

CHAPTER FOURTEEN HORMONE TREATMENTS

By Drs. E. David Crawford, Aubrey Pilgrim, Stephen Strum, Mark Scholz, Bob Leibowitz, and Eric Small
Contributions by Ralph Valle and several other PCa Survivors

Drs. Strum and Scholz have written extensively about hormone therapies. Much of this chapter is taken from their writings which are available from Gary Huckabay's Rattler site, www.prostatepointers.org. You can log onto the site and use the search engine to find almost anything you need to know about hormone treatments. If you do not have a computer, by all means you should get one. If you have advanced prostate cancer, a computer can help in your survival.

PSA and Early Detection

The PSA test was not generally used before the mid 1980s. Up until 1989, when men were first diagnosed with prostate cancer, 60 to 70 percent of them already had metastatic cancer outside the prostate. Now it is just the opposite. Because of the simple PSA blood test, when now diagnosed, about 75 percent of all prostate cancers are localized within the prostate gland. When still within the prostate gland there are several treatment options. When localized, there is an excellent chance for cure. If the cancer has metastasized outside the prostate, it is systemic. That means that it may be in the entire system. When this happens, there is no way of removing or killing all of the cancer cells. The prognosis is not very good for metastatic cancer. There is no cure, but there are several treatments that can keep the person alive and relatively comfortable for many years. **The answer to cancer is early detection.**

Prostate Cancer and Testosterone

Most prostate cancer cells must have testosterone and androgenic hormones in order to live and thrive. It is like food to them. Take their food away and many of them will die. So one of the better ways to control prostate cancer, especially if it has metastasized and spread throughout the body, is to control the hormones. Some metastatic cancers may cause a very high PSA, as high as 6000 ng/ml or more. In many cases, combined hormone therapy (CHT) can dramatically reduce the PSA to undetectable levels. There are other metastatic cancers that may have a very low PSA because the cancer cells have mutated to the point that they can no longer make PSA.

At one time, very few patients were put on hormonal treatments except those with metastatic prostate cancer. Recently, hormonal therapy is being used extensively as neoadjuvant and adjuvant treatments. (Neoadjuvant means that it is used before the major treatment such as a radical prostatectomy, different types of radiation treatment or cryosurgery. Adjuvant means that it is used in addition to the major treatment.) Some doctors are now using CHT as the primary and only form of treatment. Many of them are having excellent results

with CHT as the first line of treatment. It is one of the least invasive treatments designed for a halt in progression, or a remission or even a cure.

Why CHT Works

CHT suppresses the testosterone and other androgens that the cancer cells need in order to grow and survive. Without the hormones, many of the cells starve to death. CHT may cause a vast reduction in the size of a tumor.

In some cases, there may be a few cells that do not depend on the hormones. These are the hormone independent cells. These cells can live and grow without testosterone or androgens. This is called hormone refractory. These are the cancer cells that usually kill a man. This is why it is so important to treat the cancer early before it has a chance to metastasize. Again, the answer to cancer is early detection and treatment.

Acronyms

This chapter concerns combined hormone therapy or treatment (CHT). Here are a few acronyms that all mean the same thing:

AAT- Anti-androgen therapy

ADT- Androgen Deprivation Therapy

AHB- Anti Hormone Blockade

AST- Androgen Suppression Therapy

CAA- Complete Androgen Ablation

CAB- Combined Androgen Blockade

CAD- Complete or Combined Androgen Deprivation

CHD- Complete or Combined Hormone Deprivation

CHT- Complete or Combined Hormone Therapy

MAA- Maximum Androgen Ablation

MAB- Maximum Androgen Blockade

NAA- Neoadjuvant Ablation, (hormone therapy before surgery or radiation)

NAB- Neoadjuvant Blockade

TAA- Total Androgen Ablation

TAD- Total Androgen Deprivation

TAS- Total Androgen Suppression

IAD- Intermittent Androgen Deprivation

IAS- Intermittent Androgen Suppression

ICHT- Intermittent Combined Hormone Therapy

IHB- Intermittent Hormone Blockade

IHT- Intermittent Hormone Treatment

We have no doubt that there are many other acronyms that all mean the same thing for this therapy. There must be several people who sit up at night thinking up new acronyms for this single type of treatment. There should be some kind of law or standards for the use of acronyms.

Brand Names and Generic Names

Most drugs may have two or more names. There will be a generic name and a brand name. There are two main companies who manufacture the LHRH drugs. TAP Pharmaceuticals makes Leuprolide acetate, brand name Lupron. Zeneca makes Goserlin Acetate, brand name Zoladex. Amgen has a new drug called Abarelix and Alza has developed a one year implant they call Viadur. This drug will be marketed by the Bayer Company.

The antiandrogens are Eulexin, brand name Flutamide made by Schering Corp. and Bicalutamide, brand name Casodex, made by Zeneca. Another anti-androgen that is not used very often in this country is Nilandron, generic name Nilutamide, made by Marion Roussel.

Monotherapy

We have known for some time that both normal prostate cells and cancer cells rely on testosterone to grow. As early as 1893 doctors were doing castration on patients who had obstructions due to BPH. Later it was used for prostate cancer. There was a marked improvement in about 85 percent of the patients.

Castration or orchiectomy is still done today as a treatment. But we now have luteinizing hormone-releasing hormone (LHRH) drugs that can prevent the release of testosterone produced in the testes. Taking the LHRH drugs essentially causes a chemical castration. But, unlike a surgical castration, the chemical castration can be reversed by stopping the drugs. Castration alone, or taking one of the LHRH drugs alone, is called monotherapy or mono hormone treatment. Treatment with one of the antiandrogens may also be called monotherapy.

Normal Testosterone Levels

According to an article by Dr. Donald Coffey in Campbell's Urology, the level of testosterone can vary from 300 nanograms per deciliter (ng/dl) up to 1100 ng/dl of blood. That is a very small amount. A nanogram is one billionth of a gram. It takes 28 grams to make one ounce. A deciliter is one tenth of a liter. A liter is 33.8 ounces, so a deciliter is 3.38 ounces. A normal young man will produce a total of about 6 milligrams (mg), or 6 hundredths of a gram, per day. As we get older we produce less testosterone.

According to Dr. Coffey, the level can vary from day to day and even during the day. It is usually highest in the morning. The adrenal glands sit on top of each kidney and produce androgenic hormones in both men and women. The amount of adrenal hormones produced is about 24 mg per day or about four times more than testosterone. These hormones can be transformed into testosterone. But Dr. Coffey says that less than one percent of the circulating testosterone is derived from the adrenals.

Suppression of Hormones Surgically

In the 1940's Dr. Charles Huggins discovered that the androgenic hormones produced by the adrenal glands were quite similar to testosterone. But very little of the androgenic hormones were utilized by the prostate and cancer cells as long as there was plenty of testosterone. However, the prostate and cancer cells are very resourceful. They prefer testosterone, but if it is not present, they will use the androgenic hormones. When testosterone is present, only about 5% of the hormones used by the cancer cells come from the adrenal glands. So even though the testes have been removed, the cancer cells may still get enough hormones from the adrenal glands to thrive. The cancer cells favor the dihydrotestosterone (DHT) form of testosterone. When the testosterone is suppressed, the cancer cells may convert a much larger amount of the adrenal hormones to DHT.

Dr. Charles Huggins studied prostate cancer and hormones for several years. In 1941 he did bilateral orchiectomies on 21 patients who had advanced metastatic prostate cancer. This brought improvement of pain and symptoms in 15 of the 21 men. In 1953 he performed a bilateral adrenalectomy on several patients in addition to orchiectomies. This procedure worked quite well except that at that time it was not possible to replace the vital adrenal hormones that one must have to live. The cancer growth was slowed in most instances, but the patients died due to the lack of the essential and vital adrenal hormones. Today we have several synthetic hormones and drugs that were not available just a few years ago. Dr. Huggins received the Nobel Prize in 1966 for his pioneering work in prostate cancer research.

Among the long term side effects of castration are hot flashes, osteoporosis, fatigue, loss of muscle mass, anemia and weight gain.

Chemical Castration

There are several drugs that can be used to accomplish a chemical castration. One of the advantages of a chemical castration is that it is reversible. A disadvantage is that the drugs must be taken frequently and are very expensive. Most men will choose the LHRH castration rather than an orchiectomy.

If a man is given estrogen, it will nullify and overcome the effects of testosterone. Conversely, if a woman is given testosterone, it will nullify and overcome the effects of estrogen.

One of the early drugs used for chemical castration was diethylstilbestrol (DES), a synthetic form of estrogen. It is still used in some patients today. It is fairly inexpensive but it can possibly cause cardiovascular side effects. The original dosage was 5 mg/day. Later studies found that 1 mg/day was just as effective. If DES is used, the patient should be closely monitored for cardiovascular problems such as blood clots.

Honvan is a form of high dose DES diphosphate. It has been injected into patients who have become hormone refractory for prostate cancer (HRPC) at doses as high as 1000 mg/day. It is used in Europe and in some of the Mexican clinics. It has worked well in some men.

There are estrogen skin patches that some women have used for hormone replacement after menopause. Some oncologists are using these patches on men as a hormone treatment. Dr. Fernand Fremoli of Rosario, Argentina, has been treating a group of HRPC patients for some time with estrogen patches. He has had some very good successes. The estrogenic compounds may cause liver problems when taken orally. The absorption into the blood stream from the patches helps to avoid some of these problems. But the men still have to be monitored for any cardiovascular or heart problems.

When a man becomes HRPC it is usually because the androgen receptors (AR) of the cancer cells have become mutated. But the cancer cells may have functioning estrogen receptors (ER). This is why DES and estrogen may work for HRPC. The herbal compound PC-SPES also has an estrogenic effect.

How the Chemical Castration Works

A gonadotropin-releasing hormone (GnRH) acts on the pituitary to cause it to release a follicle-stimulating hormone (FSH) and a Lutenizing Hormone (LH). These hormones occur naturally in the body. They stimulate the testes to produce testosterone. By slightly altering the chemical composition of the natural hormones, we now have Lutenizing Hormone Releasing Hormone (LHRH) drugs that are over 100 times more potent than the naturally occurring hormones. The LHRH drugs stimulate or help in the production of testosterone so are called agonists. See figure 14-1.

The hypothalamus, a small gland in the base of the brain, acts very much like a thermostat. A thermostat may constantly check the temperature in a room, then send a signal to the furnace or air conditioner to send more heat or cooling. Much like the thermostat, the hypothalamus constantly checks the level of testosterone in the blood stream. The hypothalamus exerts its control over the amount of testosterone in the blood stream by producing a luteinizing hormone-releasing hormone (LHRH). When testosterone falls to a certain low level, the hypothalamus produces LHRH and sends it to the pituitary. The pituitary is a pea sized master gland in the center of the brain. When the pituitary detects LHRH in the blood from the hypothalamus, it sends a luteinizing hormone (LH) to the testes and tells them to produce more testosterone. When the hypothalamus determines that enough testosterone is present in the blood stream, it stops producing LHRH.

At first the pituitary responds to the abundant synthetic and normal LHRH hormones by producing more and more of the LH hormone. This stimulates the testes to produce more and more testosterone. It may take a few days, or even

weeks, but the constant bombardment of the pituitary by the powerful synthetic LHRH agonists finally causes it to become insensitive. The pituitary finally gets to the point where it ignores the LHRH and stops making LH. Without the LH stimulation, the testes stop producing testosterone. These drugs will eventually reduce the testosterone to castrate level and keep it there as long as the patient takes the drugs. Castrate level of testosterone may be 10 to 20 ng/dl.

Zoladex and Lupron are synthetic analogues of the LHRH hormones. These drugs are equivalent to having an orchiectomy. Zeneca did a clinical trial that included 496 men. Of these, 242 were given Zoladex and 254 underwent bilateral orchiectomy. There was no significant difference in survival between the two procedures. If Flutamide, a drug that blocks the uptake of the adrenal hormones, was added to the Zoladex for combined hormone therapy, the average survival rate was 7.3 months longer than patients who had monotherapy.

Flare

Using the LHRH drugs alone can be the cause of a “Flare Phenomenon”. When an LHRH agonist is first started, it paradoxically causes a sharp rise in the pituitary hormone LH. The LH rise stimulates the testicles to increase testosterone production during the first 5-12 days after initiation of the LHRH agonist. This increase in testosterone stimulates prostate cancer cell growth and is termed flare. See figure 14-2.

Why is flare prevention important?

In patients with advanced disease and subclinical spinal cord compression, flare can precipitate full cord compression and paralysis. If there is PC growing close to a nerve root flare could result in pain in the distribution of that nerve. In patients with PC involving lymph nodes close to the ureters, flare could increase nodal disease and cause early compression of the ureter(s). Obstruction of both ureters could lead to kidney failure. Increasing disease in bony sites often leads to bone pain during times of flare.

Flutamide, Casodex, Nilutamide or any anti-androgen given prior to Lupron or Zoladex can be used to block flare reactions. Other agents like Nizoral, DES or Cyproterone acetate can be used to prevent flare.

It may take one to four weeks after administration of an LHRH agonist to bring the testosterone down to castrate levels. In some cases this may be too long to have to wait. If an immediate effect is needed, a bilateral orchiectomy, Nizoral or Abarelix can be used.

Time Release Drugs

The LHRH drugs are in time release formulation. When first developed, the LHRH drugs were given every 28 days. The formulation was then increased to a three month implant, actually 84 days, now they are available in four month or

112 day formulations. A new LHRH drug implant Viadur, developed by the Alza Corporation, is good for one year.

LHRH Antagonists

Lupron, Zoladex and Viadur are agonists. These agonists initially stimulate the production of testosterone. Abarelix is an antagonist which stops the production of testosterone immediately. It is quite similar in action to having an orchiectomy. Abarelix is produced by the AMGEN Corporation at www.amgen.com.

Antiandrogenic Drugs

The adrenal glands produce several androgenic hormones that are similar to testosterone. DHEA and the other androgenic hormones produced by the adrenal glands can be converted to dihydrotestosterone (DHT), the form of testosterone that the prostate cells favor.

Flutamide, Casodex and Nilutamide are synthetic drugs that are similar to the androgenic hormones produced by the adrenal glands. To the cancer cells, these antiandrogens look very much like the real hormones. Cancer cells have a voracious appetite.

When the antiandrogens are present, the hungry cells quickly grab them. The drugs sate their appetite, but the drugs are just slightly different chemically so that they have no nutritive value for the cancer cells. The cancer cells have specific receptors for the adrenal androgens. See figure 14-3. The receptors might be compared to a lock that will only accept a certain key. When the antiandrogens are present, the cancer cells will let these drugs in. The antiandrogens do not prevent the production of androgens, but if the prostate cell receptors are saturated with the antiandrogens, then very little of the real androgens can enter the cells.

Any one of the antiandrogens can be added to Lupron or zolodex to form CHT. These drugs can actually stop much of the growth of the prostate cancer.

Proscar and Dihydrotestosterone (DHT)

Testosterone and androgenic hormones must be converted to DHT in order for normal prostate and prostate cancer cells to use it. A 5-alpha reductase enzyme is manufactured inside both normal and cancerous prostate cells. The 5-alpha reductase enzyme is necessary for the conversion of testosterone to DHT.

Proscar is a drug that can inhibit the 5-alpha reductase and thus prevent the testosterone from being converted to DHT. Proscar was originally marketed by the Merck Corporation as a treatment for BPH. But many doctors are now using it along with other antiandrogens for prostate cancer. Unlike Lupron and Zoladex, Proscar has few side effects.

Theoretically, Proscar should be all that one needs to combat prostate cancer. It would appear to be an ideal treatment option. The man would still have his testosterone, but the cancer cells would not be able to utilize it. The Government is funding an 18,000 man study to determine if Proscar can prevent prostate cancer. It is a ten year study and it will be some time before we have the completed data.

Adapting to Flutamide

The cells in our bodies, including cancer cells, are very adaptable. Dr. Charles Myers says that some of the prostate cancer cells die when their source of testosterone is eliminated. But he says that some cancer cells can mutate and adapt to Flutamide. They use it just as if it were testosterone. If the PSA numbers suddenly start rising after being stable for some time, it may be that the cells have adapted to the Flutamide. If the PSA starts to rise while on Flutamide, often just taking the man off Flutamide will cause a dramatic drop in the PSA. You may see the acronym AAWR, which means anti-androgen withdrawal response. In many cases the PSA will go down and remain down for as long as six months or more.

Some physicians often use Nizoral (generic name Ketoconazole) and Hydrocortisone if the antiandrogens stop being effective. Nizoral was originally introduced as a drug for toe nail fungus and other fungus conditions. It is also used in shampoos for certain dandruff conditions. It can prevent the production of androgenic hormones. Hydrocortisone must be added to compensate for the vital adrenal functions that we need. Further details regarding the use of Nizoral can be found at www.prostate-cancer.org .

Neoadjuvant Hormone Therapy

Several doctors now start the patient on neoadjuvant hormone therapy (NHT) from three to six months before any major therapy such as a radical prostatectomy (RP) or external beam radiation therapy (XRT). Whenever a RP is done after the patient has been on NHT for some time, some studies indicate that there are fewer instances of extracapsular penetration (ECE) and positive margins. (ECE means that the cancer had penetrated the capsule. Positive margins means that the cancer had penetrated the capsule and had extended beyond the area around the prostate that the surgeon was able to remove). ECE and positive margins generally means that the prognosis is less optimistic.

Neoadjuvant therapy is often use before cryosurgery and brachytherapy or radioactive seed implants. Quite often the prostate may be so large that a large portion is hidden behind the pubic bone and is not accessible for seed implants. At one time they drilled holes in the pubic bone to access these large prostates. They have now found that three to six months on CHT usually reduces the size of the prostate by 40 to 50%. In some cases, they have to be careful not to reduce it so much that there is not enough left for cryosurgery treatment or seed implantation. The normal prostate in a young man should weigh about 21 grams

or three fourths of an ounce. In some older men, BPH along with cancer may cause the prostate to be from 40 grams to over 500 grams. Some prostates have been reduced to as small as 10 or 15 grams on CHT.

For recurrent cancer, combining hormone therapy with other therapies can improve outcomes and survival in many cases.

Adjuvant Therapy

Quite often after a radical prostatectomy is done, they may find that the tumor had been understaged. What was thought to be a T1 or T2 (A or B) stage tumor turns out to be a T3 or M+ (C or D) stage. In this case, the doctor may prescribe CHT for a period of time. The patient may stay on CHT for the period, then go off and on CHT intermittently while monitoring his PSA closely.

There have been some studies that indicates that CHT may predispose cancer cells to be more susceptible to radiation kill. If a patient's PSA begins to rise after a radical prostatectomy or radiation, then the treatment of choice should be CHT.

Lloyd Ney and CHT- a success story

In 1983 Lloyd Ney was diagnosed with metastatic prostate cancer. A bone scan showed 31 hot spots. One of his doctors told him that he had about three months to live. But Lloyd did not believe the doctor. Lloyd could have chosen to be castrated, but he heard of Dr. Fernand Labrie in Canada who was using some fairly new drugs to counteract the testosterone and the androgenic hormones. Dr. Labrie was pursuing the same line of attack that Dr. Huggins had tried when he removed the adrenals. The difference was that now there was no need to remove the adrenals because chemical drugs were available that could counteract the testosterone and adrenal hormones. Dr. Labrie called his treatments combined hormone therapy or CHT.

Many doctors did not accept the findings of Dr. Labrie. They pointed out that the adrenals contribute a very small amount of testosterone. They were convinced that monotherapy was all that was needed. One of the problems was that it takes years to prove something like this. To do a proper test, several men of the same age, with the same type and stage of cancer, should be randomized into two groups. One group would get the monotherapy and a placebo and the other group would get monotherapy plus an anti-androgen. Then you would have to wait until the men died to determine which was the better treatment. In some cases, this might take up to ten years or more.

Since the combined hormone treatment didn't cause any additional damage or side effects, why not go ahead and use it. Later studies were made by the Schering Company, the manufacturer of Eulexin or Flutamide. Their studies indicated that CHT had a distinct advantage over monotherapy.

Lloyd went from Grand Rapids, Michigan over to Canada, met with Dr. Labrie and began taking combined hormone treatments. Lloyd felt better almost immediately. He wanted all prostate cancer patients to be aware of the hormone treatments and that CHT should be available to all patients. He began publishing a newsletter, called the Cancer Communication. He formed a non-profit organization called **Patient Advocates for Advanced Cancer Treatment (PAACT)**. Lloyd began petitioning the FDA and Congress to approve the hormone treatments in this country.

After seeing the success of the treatments in Canada and other countries, many doctors in this country began using the hormone treatments even though they were not FDA approved. It wasn't until 1989 that the FDA finally approved the treatments. A lot of the credit should go to Lloyd Ney for his persistence. Lloyd accumulated a list of over 30,000 prostate cancer survivors who received his Newsletter. He spoke personally on the telephone with many of these men, giving them advice and counsel and hope. Thousands of these men will tell you that they owe their very life to Lloyd Ney. Lloyd died on August 19, 1998, 15 years after being told that he had only three months to live. He was 78 years old.

Almost up until the day he died, Lloyd answered the phone and talked with men who had questions about their cancer treatments. Lloyd said that he got a phone call one day and the man asked if the hormone treatments would affect his sex life. Lloyd said, "I don't know. How old are you?" The man said "94". It just goes to show that you are never too old.

Though Lloyd is gone, the PAACT organization survives. Call them at (616) 453-1477 and they will answer your questions, send you a packet of information about prostate cancer and put you on their mailing list for the Cancer Communication Newsletter. They don't ask for any contribution of any kind. But it does take money to run a foundation such as PAACT. Any money donated may be deductible from your income taxes.

Dr. Fred Lee: Prostate Cancer Survivor

In 1983, Dr. Fred Lee was 51 years old. He was a successful radiologist, a loving husband, and the father of five children. After watching a manufacturer's demonstration of an experimental transrectal ultrasound machine, he scheduled a demonstration test on himself. At that time, transrectal ultrasound was so new that no one was able to read the images. However, the salesperson commented that Dr. Lee's images looked different from what was normally seen. This led to the discovery that Dr. Lee had prostate cancer.

X-ray tests did not reveal evidence of cancer spread, and Dr. Lee was hopeful of a cure using radioactive seed implant. At that time, the procedure was performed by making an abdominal incision and manually placing the radioactive seeds directly into the prostate. Several days later, Dr. Lee discovered that his lymph nodes were found to contain metastatic prostate cancer. Because of the positive

lymph nodes, Dr. Lee underwent an additional course of external beam irradiation to the whole pelvic region. Additionally, he started taking Emcyt, which he continues to take to this very day. Emcyt is a combination drug consisting of estrogen and nitrogen mustard. It is often used as a chemotherapy.

Unfortunately, in 1986 a repeat biopsy confirmed persistence of his prostate cancer. He received an additional course of external beam to his prostate as well as four courses of hyperthermia. Dr. Lee has been rebiopsied three times since then with no evidence of cancer and his PSA remains extremely low.

Dr. Lee learned that only 50% of men with his stage of disease live for 5 years and only 10% live for 10 years. Dr. Lee decided to dedicate the time he had left to optimize the detection and treatment of prostate cancer. Dr. Lee's work defined what prostate cancer looked like on transrectal ultrasound. This led to its widespread acceptance as the preferred method of diagnosing prostate cancer. He was the co-chairman of the American Cancer Societies National Prostate Cancer Detection Project, a multi-institutional study involving over 2000 men. He has written or co-authored over 75 publications, has been visiting professor at numerous institutions, and has made countless presentations. Currently, Dr. Lee is the Director of the Crittenton Hospital Prostate Cancer Center in Rochester Hills, Michigan. Dr. Lee has specialized in doing cryosurgery. Since his arrival, over 700 cryoablative procedures have been performed at Crittenton Hospital.

Dr. Lee is now 68 years old and still going strong at Crittenton Hospital, 248-652-5611

Jerome Man, Another Success Story

Here is an e-mail from Jerry that I received in early 1997. "When I was diagnosed in 1988, I telephoned Dr. Labrie in Canada for Flutamide which I obtained during a visit to Dr. Strum in Culver City. I had been examined by doctors at the City of Hope and by Dr. Israel Barken (he should be designated as a National Treasure) in San Diego. I am now seeing a wonderful Oncologist/Urologist - Dr. Paul Brower - in Laguna Hills, California. Until September, 1995, I was employed full time as a federal agent, and retired at that time. I am 73 years old, no metastasis. Current medications include Proscar, Casodex, and lots of pumpkin seeds (a good source of zinc) and some garlic (selenium). I monitor my urine flow rate DAILY using a calibrated container, and determine the volume for a 30 second period of time. This tells me the amount of restriction of the urethra caused by the prostate or tumor. My highest PSA was 5,953 ng/ml and was last measured at 377 ng/ml".

I, Aubrey, talked with Jerry and invited him to come to one of our support group meetings. He wasn't sure he could make it. He was taking some college courses, had homework to do and had several other projects going. One other thing that kept him busy was being president of one of the largest computer user groups in the Los Angeles area.

Unfortunately, Jerry died on Aug. 24, 1998, over ten years after being diagnosed with a PSA of 5,953. He was 75 years old.

Larry Parks, an Enigma

Below is the digest of Larry Parks. He had a beginning PSA of 408. With a PSA that high, there is usually lymph node involvement and or bone metastases. But despite several tests, no evidence of metastases could be found. A biopsy showed a Gleason score of 7.

Larry began CHT and his PSA came down to as little as 0.6- but then it went back up to as high as 39. He tried several different drugs and External Beam Radiation. At the time of this writing in late 2000 his PSA is 1.76.

Larry wrote:

<I have been concerned about posting my results because, as you are well aware, this disease does not affect all sufferers equally.

Fondest Regards,

Larry>

He is so right about the statement above. Again, the first rule when it comes to cancer is that there are no rules.

There Are No Panaceas

CHT worked well for Lloyd Ney, Jerry Man and thousands of other men. Dr. Labrie has been completely vindicated for his early stand on CHT. He is honored and respected by the entire medical community. As Chief Oncologist at Laval University, in Canada, he conducts studies and research on prostate cancer. We cannot ever forget that we are all different and our cancers are also different.

Dr. Labrie has said several times that we could eliminate advanced prostate cancer and eliminate the untimely deaths of thousands of men each year. All it would take is early detection. **The answer to cancer is early detection.**

CHT Compared to Other Treatments

While there are some undesirable side effects of CHT, they are fairly mild compared to some of the side effects of the other treatments. One of the major side effects is the loss of libido. A radical prostatectomy may leave a man with an intact libido, but unable to have a normal erection. Once hormone treatments are interrupted, the libido and potency may return. If the nerves that enable erections have been severed during a prostatectomy, then the man will never be able to have a normal erection. Another side effect of a RP is that many men are rendered incontinent. Incontinence may be more of a problem than impotence. The CHT does not cause incontinence. A radical prostatectomy is major surgery. It may be quite traumatic for some men, especially older ones. CHT is much less traumatic. When compared to radiation, cryosurgery and other forms of treatments, CHT also seems to be as good as or better in many respects.

CHT3 As Primary Treatment For Clinically Localized and Locally Advanced Disease

Dr. Bob Leibowitz is an oncologist who practices in the Los Angeles area. He strongly believes in conservative treatment. He treats all of his patients with combined hormone therapy, but he goes a step further and adds Proscar, or Finasteride, to the LHRH and antiandrogens for triple blockade or CHT3. He started treating some of his patients as early as 1990 with this protocol. He now has a group of 98 patients that are being followed. Each have completed 13 months of triple hormone blockade for clinically localized and locally advanced disease.

Here are some vital statistics:

Patients	AGE	Mean Age
15	50-59	67.1
50	60-69	
29	70-79	
4	80 and over	

Patients	bPSA	Mean PSA	Mean PSA 2 1/2 yrs Off Treatment is 1.4
10	<4	13.55	
45	4-10		
24	11-20		
19	20		

Lowest bPSA = 0.39 Highest bPSA =100

Patients	Gleason	Mean Gleason
2	4	6.55
13	5	
35	6	
35	7	
5	8	
6	9	
2	10	

Note: bPSA is beginning PSA before treatment.

All men were treated with Lupron or Zoladex LHRH agonists. In addition to the LHRH agonists, the men took either Flutamide 125mg, 2 capsules every 8 hours, or 3 Casodex 50mg tablets at one time daily. (Note that the standard dose of Casodex is usually a single 50 mg tablet per day). The men also took 5mg of Proscar (Finasteride) per day. During treatment, the PSA levels became undetectable in all patients within three or four months.

Dr. Leibowitz keeps his patients on this protocol for 13 months. He then has them continue with 5mg of Proscar each day for maintenance. As of December 1999, he had 60 patients who had been off treatment for at least 12 months and some patients had been off for as long as 73 months. Average time off treatment for this group is 2 1/2 years. The mean PSA is 1.4 and is stable.

The testosterone levels of 37 men were measured before treatment. The testosterone ranged from a low of 123 to a high of 635. During the 13 months of treatment, the testosterone fell to castrate level. But after treatment the testosterone production returned. For all men off treatment for at least one year, the testosterone levels ranged from 11 and up to 893 with a mean of 403. The libido usually returned to normal along with normal sexual functions.

His original goal was to have his patients go on intermittent therapy. He would monitor the PSA and if it began to rise, he would put them back on CHT3. So far he has not had to re-treat any of his patients. He has not yet had any of this group of patients become hormone refractory.

Some may look at Dr. Bob's excellent results and think that perhaps he is a "cherry picker". But if you look at the PSA and Gleason scores, you know that it isn't so. These first 98 patients were treated sequentially. Besides the original 98 patients in this study, Dr. Bob continues to accept and treat new patients.

Dr. Bob Leibowitz can be reached at 310-229-3555, fax 310-229-3554, e-mail beewell@earthlink.net

The CHT3 treatment is one of the least invasive of all treatments. The hot flashes, no libido and other unpleasant side effects usually last for one year only or the duration of treatment. The side effects of some of the other treatments last for the rest of your life. One other big advantage is that, after treatment, the man still has his prostate. He has no incontinence and can still have normal erections, orgasms, and even ejaculations.

Another advantage of this protocol is that it is one of the least expensive. The drug costs will be approximately \$12,000 for the 13 months. Of course the office visit costs would have to be added. The cost of the Proscar needed for maintenance would cost about \$1000 per year.

Still another advantage is that there would be no hospitalization or out patient care or cost. There would be no time lost from work or recuperation.

Some men have gone on CHT and stayed on it for years even though their PSA became undetectable after just a few months. When these men finally go off CHT, it often takes a very long time for their testosterone production to become normal again. In some men it never recovers. Also many of these men never regain their libido and lost muscle mass. If a patient has an undetectable PSA

for at least a year, it would seem better to go on intermittent treatment. This may help prevent the cells from adapting to the CHT. If the PSA starts rising while off treatment, the patient can always go back on therapy.

Timing of Treatment

Like most things in life, there is a cost, or downside, to CHT. There are several side effects that severely affect one's quality of life (QOL). One of the most unhappy side effects for many men is a loss of libido. The enjoyment of sex depends on the libido and without testosterone, there is no libido.

Without testosterone, the patient may feel tired and fatigued. He may have a loss of muscle mass. Men produce both testosterone and a small amount of estrogen from the adrenals. Without the testosterone, the estrogen exerts a greater influence on the man. His breasts may become very tender and sore and may also become quite enlarged. And he may put on weight.

A very famous surgeon and a few other doctors believe that, because of the psychological and sexual side effects of hormonal treatment, it should be delayed until progression of disease. However, if hormonal therapy is delayed until the tumor burden becomes massive, a proportionally larger number of androgen-independent cells may persist after hormonal therapy and be much more difficult to control. We think that the preponderance of evidence supports early hormone treatment rather than late therapy.

Dr. E. David Crawford, Dr. E. Messing and several others did a study titled "Immediate Hormonal Therapy vs. Observation for Node Positive Prostate Cancer Following Radical Prostatectomy and Pelvic Lymphadenectomy". The study was published in a leading peer review journal and was also presented at the 1999 AUA Convention.

Between 1988 and 1992, 98 men with node positive (N+) prostate cancer (PC) who had undergone radical prostatectomy and pelvic lymphadenectomy (RP+PL) were randomized to receive bilateral orchiectomy or goserelin acetate (patient's choice) vs observation (Obs) with hormonal therapy (HT) administered upon progression.

At mean follow-up of 7.2 years, 6 of 46 men in the Early Hormone Treatment (EHT) arm had died, 2 from PC. In the Obs arm, 18 of 52 had died, 16 due to PC. Four of 46 EHT men have progressed/recurred (including the 2 who died of PC) and 5 have experienced biochemical failure (PSA 0.4) only. In the Obs arm, 29 have progressed/recurred (including 16 who died of PCa), and 10 had a rising PSA or biochemical failure. Thus, 18.8% EHT vs. 75% Obs patients have failed.

In men who had positive lymph nodes during a radical prostatectomy, early hormonal treatment (EHT) significantly prolonged survival compared with observation and delayed HT. This is the first demonstration of a survival

advantage for EHT in a randomized prospective clinical trial in which only the effects of HT on the disease itself (and not on assisting other treatments such as radiotherapy) have been tested. Extension of these results to even earlier disease settings merits further investigation.

There are thousands of men who gladly endure the unpleasant side effects of hormone treatments because the alternative is much worse.

Proscar and Flutamide or Casodex as Primary Treatment

Several men are using Proscar and high dose Casodex (150mg/day) or Flutamide as a primary treatment. This does not cause a suppression of the testosterone. It does not cause hot flashes, loss of muscle mass or most of the other unpleasant side effects of CHT. It may cause a loss of libido in a small number of men.

The man can go on this protocol and closely monitor the PSA. If it starts to rise, then he can always go to the other more radical options. This is one of the least invasive of all treatments.

Costs of Hormone Treatments

One of the easiest and least expensive ways to deprive the prostate cancer of testosterone is to simply remove the testicles or castration. The Greek term for the testicle is orchis. A more euphemistic term for castration is orchiectomy or orchidectomy (orchid plus ectomy which means excision or removal). Later a flower was discovered that had a root or bulb system that looked a bit like a testicle. Since most flowers and plants are given Greek and Latin names, it was called an orchid.

An orchiectomy is fairly simple and may have a one-time cost of less than \$2000. Even after an orchiectomy, a man may still have to take one of the antiandrogens. An orchiectomy plus an antiandrogen and LHRH plus antiandrogen are both equivalent to combined hormone therapies.

CHT can be very expensive. The International Pharmacy at www.internationalpharmacy.com lists thousands of drugs and their prices. If you are buying drugs, it is a great place to do some comparison price shopping. Here are some prices for CHT drugs:

Lupron depot (28 day) 7.5 mg	\$680.67
Lupron depot (84 day) 22.5 mg	\$2042.03
Lupron depot (112 day) 30 mg	\$2722.71

Zoladex (syringe 28 day) 3.6 mg	\$516.99
Zoladex (syringe 84 day) 10.8 mg	\$1550.98

Casodex (30 tablets) 50 mg	\$380.41
Casodex (100 tablets) 50 mg	\$1268.05

Nilutamide (90 tablets) 50 mg \$291.82

They did not list Flutamide. A local drugstore offers it at a senior discount rate of \$60 for 30 125 mg capsules. The normal dose is two capsules every 8 hours, or six per day. This would be \$12 per day or \$360 per month.

The doctor visit for the injection will add to the cost of Lupron or Zoladex. Medicare and most insurance companies pay for the drug and the cost for the doctor to give the injection. But Flutamide, Casodex and Nilutamide are prescription drugs. The doctor gives the patient a prescription and he fills it at a pharmacy. At the present time, Medicare does not pay for these drugs, but many of the insurance companies do. Hopefully, Medicare may pay for some of this cost in the future. The total cost for CHT may be \$750 and up to \$1500 or more per month or up to \$18,000 or more per year. If the man lives for ten years, it could cost over \$180,000 for drugs. Both surgical castration and chemical castration have the same side effects. Both procedures eliminate the libido, cause hot flashes, loss of muscle mass, and osteoporosis.

Since orchiectomy and CHT procedures are equivalent, you can understand why HMOs, Medicare and some doctors urge the men to undergo surgical castration. (If cost is a major consideration, castration can be accomplished for much less than \$2000. For years, farmers and ranchers have been putting a rubber band around the testicles of male animals to castrate them. The rubber band cuts off the blood circulation and in a short time the testicles just fall off. We can only hope that Medicare, HMOs and insurance companies don't find out about the rubber band).

If chemical castration is equivalent to surgical castration, why don't more men choose the less expensive orchiectomy? There are several reasons why men choose LHRH agonists. First and foremost, the chemical castration is reversible. They hope that someday soon, a magic bullet will be found that can eliminate their cancer and they will be whole again. There is also the hope that their cancer will go into remission. It does happen in a small number of cases. Some of them feel that it is bad enough to have to give up sex due to the hormone treatments. But undergoing castration removes just about the last vestige of their manhood or any hope of recovery.

Holding on to their testicles is so important to some men that they do it with both hands. Many of them feel that a man has to have testicles in order to be a man. Some have argued that there are probably other hormones and substances produced by the testes besides testosterone. So why not keep them if the drugs will do the job. Once the testes are removed, they are gone forever. We keep hoping that a new cure may be found someday that will make prostatectomies and castrations unnecessary.

Intermittent CHT

After a period of time on CHT, the PSA of many patients goes to zero or to a very low level and remains steady. In some patients the PSA becomes undetectable in a very short time. In others it may take several months. The length of time from beginning CHT to undetectable can be a fairly good prognosis of the course of the disease.

If the PSA goes to undetectable and stays there for a year or so, some doctors believe that it is beneficial to take the patient off hormones for a period of time. One reason for going off the hormones is so that the cancer cells do not become adapted to the hormones and learn to live with them. The cells in our bodies, including cancer cells, can learn to adapt to and live with almost anything. Our ability to adapt is one of the reasons for evolution.

If a person is placed on antibiotics for an extended period of time the bacteria may learn to adapt and evolve to the point that the antibiotics are no longer effective. It is quite possible that the cancer cells do the same thing when a man stays on CHT for a very long time. We know that they often learn to actually thrive on some of the antiandrogens. Some of the cells actually die when the antiandrogens are withdrawn, the antiandrogen withdrawal response (AAWR).

Going off CHT is beneficial to the patient's quality of life. Without the hormone treatments, the patient's testosterone level will usually return along with his libido. The resumption of testosterone levels will also make the patient feel stronger and feel better.

Still another reason to go intermittent is that you save the cost of the drugs. Many men go on CHT and continue on it for years, even though their PSA is undetectable. These men are at risk for the cancer cells to become refractory. Another reason to go intermittent is that millions of dollars could be saved if all the men whose PSA has gone to undetectable and stayed there for at least a year went intermittent.

While off the hormone therapy, the PSA level is closely monitored and if it begins to rise, the patient resumes the CHT treatments. Several men are trying intermittent therapy. Some men go off all drugs. Others go off the Lupron or Zoladex and take an anti-androgen such as Flutamide or Casodex along with Proscar. This allows them to regain their libido and overcome the constant fatigue.

Dr. Strum's Intermittent Therapy Protocol

We believe in a prolonged exposure to CHB with nondetectable PSA reached and sustained for 12 months. In our study population the average time OFF therapy after the above is achieved has been 20 months with the longest time off

48 months. If the patient's PSA begins to rise, when it gets to about 5 ng/ml we restart them on CHB.

Our initial period is 12 months of NONDETECTABLE PSA (NDPSA). We follow this, upon reinitiation of CHB with the same approach: 12 months of non-detectable PSA. So far no one has failed this approach. We have been doing it for over 7 years.

Dr. Strum has published the results of his studies. As of this date, in mid 2000, it is the largest trial of patients on IAD with the longest followup. Some patients have been off treatment for over 8 years with a flat PSA.

His article on Intermittent Hormone Blockade was published in the 2000 February issue of The Oncologist. You can view the abstract and the full length o article by going to:

<http://theoncologist.alphamedpress.org/cgi/content/abstract/5/1/45>

Drs. Strum and Scholz have a web site or a HOMEPAGE at : www.prostate-cancer.org (see their papers, software, resources, etc) for other resources such as the PCAB (Prostate Cancer Address Book) with phone numbers, addresses and e-mail of outstanding people in the world of PC. PC PAPERS AND COMPUTER SOFTWARE: go to their website to download these without charge. Also see CLINICAL RESEARCH PUBLICATIONS in peer-reviewed journals written by Strum & Scholz.

Web: www.prostate-cancer.org

A Few Patients Who Opted For IAS

W.J.KENNEY wjkenney@prodigy.net

I was diagnosed with a PSA of 49.8 in 1992. I was treated with RP and then with External Radiation Therapy. Have been on CHT on and off since then. Off for as long as 24 months sometimes. Now over 8 years since diagnosis.

BILL CANNON CarlsbadBill@prodigy.net (Bill Cannon)

I had an RP in 1992, started CHT in February, 1995 with a PSA of 18- and stopped in July, 1995. PSA WAS 0.1 in August, 0.64 in November. Have been on and off several times. As of August 2000, I continue on Intermittent.

GEORGE McCALL mccalls@earthlink.net

I had a PSA of 14.7 July 7, 1994, Gleason was 1+2=3. Chose to watch and wait. April 11/95 PSA was 20, May 16, PSA 27. Went on CHT in June, 1995 as an initial treatment with a PSA of 27. Stopped CHT in September 95 with PSA of 0.3. May 96 PSA was 6.3, August 9.0, November PSA was 8.3 after 13 months off CHT. October, 1997... PSA increased to 17.4. At 77 years old, went to Dr. Gordon Grado in Scottsdale, AZ and had Seed Implants. Minor side effects;

Last PSA 0.3 in June 1999. October 1999- The only lingering side effects I experience are decreased libido, frequent and slightly burning urination. I will be 80 years old in a couple of months, so I feel very fortunate to have fared this well with this terrible disease.

Editorial Note: Note that George's Gleason was 1+2=3 with a PSA of 14.7. He had an enlarged prostate, probably due to BPH which can produce PSA. But his PSA continued to rise and was almost doubled from 14.7 on July 7, 1994 to 27 on May 16, 1995. No doubt this indicated an aggressive cancer. The Gleason Score of 1+2=3 was probably an error.

CHARLES CLAUSEN cclausen@magick.net

Born 7/37, 1/94 PSA 9.9, Gleason 3+4, bone scan neg, cT2c or cT3a (acid phosphatase 0.4, normal on assay = 0 to 0.8)

3/94 RP at UCSF, pT3aN1 (4 cu. cm. volume of tumor, extensive perineural and vascular invasion, extensive extracapsular extension in right posterior lobe with focal extension to surgical margin, sv & vas neg, 0.4 cm. met in 1 of 10 lymph nodes)

Since his RP in Jan. 1994, Charles has been on and off CHT three times. His on cycles have been for as long as 8 months, his off periods have been as long as one year.

Charles uses the ultra-sensitive PSA tests. He is quite knowledgeable about it and wrote the article on ultrasensitive PSA in Chapter 6. He spends a lot of time on the Internet answering questions.

DON SWIRNOW swirnow@qwestinternet.net

DOB=7/20/32, Dx=8/92, PSA=21, Gleason of 7, aborted RP in 9/92 due to one bad lymph node. CHT started in 10/92 giving PSA of 1.0 in 12/92, less than 0.1 from 4/93 thru 3/96 when CHT stopped. Five needle biopsy in 3/96 all negative for PC. PSA on 6/4/96 was 0.1 and 0.39 on 9/4/96. Started Proscar (5mg 2x/day) on 8/1/96. MRI/MRS in October showed no detectable cancer in prostate or seminal vesicles or lymphs. On 11/5/96 reduced proscar to 5mg per day due to gynecomastia.

He has been off CHT for as long as 18 months or more before starting again.

"I guess I should have been dead years ago". ☺--Don

Editorial note: Don has spent a lot time learning about prostate cancer. He devotes a lot of time to the Internet answering questions and helping others.

Orchiectomy and IAS

Here is an Internet post from Dr. David Michener who had an orchiectomy:

"Subj: [PP] Testosterone replacement clearing house
From: bermich@EARTHLINK.NET (david michener)

I am seven years into hormone blockade beginning with one year of Lupron followed by orchiectomy with gratifying PSA response but considerable aggravation from side effects. After following the positive reports from intermittent blockade I have been working with my oncologist to simulate intermittent by getting testosterone supplements.

After eight months of monthly IM testosterone enanthate I have been very pleased with the results. The PSA has gradually approached 5 which may be a good cut-off point. In any case, I am aware that there are others out there post orchiectomy who are looking for something better. I know that both Dr. Strum and Dr. Leibowitz have such patients and I assume that there are others.

I would be glad to hear from any of you and to provide a point for collection of our pooled data. Your identification can remain anonymous, if you wish and I would be happy to distribute whatever information we obtain. Specifically, it will be helpful to know what routes of administration work (I know that transdermal gel and oral DHEA have been tried) and what cut-off points have been determined.

Certainly, the responses of circulating testosterone and PSA levels will be of interest. Let me know of any interest and I'll be glad to share.

David P. Michener, M.D. MPH"

There are other men who have had an orchiectomy who are experimenting with testosterone replacement.

Here is some information from Dr. Bob Leibowitz:

"I am now treating men with testosterone replacement therapy. All were previously surgically castrated. All had undetectable PSA's; hence, they were hormone sensitive. They wanted to be on intermittent androgen blockade, but lacked the necessary equipment to produce their own testosterone.

When I reviewed the information available on why it is generally felt that testosterone replacement is contraindicated in a man with metastatic prostate cancer, I concluded that this statement is accurate for any man with hormone resistant or hormone refractory disease. If, however, you are still hormone sensitive, then testosterone may not be harmful (my opinion for these men only). Do not apply this rationale to your situation; this has the potential to worsen your prostate cancer and hasten complications and/or even death.

If testosterone were harmful for all men with prostate cancer, then no one should ever be allowed to stop hormone blockade, since stopping blockade almost always results in your testosterone rising to pre-hormone blockade levels. Intermittent hormone blockade would not be allowed if all doctors believed that testosterone is harmful to all men with prostate cancer.

One patient has been on testosterone replacement for about one and one-half years. His PSA is about 0.26 and not rising. He feels much better; much stronger; and hits his golf ball 25 yards further than pre-testosterone days.

Another patient has been treated with testosterone for over one year and has a stable PSA of 0.4 (by a different PSA assay). He also feels much better and has improved his golf game.

One other patient has only been on treatment a few months. He still has an undetectable PSA.

I must stress that any decision to consider testosterone replacement therapy must be made on an individual basis, and I urge you to never try it if you are hormone resistant at all. Your PSA will rise if you do."

Several of the men being treated by Dr. Leibowitz belong to the various support groups in the Los Angeles area. Many of them are personal friends of co-author Aubrey. Here is a letter that was received from one of them:

"Dear Aubrey,

The success of my treatment should give encouragement and optimism to others. It all started with a radical in 1988, stage C, Gleason 3+4, positive margins. Remember this was before PSA. I had 6700 rads of broad beam radiation after the surgery. In 1993, I had a rising PSA that was doubling every 2 weeks. My choice at that time was to have an orchiectomy. This is a choice that most would not make, but I think it was a good decision. Later I added Casodex and Proscar to my regimen. My PSA has been undetectable ever since. It is quite likely that the triple hormone blockade therapy might have been equally effective, but I did not know about it at that time.

To counteract some of the detrimental side effects of the CHT, I have now been off Casodex for 1 1/2 years and only on Proscar maintenance. After many months of study and analysis, I have now begun using a rub-on gel form of testosterone supplementation. My testosterone level has risen to 125 while my PSA is still undetectable.

This last 11 years has caused shock, anxiety and despair. But it has also caused excitement, acceptance and a sense of accomplishment. I am winning the battle.

James, E. Ahrens, Ph.D."

Osteoporosis

Osteoporosis is one of the symptoms of Androgen Deprivation Syndrome. Osteoporosis is quite common in post-menopausal women. One reason is due to the lack of estrogen. (The prefix osteo is from the Greek for bone, as you might guess, porosis means porous). Osteoporosis is also one of the major side effects of long term CHT. I wrote about my friend, Jerry Man, earlier. He had had a PSA of 5,953 in 1988. He was on CHT for ten years. He claims to have lost almost six inches in height. Some of that was due to his "dowager's hump", which is often seen in older women.

Osteoporosis is a serious problem for men on long term CHT. Many doctors do not assign enough significance to it. Bones are easily broken and may take a very long time to heal. Fractures of the spine, hip and wrist are common.

There is some information about osteoporosis at this Merck web site:

<http://www.merck.com/product/usa/fosamax/cns/dosing/dosing.html>.

This site talks primarily about women, but osteoporosis affects men on CHT in the same way.

Treatment for Osteoporosis

Bisphosphonates are one of the treatment options. Fosamax (Alendronate Sodium) is often used. FOSAMAX^{*} (alendronate sodium) is an aminobisphosphonate that acts as a specific inhibitor of osteoclast-mediated bone resorption.

Bisphosphonates are synthetic analogs of pyrophosphate that bind to the hydroxyapatite found in bone.

PC-SPES

Several men are taking PC-SPES as a primary treatment or as a treatment for recurrent prostate cancer. In most men, it lowers the PSA and appears to control the cancer in the same manner as CHT. However there is no long term data as to its efficacy. Dr. Eric Small of the University of California at San Francisco is doing one of the few studies of the herbal compound. The article below is taken from Dr. Small's study.

PC-SPES (PC stands for prostate cancer, SPES is Latin for hope), a dietary supplement, is a combination of eight Chinese herbs that have long been used in Asia to treat various medical conditions. It is commercially available at health food stores as an over-the-counter supplement for the treatment of prostate cancer; however, due to the possible side effects, it is recommended that PC-SPES be taken under the supervision of a doctor.

UCSF has treated 70 patients with PC-SPES. Half had hormone-sensitive disease (had never before received hormonal therapy), and half had received hormones and had developed hormone resistant prostate cancer.

In brief, our findings suggest that patients who have never been treated with hormones will virtually all have a significant response to PC-SPES. One hundred percent of patients had a decline in their PSA, and 56% of patients achieved an undetectable PSA. However, this was felt to be due to the hormonal effects of the drug, which resulted in a dramatic decline in the male hormone testosterone in over 80% of patients. Ninety-two percent of these patients developed breast tenderness or swelling, symptoms that are very reminiscent of treatment with hormonal therapy. Thus, we feel that at a minimum, this product has hormonal effects, at least in patients with hormone sensitive disease.

However, we were surprised that in hormone resistant prostate cancer patients (patients who had already received hormones, and despite hormones had developed growth of their cancer) that approximately 60% of patients had a significant PSA decline (defined as a decline of more than 50%, lasting for at least a month). Furthermore, in those patients who were tested, some patients had improvement in bone scans and other measures of disease. Thus, we believe that PC-SPES probably has some activity in patients with hormone resistant prostate cancer.

It is important to note that for both groups (both hormone sensitive and hormone resistant) we do not know how long PC-SPES will work, and what, if any, long-term complications exist. Short-term complications have been reasonably mild.

The retail cost of PC-SPES through the manufacturer, Botanic Lab, is \$108 per bottle of 60 capsules. At 9 capsules per day, the cost for a month of therapy is \$453.00. Unfortunately, at this time there are no insurance companies, HMOs, Medicare or other third party payers that pay for the use of PC-SPES. This may change over time, but for the time-being the cost of PC-SPES unfortunately must be borne by the patient.

A supply of PC-SPES may be obtained from Botanic Lab, 2900 B Saturn Street, Brea, CA 92821. The phone number to order the drug is 800-242-5555. Botanic Labs' website is <http://www.botaniclab.com>.

PC-SPES On-Line Support Group

There is another PC-SPES web site at www.PC-SPES.com. They have a lot of up to date information about the product. They also have an on-line support group that you can join. This group is made up primarily of patients who are taking PC-SPES. You can e-mail them with questions or suggestions.

Why PC-SPES May Be Effective

PC-SPES has a phytoestrogenic component. Prostate cells have androgen receptors (AR) and estrogen receptors (ER). Even those cancer cells that have become hormone refractory may still have estrogen receptors so they will respond to estrogen therapy. Estrogen patches and DES may provide an equivalent therapy at a much lower cost.

Treatments for Hormone Refractory PCa

There are several chemotherapy treatments that can be used if the patient has become hormone refractory (HRPC) . One of the more promising treatments seems to be taxotere. We will talk about that and other treatments in the next chapter.