



POTPOURRI OF PROSTATE PEARLS AND INSIGHTS

The Value of Scans For Staging Prostate Cancer (CaP):

The Absence of Proof is Not Proof of Absence - My office overlooks Beverly Hills High School, their athletic fields, basketball court, and running track. At any given time, we might see five or six people playing basketball. If we were flying in a plane at 32,000 feet and looked down, we would be unable to see anyone playing basketball; we would not be able to identify the basketball court, athletic field, or even the school. Carrying the analogy a step further, if we flew over the Rose Bowl on New Year's Day and looked down, we **would** be able to observe some activity. But, it takes a Rose Bowl full of cancer cells before you get an abnormal bone scan, CT scan, MRI scan, or any other type of scan.

Unfortunately, when a patient is told by their urologist and/or radiation therapist that their scans are normal and that there is no evidence of metastatic disease, patients logically conclude that their prostate cancer has not already spread (metastasized). However, since it takes a Rose Bowl full of cancer cells to cause an abnormal scan, it means that normal scans are absolutely **worthless** for trying **to exclude metastases**. But most patients do not understand the severe limitations of scans. They are not educated, and what is tragic is the fact that most patients place too much trust in the first prostate cancer doctor they see. Most patients tend to follow the recommendations of that first CaP doctor. Believing that the normal scans "prove" local disease only, and exclude the possibility of metastatic disease anywhere in the body, men then consent to radical prostatectomy, radiation therapy, seeds, or other local treatments. If patients truly understood that normal scans are meaningless to exclude metastatic disease, I believe that far fewer men would consent to undergo radical local procedures.

It is usually accepted that 50-70% of a vertebral (spinal) bone must be destroyed by cancer before you see an abnormal x-ray. Bone scans do not become abnormal until approximately 10-15% of the bone is replaced by cancer cells. Since there are two billion cancer cells in one inch of cancer, think of how many cells must be present before they cause an abnormal bone, CT and/or MRI scan. Lymph glands identified on CT or MRI scans are not considered abnormal until they are larger than 1

centimeter (10 millimeters). One centimeter equals approximately four-tenths of an inch; one inch, two billion cancer cells; therefore, 0.4 inches of tumor contains hundreds of millions of cancer cells.

Almost always doctors recommend the treatment that they administer. Urologists urge radical prostatectomy; radiation therapists advise radiation therapy and/or seeds. Some surgeons or radiation therapists may emphasize that their unique skills, techniques, or type of radiation therapy give better results with higher success rates compared to others in their field. This is not the case for men treated with triple hormone blockade®/Leibowitz protocol because any doctor can prescribe and administer the same medicines that I pioneered. To be sure, it is essential to use the exact protocol we use, but that information has been published and is available at no charge. This means that you do not have to see us in order to be treated with triple hormone blockade®.

The best advice anyone can give to a patient with newly diagnosed prostate cancer is to go to several different prostate cancer men's support group meetings before deciding how to be treated. He will hear men lament, "If only I knew then what I know now, I never would have allowed radical prostatectomy or radiation therapy, seeds and/or cryo-therapy." Talk to the men and/or their significant others who attend these support group meetings, and find out how their quality of life has been permanently affected. You will also learn that the frequency of side effects resulting from radical local therapies are far greater than the complication rates quoted to you, and that the chances for success are far lower.

In spite of failing to inform patients that normal scans do not by any means exclude the presence of metastases, patients are often told by their urologist and/or radiation therapist that **if** their prostate cancer cells have not spread beyond the prostate, then the **radical** local therapy should "cure" them. If there was a way to know for certain that all of your prostate cancer cells were limited to one of your fingernails, then removing the fingernail cures you. If, through Divine Intervention, you knew that all of your prostate cancer cells were confined to the prostate, and if surgery itself does not spread cancer cells (which it has been shown to do), then you could be cured with a radical prostatectomy. But this is a circular argument. The most important word in "If they are

all in one place," is the word, "If." Prostate cancer cells have had ten or more years to spread before a man is diagnosed. This gives cancer cells a long time to escape from your fingernail and/or your prostate gland before your diagnosis/treatment. Radical local therapies cannot cure you if significant numbers of prostate cancer cells have escaped from your prostate before or during surgery. Autopsy studies show that 27% of men in their 30's, and 34% of men in their 40's already have prostate cancer. These are standard **invasive** prostate cancers, not some premalignant condition or noninvasive cancer. Each decade of life increases the incidence of prostate cancer in men by approximately 10%, so that ultimately 80% of men in their 70's and 80's have prostate cancer. Since invasive prostate cancer is already present in such a high percentage of men younger than 50, we can see that prostate cancer cells almost always have had one or more decades to grow, mutate, and even spread long before the disease is diagnosable. The next time you hear a doctor tell a patient that he has "early" prostate cancer, you know that the statement is essentially an oxymoron. Studies have been done where men with clinically localized prostate cancer have samples from their bone marrows obtained prior to the start of their radical prostatectomy. An amazing 74% of men believed to have "early" clinically localized prostate cancer already have PSA secreting cells in their bone marrow. Men with BPH do not have PSA secreting cells in their bone marrow. Urologists will not dispute these facts, but argue that not all of these cells will become viable islands of metastatic disease. But men with these cells have higher rates of recurrence.

Does Surgery Disseminate or Accelerate the Growth of Cancer?

In the journal, *Lancet*, 1996; 347:260, author Baum, M., asks the question, "Does surgery disseminate or accelerate cancer?" Here is an enormously profound statement with major implications for anyone considering radical prostatectomy, radiation therapy and/or seeds. An article reported in the *Scandinavian Journal of Urology and Nephrology*, 1995; 172:65-77, by Iversen, P., et al., found no survival benefit for radical prostatectomy versus **no** treatment for prostate cancer patients randomized to radical prostatectomy plus placebo versus placebo alone. Imagine that. Does it surprise you that treatment with a placebo pill is as effective as radical prostatectomy? This was a prospective randomized study that followed 111 patients for 23 years. If you previously had a

radical prostatectomy, did your urologist inform you prior to surgery about this study that did not find any survival advantage to radical prostatectomy. In this study, radical prostatectomy did not even reduce the risk for developing metastatic disease compared to patients who were treated only with a placebo pill. What makes this study even more impressive is the fact that there was an average 23-year follow-up for these patients. Therefore, the study could not be criticized by claiming that if only patients were followed a little longer, the group treated by placebo would have been found to have an increased risk for developing metastatic disease.

The NCI today is conducting the PIVOT Trial, which stands for Prostate Intervention Versus Observation Therapy. This study is once again comparing radical prostatectomy to no treatment. If you have newly diagnosed clinically localized prostate cancer, and went to the NCI and asked to participate in one of their ongoing clinical trials to help determine the best treatment for men with so-called clinically localized prostate cancer, the computer would randomly assign you to one of two arms. In one arm, you would have a radical prostatectomy; in the other arm, your treatment would be observation therapy, which is another term that means no treatment. If you have newly diagnosed prostate cancer, and asked to enter their current high priority prostate cancer treatment trial, there is a 50% probability you would be told, "We are not going to treat you, we are only going to follow you."

If the value of radical prostatectomy, or radiation therapy, or seeds had already been proven to be both necessary and effective, the National Cancer Institute could not do a study in which 50% of men receive no treatment other than observation. This should convince our readers that the value of radical prostatectomy for improving overall survival for men with prostate cancer remains to be proven. To Compassionate Oncology, this means that radical prostatectomy as a treatment option for prostate cancer must still be considered experimental.

Why the Word "Cure" Does Not Appear in the Consultation From Your Radiation Therapist:

What are your chances for "cure" if you are treated with radiation therapy and/or seeds? Get a copy of your radiation

therapy consultation. The word "cure" will not appear in the consult. The doctor will use terms such as "success," "control," "remission," or other poorly defined adjectives. Ask him to write down in your medical record your chances for "cure," and have him define the word cure in your records. Ask your urologist and radiation therapist:

1. Will your treatment prolong my life?
2. Will your treatment improve or worsen my quality of life?

Then ask him to give you a copy of your medical record with that information recorded. Ask him/her for the specific medical references that confirm his answers. If he/she cannot provide you with the references, it is because they do not exist. Do not accept anything less than the references that confirm the promised **cure** rates. By the way, in modern radiation therapy literature, there are over 55 different definitions for "cure." For men treated by radical prostatectomy, there are approximately 50 different definitions of cure. By choosing a different definition of cure, you are able to markedly improve your reported "cure rates." Were you aware of this "sleight of hand;" I mean, this interesting way to improve cure rates without changing anything except your definition of cure? Many radiation therapists do not even agree on what PSA level to use to define "success," let alone cure. But all you as the prostate cancer patient really care about....is cure. Total and permanent cure. If it comes back, it was not cured. The burden of proof as to whether local therapy can cure you lies with the radiation therapist and urologist. If they cannot provide references that show radiation therapy or radical prostatectomy is both necessary and effective, why risk all of those side effects?

Hormone Blockade: Continuous, Intermittent, or?

Dr. Bob is certain that the most effective way to use hormone blockade is neither continuous, nor intermittent, since both of these methods hasten evolution to hormone resistant/refractory prostate cancer. The "best" way to use hormone blockade (opinion) is to treat with one 13-month cycle of triple hormone blockade@Leibowitz protocol for patients presenting with previously untreated, low-risk or intermediate-risk, clinically localized prostate cancer. For those who disagree with me, one of my original and favorite quotes is: "Everyone is

entitled to their own (wrong) opinion" (even me). For men who have previously been treated with hormone blockade, my approach to controlling their prostate cancer is to use all effective medications to postpone, or hopefully prevent, the need to go back on another cycle of hormone blockade. You cannot develop hormone resistant or hormone refractory prostate cancer unless you are re-treated with another cycle of hormone blockade, since the definition of those conditions is a rising PSA while on hormone blockade. If we can find effective, non-hormone blocking medicines to control a rising PSA, then you can remain off hormone blockade. **I am certain that the longer you are off hormone blockade, the much longer you will live** (opinion, but the logic, to me, is essentially irrefutable, and the only possible interpretation). Every time you are treated with another cycle of hormone blockade, your time on hormone blockade lengthens, your time off hormone blockade shortens, and the PSA nadir on each subsequent cycle of hormone blockade is higher. This occurs because there are ever increasing numbers of hormone resistant cells remaining after each subsequent hormone blockade cycle; each cell makes PSA; therefore, the greater the number of these resistant cells, the higher the PSA nadir. You can recognize this pattern as evolving hormone resistant prostate cancer.

Continuous hormone blockade is the worst way to use hormone blockade since it essentially always evolves to hormone resistant/refractory prostate cancer (HRPC), and does so faster than IAB. Intermittent androgen blockade (IAB) is far superior to continuous androgen blockade (CAB), if for no other reason than the fact that when you are off hormone blockade, your quality of life markedly improves. This is fact, not opinion. Beginning in 1992, I no longer used CAB on any patient except a minority of men with metastatic, hormone refractory prostate cancer. Our CaP experts review the same medical articles that I do, but their opinions almost always seem so distant and different from mine.

Since 1994, I have written that IAB will be found to be far more effective than CAB. At the Sixth Annual Massachusetts Prostate Cancer Symposium on May 21, 2003, I was one of two keynote speakers; the other was Dr. Phil Kantoff from Massachusetts General. The sponsors included Massachusetts General Hospital Cancer Center, Dana-Farber/ Harvard Cancer Center, Tufts-New England Cancer Center, Beth Israel Deaconess Medical Center (also a Harvard Hospital), the American Cancer

Society, and others. I was the only doctor at the Symposium who expressed the opinion that intermittent androgen blockade was superior to continuous androgen blockade. A few years earlier, at the same conference, I was one of many prostate cancer specialists that participated in a panel discussion on IAB versus CAB. Some of the other participants included Dr. Philip Kantoff, moderator; Dr. Anthony D'Amico, a Harvard radiation therapist; Dr. Glen Bubly, a Harvard oncologist; Dr. Mark Garnick, a medical oncologist; at least one Harvard urologist, and a number of other nationally acknowledged prostate cancer experts. Dr. Kantoff, the moderator, asked the panelists whether they recommended IAB. Everyone said no, except for Dr. Bob. Dr. Kantoff then asked the panelists to predict whether ongoing or future studies would prove CAB or IAB superior. Not being shy, I spoke first, and stated that I was certain that treatment with IAB prolongs survival compared to CAB. When polled by Dr. Kantoff, every one of the other panelists stated that CAB would be found superior.

Ever since the term IAB was first used, CaP national and most international experts essentially had universal agreement that you should never recommend using IAB. They told us that CHB was the "standard of practice" and throughout the 1990's that was their final word on the subject. Beginning perhaps around 2003 or 2004, there was a slight change in their position. They still admonished us to only use CHB in our practices for all CaP patients except for patients registered in a clinical trial comparing CHB to IAB.

Like myself, the reader might wonder how did CHB become the standard of practice? How many studies were done before it was accepted as standard of practice? How many other methods of HB were tested against CHB? These latter questions are easy to answer - none and none!! How can I be so certain? Because the first hormone blockade used to treat metastatic Cap was orchiectomy (castration) and that procedure is not reversible surgically. Many years ago, I wrote that "castration should be outlawed." Now, I feel that way more strongly than ever.

In February of 2007, at the Third International Symposium on Prostate Cancer jointly sponsored by ASCO, AUA, etc., I again had the opportunity to address a panel following some lectures. I asked about their use of CAB versus IAB. They each stated that they do not recommend IAB for any of their patients. I then asked their opinions regarding the outcomes of ongoing

studies comparing continuous to intermittent HB. They all responded that they were convinced CHB would be proven to be more effective than IAB. Under my breath I mumbled: "Everyone is entitled to their own wrong opinion."

To reiterate and re-emphasize their opinion, our CaP experts in April 2007, got together and published brand new joint guidelines by ASCO/AUA for using hormone blockade. Once again, they concluded that IAB should only be used in the context of a clinical trial. These practice guidelines, as they are called, are gradually becoming mandates. Insurance companies are already using some ASCO "guidelines" for other oncology conditions to determine whether to reimburse for certain treatments or not. I believe that we are losing the option to individualize treatments. "They" want us to use a one size fits all approach to treating cancer. Patients need to protest or we will not be able to treat them other than by "clinical guidelines."

For the past 14 years, we have been "taught" not to use IAB. The correct and the only correct form of HB to use is continuous. Our experts have spoken the same message for the past 14 years. But in the August 10, 2007 issue of Oncology Times, Dr. Phil Kantoff stated that IAB "is at least as good as, if not better than CAB." I first read this September 5, 2007, and sent a letter to Dr. Kantoff to confirm the facts in the article. Dr. Kantoff, being the true gentleman that I have always admired and respected (in spite of differences of opinion regarding certain CaP treatments) acknowledged that the information in the article was correct. There are some IAB exceptions that we both agree upon, especially for a patient whose PSA does not fall "low enough." He went on to tell me that he was flattered that I agreed with his interpretation of the data.

More recently I believe that another expert, Dr. Ian Thompson, now agrees that IAB should be considered a "standard treatment." But for the past 14 years, those of us who used IAB were criticized (loudly and continuously). It seems that we practiced "bad" medicine for 14 years, but then our experts decided that today it is good medicine. What is ironic is that "they still believe we were wrong for those 14 years and they were correct. I know my patients are happy they were treated the "wrong way" since it turned out to be the "right way."

POTPOURRI.....

Page 9

I am happy to be able to declare victory for IAB over CHB. This means that CHB moves from the #1 position to #2 according to the experts, and IAB from #2 to #1.

Now we need to "show off" our treatment results which prove that the best form of hormone blockade is a single cycle of Triple Hormone Blockade®/Leibowitz protocol followed by Proscar, 5 mg once a day, so-called finasteride maintenance® therapy.

In order to postpone and, hopefully, prevent the need to go back on another cycle of HB, in patients whose PSA rises too rapidly and/or too high, we have, fortunately, **pioneered an extraordinarily successful treatment option that is not chemotherapy, is not hormone blockade, and enhances your immune system. Isn't this exactly what you are looking for?** The name of this treatment option is prostate cancer antiangiogenic cocktail (AAC). Space permitting, and if the creek does not rise too high, we will elaborate on AAC in the next (exciting) edition of PAACT Newsletter. Stay tuned.....

As always -

Be happy,
Be well,
Live long and prosper,

DR. BOB

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