longer local.

PSA Era: The PSA was introduced in the mid 1980s and used to monitor patients who elected to delay treatment after initial diagnosis. New definitions sprung up to replace the traditional Watchful Waiting (see table below). The utility of the PSA created a different approach to deal with progression of disease. It gave information early enough to still enable local primary treatment with curative intent. During the same period of time, nomograms appeared on the scene. Nomograms are derived statistically from grouping historical data on large groups of patients. The items looked at in these nomograms included

Clinical stage, Gleason Grade, and PSA. These initial nomograms tried to predict the pathological findings after radical prostatectomy. The nomograms expanded into other stages of disease like recurrent disease after primary local therapy. Some of them tried to predict success of treatments like the Kattan Nomograms predicting recurrent disease after radiation. The PSA also pushed Watchful Waiting into other stages of disease such as biochemical failure and hormone refractory disease. In both of these scenarios, there are no symptoms to alert us, but there is evidence of progression. Therefore, patients in these stages can utilize the same monitoring tool of Watchful Waiting. You can see from this how Watchful Waiting extended its impact on all stages of disease once the PSA era was in full swing.

Tumor Markers and the Era of Sophisticated Imaging: We were and are overlapping this period with the PSA period because some of the new monitoring tools were available at the same time that the PSA became available. We are now developing a better understanding of the molecular basis of diseases. Because of that, more attention is given to the molecules related to prostate cancer and these are the tumor markers. There are many new tumor markers. Most of them are used as research tools, but some of them are available commercially which means they have been used “off the shelf” for patients who wanted more aggressive monitoring. Here are some of the names of the new tumor markers in the blood and in the pathological tissue: CGA, NSE, CEA, IGF-1, BCL-2, P53 TGF-B1 & Il6SR, Thymosin B-15 and the list goes on.

Other developments based on molecular understanding have enriched our monitoring capabilities. Functional imaging such as spectroscopic MRI is a prime example.

The availability of these tumor markers and new imaging is starting to change the paradigm related to whom to treat, when to treat and how to treat. The new monitoring tools are now applied not only at the time of diagnosis but also to the more advanced stages of disease such as biochemical failure after treatment and hormone refractory disease.

Here are some of the definitions related to Watchful Waiting as they have appeared in the scientific medical literature over the past 10 years.

These are just some of the publications and views of experts in the field.

Definition	Paradigm	Reference
Watchful Waiting	Conservative approach to avoid side effects of treatment	Gerber, GS University of Chicago 1994
Watchful Observation	Monitoring PSA Doubling To guide treatment intervention for patients managed conservatively with watchful observation alone	Choo, R University of Toronto, Canada July 1, 2001
Selective Delayed Intervention	Selectively delayed intervention based on predefined criteria of disease progression	Choo, R Toronto_Sunnybrook Regional Cancer Center University of Toronto, Canada Apr 2002
Expectant Management	Expectant management with Selective Delayed Intervention	Klotz, L University of Toronto, Canada Sept 2002
Expectant Management	Ultimately patients receive active treatment despite initial waiting period	Meng, MV University of California San Francisco, Dec 2003
Delayed Therapy	Delayed therapy with curative intent	El-Geneidy Oregon Health & Science University March 2004
Temporarily deferred therapy	Younger patients' eligible to defer their decision when to be treated and that is the primary treatment. The number of comorbidities a patient has	Carter, CA Uniformed Services University of the Health Sciences Bethesda, MD Feb 2005

	will influence the type of secondary therapy.	
Active Surveillance	A new strategy aiming to individualize the management of early prostate cancer by selecting only those men with significant cancers for curative therapy.	Hardie, C The Royal Marsden and Institute of Cancer Research, Surrey, United Kingdom May 2005
Active Surveillance	Identify the minority of patients with aggressive disease and offer them curative treatment while sparing the remainder population the morbidity of unnecessary treatment	Klotz, LH University of Toronto Ontario, Canada June 2005.

Maximum Surveillance and Minimum Intervention: Choo and Klotz were the first to report on a prospective active surveillance protocol. The table above gives the historical review of shaping and reshaping the new paradigms of Watchful Waiting. Out of my own long career devoted to prostate cancer, I came to a personal conclusion to apply the dictum: Maximum Surveillance and Minimum Intervention. Maximum Surveillance is always active and always objectified by the doctor. The Minimal Intervention is a decision that has to be taken by the patient in choosing the least aggressive treatment. My dictum has stood the test of time with countless patients whom I was and still am in contact with, now as their personal Coach.

The Future: With the advent of gene-molecular fingerprinting, our suspected cancer cells will be able to receive correct, individualized treatment. These approaches will take away the guess work and the waiting periods. Each individual will receive his treatment according to his private, personal and specific fingerprinting of his tumor. No more relying on

statistics formed by groups as published in medical journals. I believe that this future is quickly approaching. I am proud to tell you, the reader, that PC-REF is an active player in realizing this future. Through patient donations and support, we have given a seed money grant in 2005 to a researcher at Johns Hopkins to investigate the genetic fingerprinting of prostate cancer cells in metastatic disease. Let's continue to open the door to a better era as we move into 2006.

To learn more about surveillance and interventions with the new paradigms described in this article, the following PC-REF services are available. "ASK DR. BARKEN" a free, weekly telephone call in show, every Tuesday evening at 6 pm Pacific, 9 pm Eastern, toll free 1-877-727-3301. Also available is individual Coaching with Dr. Israel Barken for which a donation to PC-REF based on time is expected. Money raised through Coaching goes toward funding new research for prostate cancer. In helping yourself, you can also help others.

Prostate Cancer and Diet

By Charles E Myers Jr., M.D.

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As many of you know, I was diagnosed with poor prognosis prostate cancer in February of 1999. Fortunately, I remain in remission. In part this is due to the aggressive initial treatment I received and in part I think it is due to the program I've developed to suppress cancer recurrence. An important part of that program is diet and I've naturally been very interested in updating it as research on prostate cancer develops. If you want to get a sense of this literature, go to PubMed (www.pubmedcentral.nih.gov/) or Google Scholar (<http://scholar.google.com/>). One of the first things you'll notice is that there are more than 1,000 papers on the broad issue of the impact of diet and nutrition on prostate cancer. The next thing you'll notice is that there are almost as many controversies as there are articles. Of course, there is another complication: most men with prostate cancer are also at risk for high blood pressure, diabetes, and heart disease as a result of elevated cholesterol. In my own family, there is a strong history of high blood pressure. With these issues in mind, I've tried to se-

lect the most prudent diet for general health while also preventing prostate cancer relapse.

This drive led me to focus on a Mediterranean diet. The literature supporting the Mediterranean diet is vast. Among the clinical trials that support the diet, I've found two particularly persuasive in terms of general health. The Lyon Diet Health study looked at 605 people in the intensive care unit with their first heart attack. Half followed a version of the Northern European diet with modest cholesterol restriction. The other half followed a Mediterranean diet patterned after that found on Crete. After four years the number of new heart attacks decreased by 50%, while the number of new cancers decreased by 60%. The second study is the HOPE trial. In this study, researchers followed close to 2,300 subjects between the ages of 70-90 for more than 10 years. Researchers also looked at four life-style issues and the risk of death from various causes. The four life-style issues were: not smoking, exercise, moderate alcohol consumption, and the Mediterranean diet. Overall, those who incorporated all four positive life-style habits had close to a 70% reduction in death rate compared with those who had none of these. The Mediterranean diet accounted for about a 25% reduction in overall deaths as well as deaths from cancer and heart disease.

There is less extensive information on prostate cancer and the Mediterranean diet, but I find it quite persuasive. Saxe and his colleagues took a group of patients who had recurred following radical prostatectomy and placed them on the Mediterranean diet. Their PSA doubling time was 6.4 months before the diet change and 17.7 months afterward. This is nearly a 2/3 reduction in the growth rate of the cancer. This alone has the potential to triple the lifespan of these patients.

Another factor I find persuasive is that laboratory data on how food components control prostate cancer growth show that it is plausible that the Mediterranean diet will suppress prostate cancer growth and spread. For example, there are now over 120 papers that link the fatty acid arachidonic acid to the growth and spread of prostate cancer. Aspirin, ibuprofen, and other nonsteroidal anti-inflammatory drugs work by blocking arachidonic acid and also appear to have a favorable impact on prostate cancer progression. Arachidonic acid is found in large amounts in meat.

The Mediterranean diet as practiced on Crete limits red meat to once a month and white poultry to once a week. The major daily sources of protein are beans, nuts, and grains. This diet is quite low in arachidonic acid content, but not low in fat. In fact, there's a relatively high fat content in the form of olive oil and nuts, such as almonds, pistachios, and hazelnuts. All of these are sources of monounsaturated fat: a form of fat that markedly reduces "bad" or LDL cholesterol. In the laboratory and in clinical studies, this type of fat doesn't stimulate prostate cancer growth and spread. While it is now popular to recommend a low fat diet to men with prostate cancer, there's no basis for excluding olive oil or these nuts from your diet and they actually have a dramatically favorable impact on general health.

The Mediterranean diet is also rich in fish and the fat found in fish—DHA and EPA—blocks the adverse effects of arachidonic acid. Adding fatty fish represents another step away from a low fat diet that actually improves overall health.

The Mediterranean diet is also rich in tomatoes and other vegetables, especially dark green leafy vegetables like broccoli, kale, and spinach. Among other things, these provide lycopene and lutein, two natural compounds that appear to suppress prostate cancer.

Evidence in favor of the Mediterranean diet is everywhere in the medical literature. For example, there have been a number of recent studies suggesting that pomegranates may be beneficial for men who have prostate cancer. This fruit is one of the classics of the Mediterranean diet, both as a fresh fruit and as syrup you can use when the fruit is out of season.

The Mediterranean diet itself encompasses a wide variety of foods, but there are some products that make the diet a tasty and attractive alternative for me. (Note that I have no financial link of any kind with these products.)

Special Lentils

Beans and other legumes are great for your health and offer protein free of cholesterol and arachidonic acid. But beans are not without problems. First, they can take a lot of time to cook from scratch. Also, there is the problem of intestinal gas—as I'm sure your wife can attest to! Lentils, on the other hand, don't cause gas and are quick to cook. Now, the len-

tils you find in the stores may take up to an hour to cook, and while tasty, they are not really special. But there are gourmet lentils that are much smaller and have their own unique flavor. Because of their small size, these often cook very rapidly. I have found <http://chefshop.com> one of the best internet sites to learn about these special lentils and get samples to try. You can also find these on Amazon.com. Some unusual lentils include: beluga lentils, which are tiny black beans that cook in 20 minutes or less and have a rich, smoky flavor. Pardina browns are another great small lentil with a rich nutty flavor and again cook in 20 minutes or less. You are more likely to find small French green lentils in local gourmet stores. You can get fancy in how you cook these, but I love to sauté diced celery and onion, add the beans and water and cook. While the beans are cooking, I crush garlic into olive oil—my current favorite is rosemary-flavored oil—and let sit until the beans are cooked. At that point, I add garlic and olive oil and salt to taste. (As I explained, this isn't a low fat diet!)

Sardines

Sardines are rich in heart healthy fats, are very low in the contaminations found in many fish, and are a key part of the Mediterranean diet. Unfortunately, commercially available sardines range greatly in quality. The brand I've found consistently good is King Oscar. My favorite is the double layer sardines packed in olive oil.

Avocado Oil

The taste alone makes avocado oil a special treat. There are practical advantages to the oil, though, such as the fact that it is very stable at high cooking temperatures: it doesn't break down until temperatures exceed 600 degrees F. But what I really love is the flavor of the best Avocado oils: they have a rich golden hue and an almost buttery aftertaste. The best brand I have sampled so far is the Elysian Isle Gourmet Avocado from New Zealand. The oil is produced by cold pressing and is clearly made with care. You can find the product at several sites on the internet, but I suggest you use Google to find the best deal.

Albamarle Pippin Apples

Among alternative medical practitioners, there's a wide-spread myth that sugar feeds prostate cancer. Many men therefore eliminate fruits and other sweets from their diet. But in truth, there isn't one shred of scientific evidence to support this idea. Studies by

Dr. Giovannuci and colleagues at the Harvard School of Public Health show that the greater the intake of fruits and sugar, the lower the risk of metastatic prostate cancer. And it appears that diabetics, with their high blood sugar levels, are at a reduced risk of dying of prostate cancer. One argument I've heard in response to all this is that the PET scan is successful in visualizing cancers because cancers take up the radioactive sugar used. Well, PET scans are useless in visualizing prostate cancer in all but the most aggressive cases because this is one cancer that does not take up sugar in any great quantity.

Now, a key element of the Mediterranean diet is that it is rich in fruits like dates, figs, pomegranate, grapes, and oranges. My favorite fruit is an apple that has been grown in our part of Virginia since pre-Revolutionary times: the Albemarle Pippin. The Albemarle Pippin was a favorite of Thomas Jefferson and Benjamin Franklin and was a major export item from America to Europe in that time. Even today, the website devoted to Monticello describes this apple (<http://www.monticello.org/gardens/inbloom/>). Unfortunately, the Albemarle Pippin has largely disappeared from American commerce. It bears only every other year, the trees take their own sweet time maturing and the fruit is a dull green color mottled with brown. But each fall, here in Albemarle County, Virginia, a few local orchards have the apples for sale. My wife and I make sure to buy them by the bushel. Fortunately, they store very well and actually taste better after months of storage. In fact, I think they are reaching their peak right now. The flavor is rich, complex, and aromatic with a perfect balance between sweet and sour.

Freeze Dried Raspberries

You've heard of frozen raspberries, but what about freeze-dried? Freeze-dried fruits are fantastic: you can just pop them in your mouth like candy and the flavor gradually emerges as you chew. The drying concentrates the flavor. I've never tasted anything like this with the fresh berries. You can also quickly crush these berries into a powder that can be added to tea or put on top of other fruits. One of my favorites is to take Concord grape juice or pomegranate juice, add the raspberry powder and heat until it steams. We buy cans of 3.5 pounds of raspberries freeze-dried at the peak of freshness from <http://www.store.honeyvillegrain.com>.

What do you spread on toast?

When I tell patients that they will need to do without butter, many ask in astonishment: "What do you spread on toast, then? Luckily, there are many options. Almond butter is a great tasting yet healthy alternative. I also love garlic crushed in olive oil plus a little salt. But my real favorite is home-made hummus. Nothing could be easier to make. I place cooked chickpeas (garbanzo beans) in a blender with ground up sesame seed butter (tahini) and olive oil. Sometimes I use olive oil and a bit of water instead of tahini. This base can then be flavored in many ways. One of my favorites is to add hot pepper, but the variations are endless. Finally, when only the flavor of butter will do, I use one of the butter-flavored salts like Butterbuds.

La Cucina Italiana

This is a wonderful monthly magazine, written in English, but devoted to Italian food. While many of the recipes contain meat or dairy fat, each issue has at least several new ideas you can use. It's also a great way to find out about internet and mail order sources of Mediterranean food items. You can even find out how to rent a villa in Italy if you want and can afford to. You can subscribe at www.italiancookingandliving.com or call toll-free at (888) 857-7016.

I hope these products and ideas show you that adopting a Mediterranean diet need not be a burden but an adventure that has the side effect of improving your overall health while helping keep your prostate cancer from recurring.

Complete Remissions Are Important

By Charles E Myers Jr., M.D.

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(Note: this is excerpted and somewhat modified from a recent issue of the Prostate Forum devoted to the treatment of young men with prostate cancer)

We can now cure a number of cancers even if they are metastatic. This is true for acute lymphocytic leukemia in children, Hodgkin's disease, nonHodgkin's lymphoma, and testicular cancer. In each of these diseases, cure is most likely if the patient rap-

idly enters a complete remission, typically within 4 months of starting treatment. If we can't create a complete remission, cure simply isn't possible. For each of these cancers I just mentioned, complete remission means that we can find no evidence of cancer after treatment. Among individuals who attain a complete remission, some have microscopic deposits of cancer that will re-grow over time. Thus, the ultimate measure of successful treatment is when the person remains in complete remission for years after treatment is over. This is called a durable, unmaintained complete remission. As you'll see, it's possible to attain complete remission in men with metastatic prostate cancer, but these remissions are not durable if they aren't maintained. Nevertheless, my approach to men with metastatic disease is governed by the knowledge that it's now possible to place many into complete remission. Based on what we know about treating cancers with drugs, this approach is likely to give any man the best chance of long-term survival.

So, complete remission in men with metastatic prostate cancer means that no evidence of the cancer can be found. By this I mean that the PSA is less than 0.05 ng/ml. Furthermore, bone scan and CT scan results show no evidence of remaining cancer. My current views on this subject were formed following a provocative discussion with David Crawford, the head of Urology at the University of Colorado. In 1989, he published a major randomized controlled trial comparing Lupron alone with Lupron + Eulexin. In this trial, Crawford and his colleagues noted that a certain proportion of men with advanced metastatic disease entered complete remission on hormonal therapy. In our discussion, that so influenced me, he expounded upon this by noting that many of these men remained disease-free for many years. It is important to note that the men in the trial were on continuous hormonal therapy, so these are not unmaintained complete remissions.

As I mentioned in Volume 9 #5 (Prostate Forum-Hormonal Therapy I), I commonly use intermittent hormonal therapy and what has surprised me most about this approach is that there are a proportion of men who remain in complete remission for years after treatment ends. Dr. Robert Leibowitz of Compassionate Oncology reports that this is common if we administer Proscar during the time patients are off hormonal therapy. My own experience with inter-

mittent hormonal therapy supports the contention that drugs that prevent the synthesis of dihydrotestosterone (DHT), like Proscar or Avodart, do what Dr. Leibowitz claims – they help maintain complete remission. One of the first patients I treated in this fashion started hormonal therapy in April 1996 and stopped in April 1997. Since then, we've used Proscar to maintain his disease; his PSA has remained undetectable for more than 8 years despite having a normal testosterone for more than 6. Thus, while it is possible to attain a complete remission in metastatic prostate cancer, these remissions are not durable if they are not maintained.

Based on these experiences, I divide prostate cancer treatment into two phases. The first phase focuses on attaining a complete remission. The second phase is designed to delay or prevent disease recurrence. In large part, all of my efforts are focused on either obtaining as complete a response as possible or in looking for better agents to maintain a remission.

My current program for newly diagnosed men with metastatic cancer is to first try to induce a complete remission with triple hormone blockade® using LHRH agonists, such as Lupron, Trelstar, Eligard or Zoladex, combined with Casodex and either Proscar or Avodart. If the patient does not enter a complete remission with this program, I use second line hormonal therapy with agents such as ketoconazole, transdermal estrogen, or aminoglutethimide. Taxotere-based chemotherapy is only initiated after second line hormonal therapy is no longer causing the PSA to decline. The advantage of this approach is that many of my patients don't receive chemotherapy and thus are spared the side effects of this form of treatment.

Prostate Cancer and BPH

Dr. Bruce West
Health Alert
www.healthalert.com

"I thought you would like my recent PSA info! If you recall, I started out two years ago with a PSA of 66.6. My blood PSA this week is now 0.4! Who says this Standard Process stuff doesn't work miracles."

This is a quote from a friend who was faced with sudden, aggressive prostate cancer at a young age. In fact his doctor told him to go home, get his affairs in

order, and plan for some aggressive surgery and toxic treatments. He opted to *ignore* his urologist's recommendation and start on a nutritional protocol, *with no medical treatment at all*. The rest is history – he is cured. Here's the great news about prostate cancer...

What happens when you find out you have prostate cancer? Your doctor recommends a prostatectomy, radiation, seed therapy (brachytherapy), watchful waiting, Lupron injections, and/or some other treatment. What should you do? That is a question that tens of thousands of men are faced with each year. In 2006 alone, it is expected that over 230,000 men will be diagnosed with prostate cancer. And not one in one thousand are prepared with adequate information to make the correct decision. This includes both patients and doctors.

Choosing the right kind of therapy has a lot to do with the aggressiveness of the cancer and your current age. If you are in your late '70s to '80s and your cancer is not aggressive, watchful waiting may be perfect for you. However, if the cancer is aggressive, you must take action – and some form of therapy must be considered.

Alternatively, if you are younger and the cancer is not aggressive, you may want to reconsider the medical "gold standard" of radical prostatectomy. Why? Because prostate cancer is *overwhelmingly likely to recur* after surgery given the many years you have left to live. In almost all cases, the cancer is already throughout the body at the time of diagnosis. And if you're younger and have an aggressive cancer, you must take action. But the gold standard of surgical therapy may be wholly inadequate, or even dead wrong.

Prostate Cancer is Systemic

The first factor for all prostate cancer sufferers to fully understand and accept is that prostate cancer, once discovered, is rarely if ever confined to the gland or prostate capsule – even though your doctor may tell you with certainty that the cancer is confined to the prostate gland. The sad fact is that the overwhelming majority of men diagnosed with prostate cancer, regardless of age, have had microscopic spread of tumor cells *long before the diagnosis was made*.

The most rapidly growing number of prostate cancer sufferers in the United States are those men who have already been "cured" with radical surgery and/or radiation. These men make up the largest number because they still have identifiable PSA in their blood – indicating persistent cancerous cells throughout the body – despite aggressive, radical therapy. This recurrence of rising PSA takes place in *the overwhelming majority of men* diagnosed with prostate cancer and treated with the medical "gold standard."

No doctor can tell you that your cancer is confined to the gland. The real prostate cancer survivors are those men who have had the cancer cells starved out of existence, and/or those men whose immune system is able to eliminate the cancer seeds and cells that are released into the bloodstream. These inevitably settle or nest in the bones, attract a blood supply to themselves, and grow. This takes place in almost all prostate cancer sufferers.

Once you understand this phenomenon, it is easy to understand that settling for *any local treatment alone* is inadequate. Local treatment includes radical prostatectomy, radiation therapy, seed therapy, or cryotherapy. All local therapies are designed to remove or destroy the prostate gland. Treatment usually comes with the assurance that "we got it all." In truth, there *has never been any study* that shows that any local (even radical) therapy is both necessary *and effective* in the treatment of prostate cancer.

Amazingly, despite aggressive local therapy, men who receive surgery or radiation are equally likely to die from prostate cancer as those men who have taken no action. Or in other words, if you are young enough, and the cancer is aggressive enough, and you take no other action, the cancer will come back and try to kill you.

For men with PSA recurrence, your PSA will slowly rise and unless something else is done (usually hormone blocking therapy), the cancer will debilitate and even kill you – despite the quote "we got it all." So you need to take action – and that action is most often a combination of a powerful nutritional protocol and/or Triple Hormone Blockade® (THB). With this type of therapy there is *rarely the need for any local therapy at all*.

You read that correctly. There is no need for radical prostatectomy or radiation therapy. That means no drastic or enduring side effects from surgery: urinary incontinence, fecal incontinence, impotence, diapers, and more. That means no radiation damage to your bowels. That means no hospital and all the inherent risks of disease or death that come with a hospital visit. In fact, therapy of this type is now considered the “Platinum and Diamond Standard.”

Triple Hormone Blockade® Therapy (THB)

This remarkable therapy, started by Robert L. Leibowitz, M.D., involves 13 months of hormone blocking medications. The hormones eliminate testosterone (androgens) from the body, starving the prostate cancer out of existence. It can be tough – with side effects such as hot flashes, temporary change in sexual function, decreased energy, and in rare instances breast growth. But it is only for 13 months and there is no other medical therapy that can measure up to its results.

Triple Hormone Therapy works best when started early – even though lots of men with advanced prostate cancer have had excellent results. So when first diagnosed, you would want to consider getting in touch with Dr. Leibowitz at Compassionate Oncology Medical Group in Los Angeles (www.prostateweb.com or 1-310-229-3555). According to Dr. Bob, virtually all men can tolerate these reversible side effects for 13 months.

In my opinion it is not too high a price to pay for a potential prostate cancer cure. Surely it beats having your prostate removed, then waiting around with your fingers crossed hoping that “they got it all.” Dr. Bob has a long list of prostate cancer survivors who are willing to serve as volunteers to answer questions. For this type of therapy, information, and counseling, do not hesitate to give his office a call.

Nutritional Therapy

Always include a powerful nutritional protocol to accompany other therapies. My friend with the PSA of 0.4 opted for a nutritional protocol alone – without any local treatment and without Triple Hormone Blockade® Therapy. The basics of a protocol for men with prostate cancer are the very same basics he used. The products and dosages that can work include *Arginex* (6/day), *Cataplex E* (6/day), *Cyruta-Plus* (9/day), *Prostate* (3/day), *Cataplex F* (6/day),

and *Immuplex* (3/day). This kind of nutritional therapy combined with THB® is powerful indeed. If you remember that all prostate cancer is systemic, and you use the right kind of therapy, you can beat this disease.

Benign Prostatic Hypertrophy

If you only have benign prostate hypertrophy (BPH), remember that this can be helped nutritionally also. We use three to nine *Palmettoplex* capsules with three to six *Cataplex F* tablets daily with great results. If your prostate is just too big to shrink, there is a wonderful medical procedure that is safe and effective called *Green Light PV*, which is short for Selective Photo Vaporization of the Prostate.

In this procedure, an 80-watt laser is used to vaporize some of the excess tissue in the prostate gland that is blocking the urethra and holding up urine flow. It is done with a catheter and a tiny laser. It takes about a half hour and usually provides profound and long-term relief without the problems and potent side effects of a surgical reaming out of the prostate gland (TURP).

There is almost no risk of infection; nothing is cut; and problems with impotence, nerve damage, incontinence, and more are now a thing of the past. About two millimeters of prostate tissue surrounding the urethra is vaporized, eliminating the pressure and stricture that causes urinary problems. You can find out about Green Light PV on-line at www.laserscope.com or call them at 1-800-356-7600 for a referral doctor.

But even this seemingly benign technique can carry problems if the doctor performing the therapy does not have the necessary skills. To avoid an urologist who may only have a weekend seminar under his belt, I suggest you go to skilled and experienced men who have performed lots and lots of these procedures. In the Detroit area call Dr. Mahmood Hai (1-734-595-1166). In the Los Angeles area call Dr. Thomas Bogaard (1-213-483-6830). I have checked on both these doctors and visited Dr. Bogaard. Be assured you will get the best procedure at either of these clinics.

Even if you have Green Light PV treatment, it is always best to use *Palmettoplex* and *Cataplex F* to give you the bet odds of superior results. So whether

you have a prostate that is just a nuisance, or one that can be life threatening, always remember to use a protocol that really works. And don't put all your eggs in one basket with the standard medical approach of local therapy. It could cost you your life.

Get Treatment for Cancer-Related Depression

Coping Magazine
March/April 2005

Depression is not just sadness or feeling blue. It is a combination of symptoms that often includes a change in weight and appetite, in sleep and energy, in thinking and ability to concentrate, in your desire to participate in social activities, in your overall mood, and in your interest in both people and your surroundings.

These symptoms are often accompanied by feelings of guilt, worthlessness, or helplessness that can escalate into thoughts of taking your life. If you are experiencing pervasive feelings of guilt, worthlessness, or helplessness, or if you are thinking about taking your life, seek help immediately. There are many approaches to dealing with depression, including medications and the help of mental health professionals.

Some degree of depression is common in people who are coping with cancer, and some cancers are more frequently associated with depression, like those that arise in the pancreas and lung. About 25 percent of all people with cancer experience clinical depression, causing distress, impaired functioning, and decreased ability to follow a treatment schedule. Not surprisingly, depression is seen more often in people with advanced stages of cancer, and in those who have more disability from their cancer and/or poor pain control.

It is not uncommon for people with advanced cancer to experience hopelessness or a sense of helplessness when they first learn that their cancer has recurred or that the treatment has failed, whether or not there are alternative treatments available for the cancer. A period of shock, disbelief, or denial is very common, often followed by a period of depression.

With time, most people with cancer and their families are able to come to terms with what at first seems impossible to accept. For many, understanding what to expect and gaining more knowledge about the can-

cer and its progression make it easier to move forward. If the initial sense of hopelessness or helplessness persists and is accompanied by feelings of despair, guilt, and worthlessness, the possibility of significant depression should be considered. It is important that you speak with your doctor, healthcare team, or your family and friends about these feelings. Depression can make all of your symptoms worse.

Another reason it is important to talk to your healthcare team about depression is that some of the drugs used to treat cancer may make your depression worse. For example, steroids (dexamethasone, prednisone, etc.) may make depression more severe, and some biologic therapies, like interleukin-2 and interferon, can cause depression.

Both counseling and medications can make a very big difference in how you feel and improve other symptoms at the same time. There are many medications available to treat depression, some of which begin to have an effect within two to four weeks. In addition to counseling and medications, here are some other strategies to consider:

- Talk about feelings and fears that you may be having – do not keep them inside.
- Remember that it is OK to feel sad and frustrated.
- Try deep breathing and relaxation exercises several times a day.
- Don't blame yourself for feelings of fear, anxiety, or depression.
- Engage in enjoyable activities.

Depression in the setting of advanced cancer is best treated by a combination of medication, supportive therapies (such as relaxation and distraction), and counseling. Your prognosis, and therefore the time available for treatment of your depression, is an important consideration when choosing the best treatment. If you have months of treatment ahead of you, you have time to wait the two to four weeks sometimes needed to see the benefit from the majority of antidepressants. If the time is very short, stimulants (which act more quickly) may be of greater benefit to you.

Many people assume that depression is inevitable if you have cancer. This is not true. Treatment for depression has proven benefits for anyone living with cancer.

LAC-PAACT ¹UPDATE

By Gregory H. Teufel, Esq., Chairman²

Apologies for the long hiatus for this column. We are glad to have some good news to report.

In the middle of 2005, Medicare posted payment rates to Hospital Outpatient Departments for 2006 and proposed a 12% decrease in an already low reimbursement rate for prostate cryosurgery. This would clearly have limited access to cryosurgery. There had already been hospitals that stopped doing prostate cryo because of the limited reimbursement.

PAACT coordinated efforts with other interests and LAC-PAACT volunteer Gordon Woodward, Esq., a lawyer with Schnader's Washington, DC office, attended a meeting in August with Medicare officials to urge against the proposed reimbursement rate reduction.

As a result of that meeting and the efforts of LAC-PAACT combined with numerous other interested organizations, the reimbursement rates were actually increased instead of decreased, helping ensure continued access to this treatment option. We were very glad to be able to help in that effort.

The next challenge we hope to undertake is approval for off-label use of chemo's for prostate cancer. Thanks to Harry Nowicki for bringing this issue to our attention last year. The issue of off-label use of chemo's for prostate cancer is a very complex one because the use of these chemo's have primarily been in phase II trials. Hence, it is very difficult to provide peer-reviewed articles that insurance companies require for "proof of efficacy." It is extremely frustrating and depressing to see off-label use of other drugs allowed and not chemo's that have shown some efficacy for prostate cancer in the smaller trials. We are looking for volunteers to assist with address-

¹ LAC-PAACT is PAACT's legal advisory committee. Despite the name of the committee, for various reasons, we generally cannot give you legal advice or act as your personal attorney. Please do not consider anything in this article as legal advice. If you want legal advice, I encourage you to consult a lawyer in your state, so that your specific situation and local laws can be considered.

²Gregory H. Teufel, Esq. is a partner in the Litigation Department of Schnader Harrison Segal & Lewis LLP's Pittsburgh office. The views expressed are those of Mr. Teufel personally and not of the firm.

ing this issue. If this sounds like an issue that would interest you and you want to help, please contact Greg Teufel.

We want to keep you aware that the LAC-PAACT is here to help you. We are particularly helpful in addressing insurance and Medicare coverage issues related to advanced cancer treatments. Please do not hesitate to contact us regarding any coverage or other legal issues related to advanced cancer treatments. We want to help and need your help in identifying the areas of greatest need.

We are also always seeking volunteers to help with LAC-PAACT activities. Even if you are not a lawyer, you can volunteer if you are inclined to help with law related issues. Also, if you know any lawyers that would be sympathetic to our cause, please make us aware of them and them aware of LAC-PAACT. Just contact Greg Teufel regarding volunteer opportunities with LAC-PAACT.

If you have been denied coverage for an advanced cancer treatment, be sure to let us know and we will see if there is anything we can do to help.

Contact LAC-PAACT

If you have any questions or comments, or any suggestions about how LAC-PAACT can best serve your needs, please do not hesitate to contact me. The preferred method to contact me is via email at gteufel@schnader.com. You can also call me at work at (412) 577-5289, home (412) 421-7123, or on my cell phone (412) 596-6316, or send me a letter at Schnader Harrison Segal & Lewis LLP, Suite 2700, Fifth Avenue Place, 120 Fifth Ave., Pittsburgh, PA 15222 or a fax at (412) 765-3858. Please note that requests for the LAC-PAACT kit should be addressed to PAACT. Contact information for PAACT is on page 2 of this Newsletter. Please remember that this article is not legal advice and I cannot generally give you legal advice or become your personal attorney.

WHAT THE HECK HAS BEEN GOING ON IN MY WORLD-PART 10 or In Honor of the Super Bowl or Winter Olympics-Part X!!!

By Mark A. Moyad, M.D., M.P.H.

Michigan lost in the last seconds to Ohio State and all I can say is after several months of intensive post-game

psychiatric therapy, that cost thousands of dollars and involved numerous medications - it is going to be okay and I really hope Michigan wins next year (excuse me for a second - my tongue is bleeding) I think I am going to take a vacation after this column and do something relaxing like go hunting with the Vice President (what a cheap shot - no pun intended or that was a fowl joke - pun intended).

67) The penis, the heart, and overall cardiovascular disease (CVD) risk: Are they all related? (This sounds dirty and x-rated, but it really is not and if it was I would not admit it because the PAACT editors would take this article out before you read it)!?

(Reference: Thompson IM, Tangen CM, Goodman PJ, Probstfield JL, Moinpour CM, Coltman CA. Erectile dysfunction and subsequent cardiovascular disease. JAMA 2005;294:2996-3002.).

Here is a wonderful study, which I think really sends the right message. Men aged 55 years or older randomized to the placebo group (n = 9,457 participants) in the Prostate Cancer Prevention Trial (PCPT) at 221 United States (U.S.) locations were given evaluations every 3 months for CVD risk and erectile dysfunction (E.D.) between 1994 and 2003. Researchers also adjusted their results for potential confounders such as age, body mass index (BMI), blood pressure, cholesterol, diabetes, a family history of heart attack, race, smoking status, exercise level, and quality of life. A total of 85% of these patients had no CVD at the beginning of the study, and 47% of these men had E.D. The men that reported E.D. during the study or had E.D. when the study started had a significant 25-45% increased risk of having a CVD event (like a heart attack or a stroke for example). The correlation of E.D. and CVD events was in the range of risk associated with smoking or a family history of heart attack. The smaller arteries and vessels in the penis are most likely reflecting what is going on in the larger or coronary artery circulation. This is not a new thought because past studies of patients with diabetes not only demonstrate a higher risk of E.D. but also CVD. It is also important to mention in this current study of men in the PCPT that other things were significantly associated with CVD events and not just E.D. Other risk factors for Cardiovascular Disease events included:

-AGE (just getting older increases your risk of heart disease - that sucks man - I just had a birthday - feel free to send me a gift, but please keep it under a 1,000 dollars)

-Race

-BMI

-Systolic blood pressure

-HDL or "good cholesterol" (every 5 mg/dL decrease)

-Smoking

-Poor overall health status

-Family history of heart disease

-History of diabetes

-Current use of blood pressure control drugs

-E.D.

This just proves once again that many of the accepted risk factors for CVD bear some relation to E.D. The bottom line to patients is that heart health seems to be equivalent to penile health and vice versa. What this research also means is that any man that reports E.D. should also have a CVD risk analysis. E.D. may be an early symptom in patients with CVD. Now, this study may not mean much to the men that have experienced erectile dysfunction because of prostate cancer treatment, but it still should apply. Increasing your risk for heart disease only reduces the chances of regaining erectile function regardless of the prostate cancer treatment you received. If you want to increase your chances of having good erectile function then you should reduce your cardiac disease risk to as close to zero as possible.

68) Combining sildenafil (Viagra®) with an L-carnitine dietary supplement may enhance the response to Viagra® and help to restore sexual function in men after prostate surgery - are you kidding me!?

(Reference: Cavallini G, Modenini F, Vitali G, Koverech A. Acetyl-L-carnitine plus propionyl-L-carnitine improve efficacy of sildenafil in treatment of erectile dysfunction after bilateral nerve-sparing radical retropubic prostatectomy. Urology 2005;66:1080-1085.).

Researchers from Italy that have a history of working with the dietary supplement L-carnitine decided to perform a unique and small preliminary clinical study. Men, average age 60-63 years, less than 10% were obese, approximately 50% had high cholesterol, most (55%) were past smokers, and had prostate removal surgery 1-year earlier, were placed in one of three groups:

1) placebo (33 patients)

2) sildenafil (Viagra®) 100 mg on demand + acetyl-L-carnitine (ALC) 2 grams/day + propionyl-L-carnitine (PLC) 2 grams/day (32 patients)

3) 100 mg of sildenafil (Viagra®) on demand (35 patients)

It should also be kept in mind that the prostate removal surgery received by these patients was the bilateral nerve sparing type. Both (bilateral) nerve connections to the penis were left intact during the surgery making it easier to have a spontaneous erection after surgery compared to men that have only one (unilateral) nerve bundle of the two removed, or both removed, which in either case makes it more difficult to have a spontaneous erection compared to bilateral sparing. Men were followed for 4 months then evaluated. Men from group 2 taking the dietary supplement L-carnitine + Viagra® had a better response than those who just took Viagra® for 4 months. Men from group 2 had a significantly greater impact on erectile function, sexual intercourse satisfaction, orgasm, and general sexual well-being. However, men did not

have an improvement in the area of sexual desire. L-carnitine did not decrease or increase the side effects of Viagra® (headache, flushing, dizziness, nasal congestion, and nausea). Researchers from this study concluded “PLC and ALC proved to be safe and reliable in improving the efficacy of sildenafil in restoring sexual potency after bilateral nerve-sparing radical retropubic prostatectomy.” This is an interesting small study because anything that can enhance sexual function beyond what is already given should be encouraging. L-carnitine supplements do have a good safety record and they are receiving a lot of attention in several different areas. L-carnitine supplements may reduce fatigue in older individuals or those receiving treatments that increase the risk of fatigue such as chemotherapy or hormone suppression for breast and prostate cancer. Carnitine is a compound found in every cell of the human body and carries other compounds (fatty acids) to be used for energy production and antioxidant activity. One of the side effects of L-carnitine is euphoria or increased energy levels and it is this side effect that may help patients reduce fatigue. Two of the patients (6.2%) from group 2 experienced euphoria and none from group 3. One of the biggest side effects with L-carnitine in my experience is simply price - these are generally expensive dietary supplements and for patients that need to take 4 grams or 4000 mg a day this will definitely be costly (so if you are interested you should talk to your doctor about starting with a low dose - about 500 mg daily). Viagra® is also expensive. One concern I have with this study is the need to have other independent researchers confirm these findings, because this one research group from Italy has found numerous benefits with L-carnitine and have completed most of this research. Another concern in this study was that men took the Viagra® as needed or “on demand” instead of every day as was the case with the carnitine supplements. In order to truly evaluate how well the L-carnitine supplements were enhancing the impact of Viagra® the men needed to take the Viagra® daily, or at least take it on a regular schedule. Regardless, I still believe that L-carnitine has enough interesting preliminary data that some patients can use it at a variety of dosages from 500 mg – 4,000 mg a day, but compare prices of the different brands before you buy, and keep in mind that although it has a good safety record in preliminary studies that doesn't mean it won't come with a catch somewhere down the road (If you do not believe me then just read the next article.). In other words, everything comes with a catch so get your doctor's approval before using this stuff after surgery.

69) L-arginine dietary supplements for erectile dysfunction or exercise enhancement may come with a BIG CATCH in individuals with heart disease.

(Reference: Schulman SP, et al. JAMA 2006;295:58-64)
Researchers were trying to determine whether L-arginine dietary supplements given in addition to standard therapy

after a heart attack could actually improve heart health. This study was a single-center, randomized, double-blind, placebo-controlled trial for 6-months. A total of 153 patients following a first heart attack were enrolled, and 77 patients were 60 years or older (68% were men). Ejection fraction changes (a measurement of how well the heart is working where higher ejection fractions mean better function), non-invasive measures of vascular stiffness, and clinical events were recorded over 6 months. Patients were randomly assigned to receive L-arginine supplements with a goal dose of 3 grams, 3 times a day (3,000 mg/day) or matching placebo for 6 months. No significant change from baseline to 6 months in left ventricular ejection fraction or vascular stiffness measurements were found in either group, including those patients age 60 years or older. In other words, the L-arginine supplements did not improve heart health. However, 8.6% of the participants (6 individuals) died during the 6-month study in the L-arginine group compared to none in the placebo group. Due to safety issues, the safety monitoring committee closed enrollment and stopped the study. L-arginine supplements when included as part of standard therapy after a heart attack does not improve ejection fraction or vascular stiffness measurements, and may be associated with a higher rate of death. L-arginine should not be taken in individuals with heart disease. L-arginine is an amino acid dietary supplement, which functions as a precursor for nitric oxide synthase, and a potential producer of nitric oxide (NO). It has become a popular supplement for men experiencing erectile dysfunction with or without the use of proven standard erectile dysfunction prescription medications. Previous long-term studies of this supplement have not been conducted in high-risk individuals at risk for a cardiovascular event (like a heart attack). This supplement is being used by individuals experiencing erectile dysfunction, female sexual dysfunction, interstitial cystitis, those attempting to enhance overall physical function, and perhaps for many other reasons. However, based on this single trial, L-arginine supplements should be discouraged in any high-risk cardiovascular patients and perhaps anyone else until more safety and efficacy issues are resolved.

70) Can a statin drug improve the prognosis in men treated for localized prostate cancer?

(Reference: Moyad MA, Merrick GS, Butler WM, et al. Urology 2005;66:1150-1154.)

We decided to conduct a preliminary study on statin use and its impact on clinical presentation and biochemical progression-free survival after brachytherapy. This was a retrospective analysis of consecutive patients treated with brachytherapy at one institution. A total of 512 patients consecutively treated with permanent brachytherapy for clinical stage T1c-T3aNxM0 prostate cancer were included in this study. Biochemical progression-free survival (bPFS) was defined as a prostate-specific antigen

(PSA) level of 0.4 ng/ml or less. Median follow-up was 5.3 years. Adjustments for a variety of confounding variables included: statins, age, body mass index (BMI), PSA level, Gleason score, percentage of positive biopsies, perineural invasion, prostate volume, planning volume, dosimetric quality, supplemental external beam radiation, tobacco use, hypertension, and diabetes. The 8-year biochemical progression-free survival rate was 94.6% for the entire group. Pretreatment PSA level and percentage of positive biopsies were statistically significant predictors of outcome - in other words a lower PSA and prostates with less cancer increased the chances of success overall. However, a significantly lower pretreatment PSA value, percentage of positive biopsy cores, more favorable PSA density, and earlier clinical stage were found in the patients taking statins at the time of treatment. When analyzed by specific statin use, 97.8% of patients taking atorvastatin (Lipitor®) versus 94.7% taking other statins were free of biochemical progression. This was the longest reported follow-up period to date that suggests that statins, especially atorvastatin (Lipitor®), may improve most clinical presentations and may improve bPFS in men after being treated with permanent brachytherapy for clinically localized prostate cancer. An improvement in bPFS favored statin users when stratified by low-risk (100% versus 96.5%), or high-risk (90.9% versus 85.3%) for recurrence. Therefore, the use of atorvastatin (Lipitor®) especially may have improved outcomes in patients. This is obviously not proof of cause and effect, but these results support previous laboratory and epidemiologic studies, which suggest that statins may have a greater impact on presentation and progression of disease compared to incidence. Atorvastatin may have been favorable because of several reasons: the ability to enter cancer cells, half-life, overall potency, other effects, or simply because it represented the largest use of any statin compared to another. We were not able to study the newer cholesterol lowering drug known as Crestor® because not enough patients were taking this drug at the time of the study.

71) Dietary silicon consumption may improve bone mineral density in men and pre-menopausal women, especially at the hip.

(Reference: Jugdaohsingh R, Tucker KL, Qiao N, Cupples LA, Kiel DP, Powell JJ. Dietary silicon intake is positively associated with bone mineral density in men and premenopausal women of the Framingham Offspring Cohort. J Bone Miner Res 2004;19:297-307.)

This was a cross-sectional, population-based study of 2,847 participants. Dietary silicon (Si) was found to be significantly associated with higher bone mineral density at the hip in men (average age 59 years) and premenopausal women (average age 47 years), but not postmenopausal women (average age 61 years). The intake of silicon (about 30 mg/day) is among the highest for a trace element in humans. The group in the highest category of

silicon intake in this study consumed greater than 40 mg Si/day, and lowest was less than 14 mg Si/day. Major sources of dietary silicon in the diet are cereals/grains and their products such as breakfast cereals, bread, and beer. Other sources are fruits and vegetables (bananas, raisins, beans, lentils), and unfiltered drinking water.

TOP FOOD/BEVERAGE SOURCES OF TOTAL SILICON
1) Bananas
2) Beer
3) Cold cereal
4) White bread
5) Beans/lentils
6) Coffee
7) Pizza
8) Dark bread
9) String beans
10) Muffins/bagels
Other: Brown rice, pasta, potatoes...

In the Western world one of the major sources of bioavailable and bioactive silicon is beer, especially for men. This is nice to know for the moderate beer drinkers of the world. Dietary silicon may improve bone mineral density in men and premenopausal women. Estrogen levels may impact the incorporation of silicon in bone, which is why post-menopausal women may not have benefited as much. Regardless, a variety of simple and pleasurable foods and beverages may help to improve bone mineral density at the hip. Hey - thanks to this study I'm going out to have a beer right now!

72) Hey what is the status of that new weight loss prescription drug known as Acomplia® - when is it going to get approved by the FDA?

Well, it looks like we all need to be a little more patient. Acomplia® taken daily (20 mg a day) versus placebo, helped patients reduce weight by as much as 17 pounds compared to placebo over a two-year period. Individuals also lost over 3 inches in their waist, improved their cholesterol and were more likely to quit smoking while taking the drug versus a placebo. So, if this drug works so well in so many patients why is the FDA waiting longer to approve it? The FDA felt like more safety data was needed on this drug. There was a slightly higher rate of irritability and depression reported on the drug versus placebo so this is why they want more safety information. I was really surprised over the past few days that the FDA took this position, but what can you do? There was also some concern by the FDA that since this drug works by a mechanism of action that has not really received a lot of previous research they wanted to wait a little longer. Acomplia is an endocannabinoid receptor antagonist, which means it blocks some of the same receptors in the brain that are

stimulated by marijuana to give a person the munchies or increased appetite (Note from Moyad: I do not know this fact about marijuana from personal experience, but rather from reading the actual research on this product.) We need to be a little more patient and see what happens, but I do believe this drug will get approved eventually and I will keep you up to date. It is also interesting that we do not yet have really effective medications for weight loss. There are only two prescription drugs approved on the market currently for long-term weight loss. One drug is called "Meridia®" and it works somewhat by controlling appetite and impacting some brain receptors, but the overall effectiveness has been mixed and there have always been blood pressure issues with this drug. I think the medication is okay but many people do not experience significant weight loss on this product. The other drug is known as "Xenical®" and it is a lipase inhibitor, which means it blocks the absorption of fat. So, you have to get some fat in your diet for it to work well and you have to take a multivitamin daily because it also blocks the absorption of the so called "fat-soluble" vitamins (vitamins A, D, E, and K). It can come with some interesting side effects that are reduced over time, such as loose stools, and again, it works okay but not good enough to write home to momma about (if you know what I mean). The strange thing about the world of drug approval is that recently the FDA seemed to favor the over the counter sale of "Xenical®" because the patent of the drug is going to expire soon. So, soon individuals will be able to buy a lower dose of this drug over the counter? What about over the counter weight loss products? Despite what you are hearing from some so called "experts" at 2 A.M. on an infomercial there is little proof that any over the counter dietary supplement or herbal product helps you lose weight. Many of these products actually contain stimulants, which can raise your heart rate and blood pressure. This is why I have never been a fan of these products. What happens long-term to a person that takes them besides the fact that their wallet or purse becomes thinner? Not much in my experience. In a later issue we will talk about weight loss products for individuals with and without cancer. In the meantime, one of the more controversial but safer weight loss products that never gets enough attention are the dietary or dietary supplement sources of fiber. These products not only promote colon health, but give people a feeling of fullness, and as an added bonus they help lower cholesterol. You should talk to your favorite doctor about the possibility of increasing dietary fiber and/or taking a dietary fiber supplement. It comes with so many tangible benefits that I love to discuss fiber with patients, but because I am lazy and PAACT only pays me 100,000 dollars a year in monopoly money to write this column I will talk more about fiber in a later issue. Personally, I like All-Bran® cereal in the morning. It has worked well for me and is a large source of dietary fiber. The only problem I have with All-Bran® is that on

the back of the box there are pictures of people and they all look very, very old so I feel like the company is not advertising well to my age group. Fiber powders and fiber wafers or bars work well, but I am not a big fan of those dang new fiber pills because you have to take so many each day to equal a bowl of All-Bran that they are not worth it in my opinion.

HAVE A NICE DAY, AND MAY YOUR UPCOMING SPRING VACATION BE FILLED WITH CHEAP DIETARY FIBER, AND NOT EXPENSIVE OVER THE COUNTER WEIGHT LOSS PRODUCTS PROMOTED BY MANY BONE-HEADED SO CALLED "HEALTH EXPERTS."

Finally, Mark I heard you are the new editor of a medical journal by Elsevier called "Seminars in Preventive and Alternative Medicine." Is this true? Yes, it is and if you go to the web-site of Elsevier publications (www.elsevier.com or call 1-800-654-2452) you can order the same medical journal that the health professionals can use that updates the latest on diet, supplements, and drugs... for cardiac disease, different cancers, and anything else that is happening in preventive and alternative medicine. This is the end of this shameless promotion, but for some patients the medical journal should be a good source of objective education.

PS. In this column we talked a lot about erectile dysfunction (E.D.). Individuals interested in some recent medical reviews on E.D. after localized prostate cancer treatment have many articles to choose from, but a nice recent article is by Raina R, Agarwal A, and Zippe CD. Urology, November 2005, volume 66, pages 923-929. They review the nonoral treatments like vacuum constriction devices (VCD), injections, and other methods. They also review some of the oral treatments and some of the future clinical studies. This review is brief and to the point, but they do a good job in my humble opinion. The only strike against them is that they live in Ohio (just kidding - man am I asking for hate mail or what - keep in mind that of course I am joking because I was actually born at the Cleveland Clinic).

Letter to the Editor

Enclosed is a check from my father's estate. In his will he requested that this be given to PAACT.

My father believed that the PAACT organization kept him alive for many more years than he would have been if he didn't have the support and information that he received through the organization.

At the age of 90 he performed a sky dive at Sky Dive New England to promote awareness of the PAACT organization.

He passed away July 12, 2005 at the age of 93.