

EARLY HORMONAL THERAPY WORKS RIDICULOUSLY WELL

Traditionally, patients with prostate cancer were offered only three treatment options: observation (no treatment), radical prostatectomy (the alleged gold standard), and standard radiation therapy. A fourth treatment option, brachytherapy or seeds, has been increasingly offered. Since 1991, the only treatment I have recommended is primary androgen deprivation therapy without any radical local treatment. I call triple hormone blockade® the "Platinum and Diamond Standard," because I believe it is far superior to any "gold standard."

At the European Oncology Conference, September 22, 2003, Abstract 328 was presented and discussed. In a press conference held afterwards, Sir Richard Peto, Ph.D., Professor of Medicine Statistics at the University of Oxford, United Kingdom, was interviewed. Dr. Peto has gained international recognition and fame with his analysis of the adjuvant therapy for breast cancer (this refers to treatment given after surgery or radiation therapy to reduce the risk of cancer recurrence). I believe the following statement best describes Dr. Peto's analysis. "Hormonal therapy as a whole works **ridiculously well.**" Significant reductions in ten-year mortality rates have been identified in the United States and United Kingdom, as well as elsewhere in Europe. A meta analysis is a type of analysis that pools the results from all pertinent medical publications, hoping that by adding together all of the patients in each trial, it is more likely that you will identify statistically significant conclusions because of the larger sample size. Dr. Peto looked at early versus late initiation of hormonal therapy. His meta analysis concluded that early hormone blockade for prostate cancer is about as effective as it is for early breast cancer...." When asked why so many physicians are reluctant to prescribe early hormonal therapy when the **survival benefits are so great,** Dr. Peto primarily attributed this to tradition. I would interpret that as reluctance on the part of physicians to open their (sometimes closed) minds to change and allow

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themselves to learn about new and effective treatment options. "Meta analysis provides strong evidence of benefit, and when you add them (the studies) all together, they are very clear, showing improved prostate mortality...." Early use of hormone blockade reduced the probability that you would **die** from prostate cancer in the next ten years by **about one-third**, and all other deaths were **not** increased.

A very well known and internationally respected urologist, Dr. E. David Crawford, Professor of Urologic Oncology at the University of Colorado Health Sciences Center in Denver, in a telephone interview, stated "Early hormonal therapy saves lives, and can even be considered to be a cure of prostate cancer." Although not involved in this study, he states, "We have been on this bandwagon for years. When I give a talk on this, I like to start by asking for a show of hands on how many people think early hormonal therapy can be a cure for prostate cancer. I do." (Dr. Bob has never claimed early hormone blockade could cure prostate cancer, but he loved discovering that Dr. Crawford believes it can.) Dr. Crawford went on to state that "early signs of a drop in prostate cancer mortality in the 1990's **could not** have been accounted for by improved screening and detection with PSA testing because the test was too new to have an impact on death rates. At least some of the decline was likely attributable to the inhibition of cancer growth by hormone blockade." Dr. Bob comments, "It is known that 80% of men in their 80's have prostate cancer, but only 2-3% of men die from prostate cancer. Most of us will die **with** prostate cancer; not **from** it. Therefore, for most men, it is not necessary to be cured of prostate cancer in order to enjoy a normal life span." Treatment with 13 months of triple hormone blockade/Leibowitz protocol® is the least invasive treatment option for so-called localized prostate cancer, but still is a most potent and effective form of therapy. It is also the only non-chemotherapy treatment option that can kill prostate cancer cells that have escaped from the prostate and spread to places like your bones.

Dr. Crawford had been one of my most vociferous critics in the past, stating that hormone blockade could never cure prostate cancer, and that patients should never consider primary hormone blockade as a viable treatment option. During a question and answer session following one of his

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L.A. area lectures, he literally took one of my patients to task when this patient asked, "What about using hormone blockade as sole treatment for so-called, localized prostate cancer?" Dr. Crawford was extremely indignant and quite rude, stating categorically that hormone blockade is not an acceptable treatment option; period; end of discussion. Perhaps Dr. Crawford would be impressed (astonished) if he was told that this patient continues to remain in a clinical complete remission for more than six years in spite of the fact that he had aggressive, negative baseline prognostic factors. His only treatment was 13 months of triple hormone blockade/Leibowitz protocol®, followed by finasteride maintenance therapy®. It is amusing to hear Dr. Crawford say that "...we've been on this bandwagon for years." He sure wasn't on this bandwagon when he lectured in L.A. just a few years ago. However, I welcome company on the primary hormone blockade as sole therapy for prostate cancer bandwagon. I was the first to advocate this option more than 12 years ago, and remain a most vociferous spokesperson for this approach.

CAPSURE data was presented at the American Urologic Association in May 2003, and reported that from 1989 through 2001, the use of primary androgen deprivation therapy as a treatment option had risen sharply. For low-risk patients, the use almost tripled to 14.2%. For intermediate risk, it more than doubled to approximately 20%, and for high-risk, it increased from 33% to 48%. Almost one-half of men with high-risk disease selected hormone blockade as their treatment option. They investigated and discovered how poor the results were from any form of radical local therapy. Obviously, more and more doctors are either prescribing or agreeing to prescribe hormone blockade as the first and only treatment for prostate cancer patients. High risk is defined as a PSA equal to or greater than 20, or a Gleason score of 8-10, or locally advanced disease. Low risk is a PSA less than 10, a Gleason score of 6 or less, and nonpalpable or only a small abnormal area identified on digital rectal exam. Intermediate risk includes everyone else.

It seems ironic that when surgery or radiation therapy fails to control your prostate cancer, then your urologist or radiation therapist will inevitably prescribe the same type of hormone blockade that I prescribe initially. Why subject

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yourself to radical local therapies with the well-known, often permanent complications of erectile dysfunction (impotence) and urinary incontinence? One-third of men report that they use a pad, diaper, or penile clamp after radical prostatectomy. More than 60% report that they drip urine. Eight-five percent report the inability to achieve and maintain an erection firm enough to allow for intercourse. Seven percent suffer from fecal incontinence.

Imagine how you would feel if you developed one or more of these complications, but in spite of this you later required treatment with hormone blockade because of a rising PSA? Skip the radical local therapies and start with triple hormone blockade/Leibowitz protocol@.

I firmly believe that you never save your best prostate cancer treatment for later. The time to kill prostate cancer cells is now. Do not allow prostate cancer cells the opportunity to mutate and become more aggressive. If any therapy works well in more advanced disease, it essentially always works **much better** in earlier stage disease. Hence, give your hormone blockade early rather than late. When radical prostatectomy or radiation therapy fails to cure a man, the PSA doubling time shortens from three to four years pre-surgery or pre-radiation, to about four months after those treatments. Frightening, but true.

Remember, no study has ever shown any form of radical local therapy to be **both** necessary and effective.

Dr. Fernand Labrie reported in the early 1990's that for men who presented with one to five separate metastases identified on bone scan, their median survival was greater than eight years. These men didn't have bone cancer, they had prostate cancer cells in their bones. Hormone blockade can kill prostate cancer cells in your prostate, lymph nodes, and bones as well.

Patients with obvious metastatic disease to bones have much shorter survival than patients with normal bone scans, even though a normal bone scan does not exclude the possibility that occult metastatic disease exists. More than 10-15% of a bone must be dissolved before a bone scan is abnormal. It

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takes destruction of 40% or more of a bone before an x-ray becomes abnormal. There can be billions of cancer cells, with a normal bone scan. Men with abnormal bone scans have much more aggressive disease. Their prostate cancer cells have figured out a way to escape from the prostate, survive in the circulation, leave the circulation, "nest" in bones, attract blood supply to themselves, and develop successful colonies or islands of metastatic cells. Only the most aggressive cells are able to accomplish all of these steps. It is reassuring that even in men with up to five identified metastatic deposits on bone scan, eight years after starting hormone blockade, more than half were still alive in the Labrie study. Dr. Labrie used continuous double hormone blockade.

I am confident that intermittent androgen blockade is far superior to continuous blockade. I am also convinced that triple hormone blockade/Leibowitz protocol® is the most effective form of hormone blockade, and is much better than double blockade. We feel the best results are obtained using a single 13-month cycle of triple hormone blockade® up front, rather than intermittent hormone blockade. Following that first cycle of hormone blockade, use all of your supportive treatments to avoid the need for a second cycle of hormone blockade. The longer you are off hormone blockade, the much longer you will survive. You cannot get hormone refractory unless someone puts you back on hormone blockade. Examples of these supportive therapies include finasteride maintenance therapy (a small percent of our patients take dutasteride [Avodart]). All of our patients are on either one or the other. Virtually all take a COX-2 inhibitor, preferably Celebrex. The other COX-2 inhibitors we sometimes use are Vioxx or Bextra. Calcitriol and/or PEENUTS **may** have some limited beneficial effects. We have found that thalidomide is the most successful treatment option that helps to postpone or avoid the need for another cycle of hormone blockade. In our experience, more than 85% of men will respond to thalidomide by showing a decline in PSA, usually within weeks of starting therapy. You can request a videotaped lecture that discusses and explains how to avoid getting hormone resistant or refractory. Request Video #2 which is a lecture given in August 2001.

Dr. Labrie's survival figures are from a 1992 report. These

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survival statistics occurred in the era before we identified modern, effective therapies that we use for those men who fail initial hormone blockade. This information should reassure any patient with low-risk prognostic factors that almost without exception we expect them to do well for an indefinite period of time, well beyond eight years, if they are treated appropriately.

For those men who present with intermediate-risk factors, the protocol described below also confirms their excellent prognosis. The men who present with one or more high-risk factors almost always require treatment with 12 doses of mild, easily tolerated, low-dose chemotherapy in addition to 13 months triple hormone blockade/Leibowitz protocol®. None of these patients develop nausea or vomiting; hair loss is rare; most working men continue to work full time during therapy.

Men are amazed at how nontoxic this treatment is, and how well it is tolerated. We have a list of volunteers who have been treated with this protocol and are happy to discuss this treatment with you. Video #4 from October 2002 has additional helpful information.

Triple hormone blockade/Leibowitz protocol® refers to men who have never had any form of local therapy and have never had any form of prior hormone blockade. These men are treated with 13 months of triple hormone blockade® utilizing Lupron or Zoladex, three Casodex per day, and one finasteride (Proscar) per day. After 13 months, they are treated with finasteride maintenance® (Proscar maintenance therapy). For men who cannot afford three Casodex per day, I recommend Eulexin, 250 mg three times per day. I do not recommend using one or two Casodex per day. You need three for optimal results.

You can request a copy of a videotaped lecture given by me (some of my lectures are also available in DVD) to further explain in detail this information regarding triple hormone blockade®. A July 2001 lecture also describes all of the choices for local therapy as well as the side effects from each form of treatment. A lecture from May 2003 updates our triple hormone blockade/Leibowitz protocol® results, and may convince you to consider treatment with high-dose testosterone replacement therapy after your triple hormone

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blockade® has been completed. The February 2002 lecture addresses subjects including our antiangiogenic cocktail; high-dose testosterone replacement therapy; as well as different approaches for achieving optimal management of all stages of prostate cancer. Call our office for a description of these lectures. Dr. Tucker has taped a lecture given in San Diego in October 2003. A copy of that lecture is also available.

In September 2003, I presented our updated data at the Prostate Cancer Research Institute Symposium. I reported on 177 men, all with biopsy-confirmed prostate cancer. All men refused local therapy; all men were treated in a single practice, by myself or Dr. Steven Tucker. Their average age is 66. Their average baseline PSA is 11.5. Their median Gleason grade is 7. We had 71 patients with a Gleason 7; 24 with a 4+3, and 47 with a 3+4. Twenty-one of our men had Gleason scores of 8 to 10, and 85 had a Gleason score of 4 to 6, with a rare 4 or 5. The largest percentage of our patients were stage T1c or T2a; however, at least 20% were locally advanced. The first 134 men treated have a mean follow-up of 60 months. Their current mean PSA is 2.49. Ninety patients have been followed for a mean of six years, and their mean PSA is 2.8. Almost 50 men have been followed for a mean of seven years; their mean PSA is 2.678. Baseline testosterone was 388; on finasteride maintenance® 530. Finasteride (or Proscar) raises your testosterone level.

Through September 2003, we have only had to re-treat 12 men. All 12 of these patients presented with at least one high-risk prognostic factor.

As of September 2003, our disease specific survival is 99.4%. This means that only **one** patient in 177 died from prostate cancer. These results are superior to any reported surgical or radiation therapy series. Our results were published in the journal, *The Oncologist*, an international, peer-reviewed journal; see "Treatment of Localized Prostate Cancer with Triple Androgen Blockade: Preliminary Results in 110 Consecutive Patients;" 2001; 6:177-182. Our article was referenced at the 2003 AUA convention in a course on androgen deprivation therapy. The syllabus, written by Dr. Eric Small, reads "Triple androgen blockade employing simultaneous LH-RH agonist, antiandrogen, and 5-alpha-

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reductase inhibitor (finasteride) may offer additional benefit over standard double hormone blockade, particularly in the context of intermittent treatment protocols." Our work was also referenced in the *Journal Cancer*, published by the American Cancer Society.

It is immensely satisfying to me personally that my work utilizing triple hormone blockade® with finasteride maintenance therapy® has been so successful, is finally being recognized, and is increasingly accepted as an appropriate primary treatment option. Being the first to name and pioneer this approach that offers men a treatment option without incontinence and is the only treatment option whose side effects are almost always reversible, makes me proud and happy. MayoClinic.com agrees that one of the treatment options commonly used by men with (so-called) localized prostate cancer is hormone blockade. This is your Fifth Treatment Option. We believe that our results confirm our opinion that triple hormone blockade/Leibowitz protocol® is the best treatment option (hence the name, The Platinum and Diamond Standard). It avoids any form of radical local therapy. Why take the risk you might need a diaper, pad, or (God forbid) penile clamp? Avoid the possibility of fecal incontinence or soiling. About one-quarter to one-third of men, after being treated with radiation therapy, report moderate to severe gastrointestinal complications including bleeding or fecal soilage after radiation therapy. Following radiation therapy, approximately 85% of men develop erectile dysfunction within four years of treatment. Erectile dysfunction was defined as inability to get and maintain an erection firm enough for intercourse.

Start your treatment with triple hormone blockade/Leibowitz protocol®. This buys you the time needed to investigate all other options. Later, if you decide, you can add local therapy. You are not burning any bridges by starting with triple hormone blockade®. We don't recommend local therapy, but you have the option to add it at any time. Currently, about two-thirds of men treated with radiation therapy for locally advanced prostate cancer are told that they also need to take hormone blockade. No study has ever shown that radiation therapy adds to the benefit of hormone blockade. Prospective randomized trials have proven that radiation therapy **plus** hormone blockade statistically **prolongs survival** compared to radiation therapy alone. After all of

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these years, no study has shown an advantage from adding radiation therapy to hormone blockade. The value of using hormone blockade is proven. This is not just my opinion; this is proven medical fact.

Simply stated, we do not believe in any form of radical local therapy. Seventy-three percent of men, prior to the start of their radical prostatectomy surgery, already have PSA-secreting cells in their bones (bone marrow). Most experts agree that these are malignant prostate cancer cells. Not all will grow into mature metastases, but it is sobering to realize that three out of four men have these cells in their bones at diagnosis. This is one of the major reasons we believe prostate cancer is a systemic disease. This means that prostate cancer cells have already spread to lymph nodes and/or bones by the time you are first diagnosed. Since triple hormone blockade/Leibowitz protocol® is systemic therapy, it can attack prostate cancer cells anywhere and everywhere in the body. No form of local therapy kills the prostate cancer cells that have already spread to your bones or other distant sites. Dr. Peto, after analyzing the world's literature, concludes how ridiculously well hormone blockade works. Dr. Crawford has admitted (? confessed) that hormone blockade kills prostate cancer cells. Let triple hormone blockade/Leibowitz protocol® help you, too.

We have a very long list of patients who were treated with our triple hormone blockade/Leibowitz protocol® and now volunteer to answer any questions or concerns that you or your significant other may have. Please call our office for a copy of that list. Call them and hear what they have to say.

And, as always,

Be happy,

Be well,

Live long and prosper,

DR. BOB

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Note:

Triple hormone blockade® is Dr. Bob's registered trademark.

Triple androgen blockade® is Dr. Bob's registered trademark.

Finasteride maintenance therapy® is Dr. Bob's registered trademark.

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