



Hormone Therapy for Prostate Cancer – A Patient Guide

Urologic Oncology Program
UCSF Helen Diller Family Comprehensive Cancer Center
University of California, San Francisco
Phone number: 415-353-7171

Prostate cancer is the second most common male cancer after skin cancer. Hormone therapy is a type of treatment sometimes used to treat prostate cancer, although not all men with prostate cancer need or benefit from hormone therapy. Hormone therapy works by reducing the production of **testosterone** in different ways. Testosterone feeds the prostate cancer cells so starving them often prevents and controls growth. In selected patients it also improves the effectiveness of radiation therapy. The purpose of this booklet is to explain hormone therapy in layman's terms to men and their partners who may be considering or have started on hormone therapy. This booklet will cover the following topics about hormone therapy:

- How and why it works
- What are the different types
- Who is a candidate
- What are its side effects
- How side effects can best be managed

What is testosterone?

All men produce a hormone called testosterone. It is the male hormone comparable to estrogen produced in the female body. Testosterone is one of a number of different hormones called androgens that have sexual and other effects on the body.

Please Note: all words in **bold** are defined in glossary at end of document, pg. 16.

During puberty, a boy's production of testosterone increases as part of his natural physical maturity. This increase of testosterone during adolescence is responsible for male sexual maturity and fertility. Increasing levels of testosterone lead to:

- increased muscle mass
- increased body and facial hair
- deepening of the voice
- lengthening of the penis
- enlargement of the testicles
- increased libido (desire for sexual activity)
- the ability to achieve and maintain an erection and to ejaculate.

During adolescence, testosterone also aids in the normal development of the prostate gland. The prostate gland begins to produce fluids which are added to semen during ejaculation. Later in life, testosterone plays a very active role in the development of prostate cancer since it is known to assist in the growth of prostate cancer cells.

How is testosterone made?

Two different pathways produce testosterone in the male body (see *Figure 1*).

- Most testosterone is made by the testes.
- A much smaller amount is produced by the two **adrenal glands**, located just above the kidneys.
- Testosterone production begins in the brain where a gland called the **hypothalamus** sends a message to another gland in the brain called the **pituitary gland**.
- The pituitary then sends out a message that tells the testes and adrenal glands to make testosterone.

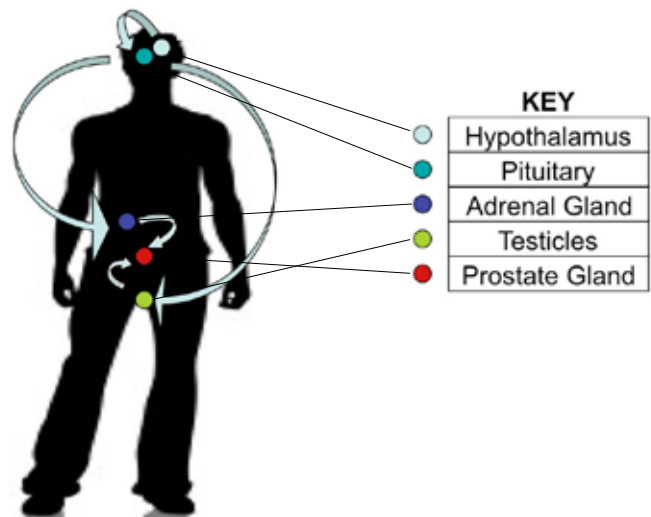


Figure 1

How does testosterone help prostate cancer grow?

Testosterone travels through the blood and eventually arrives at the prostate cancer cells. The testosterone then moves inside the cancer cell where it helps the cancer grow. One may think about testosterone as a hormone that "feeds" the cancer. The more testosterone the cancer cells have (within limits), the more the cancer can grow, thrive, and then spread to other parts of the body. In other

words, very low levels of testosterone may be sufficient to stimulate the growth of prostate cancer cells but once testosterone is in the normal range it is unclear that slightly higher levels cause more growth.

What is hormone therapy?

Since testosterone enables prostate cancer growth, one method to treat the cancer is to eliminate as much testosterone as possible. This is referred to as Androgen Deprivation Therapy.

- One type of hormone therapy, known as **LHRH or GnRH agonists**, are medications commonly used to reduce the amount of testosterone in a man's body.
- A second family of hormone therapy drugs, the anti-androgens, blocks the use of testosterone by the cancer cells.

When testosterone is reduced, prostate cancer cell growth may be slowed and the cancer almost always begins to shrink. As the cancer decreases, **Prostate Specific Antigen (PSA)**, measured by a simple blood test, will also likely decline. For men with very advanced prostate cancer and those failing local therapy (usually radiation or surgery), in general, hormone therapy will not cure the cancer, but it will greatly slow it down and may control prostate cancer for an extended period of time.

For men receiving hormone therapy to supplement primary treatment such as with radiation, the addition of hormone therapy has been shown to increase the likelihood of disease free success including enhanced survival in some patients.

Who should be treated with hormone therapy?

Hormone therapy may be recommended in the following circumstances:

- In conjunction with radiation, mostly for men with **Gleason scores** of 7 or higher. This is often given before (neoadjuvant), during (concurrent), and after (adjuvant) radiation.
- After primary radiation or surgery when PSA rises.
- As primary therapy for men unsuitable for radiation or surgery.
- In men with metastatic prostate cancer (prostate cancer which has spread to other sites in the body).

Men diagnosed with non-metastatic or **localized prostate cancer** are divided into three categories depending on the characteristics of their cancer. These groups attempt to predict the likelihood of the cancer returning after primary treatment of surgery or radiation. These are general categories and more specific assessment of risk can be obtained by using other risk assessment tables or nomograms (i.e. UCSF CAPRA, Kattan, etc). The three groups are:

- low risk
- intermediate risk
- high risk.

Men diagnosed with **low risk** prostate cancer are often treated with surgery (**radical prostatectomy**), or either **external beam radiation** or **brachytherapy** that places radio-active seeds inside the prostate. Hormone therapy is generally not recommended for use in either of these treatment options. An exception to this rule is the low risk patient whose prostate is too large to treat with an implant due to its size (e.g. > 50cc). In this case the use of hormonal therapy can shrink the prostate 30 to 50% and allow an implant to be performed. For low risk men selecting to monitor their progression on an active surveillance program, hormone therapy is not necessary.

Men with **intermediate— or high risk** prostate cancer may also select surgery or radiation. Hormone therapy is not used with surgery unless PSA continues to rise following surgery.

Men selecting radiation are usually treated with either external beam radiation or a combination of external beam and brachytherapy. These men often receive hormone therapy based on research showing some men live longer when radiation is supplemented with hormone therapy. Treatment usually begins 6–8 weeks prior to the start of radiation, continues throughout the course of radiation treatments, and lasts anywhere from 4 months to 3 years based on the extent of cancer. Your doctor will discuss with you whether or not the hormone therapy should continue after radiation treatments are completed.

Some men are not suited for either surgery or radiation for multiple reasons: for example:

- advanced age
- other medical problems
- patients' choice because of potential side effects.

Hormone therapy is an option in any of these situations. In patients with locally advanced disease it has been shown not to be as effective as hormonal therapy combined with radiation or, possibly, surgery.

When PSA rises after primary treatment with surgery and/or radiation, this is called **serologic progression** meaning a climbing PSA with no cancer metastasis visible on **bone scans**, or **CT scan**. Alternatively, a post-operative pathology report may indicate **positive margins**, meaning the cancer has probably spread outside the capsule, or identify cancer in the seminal vesicles and/or lymph nodes. This too can result in serologic progression. If cancer is evident after primary treatment and/or there is serologic progression, your physician may well recommend hormone therapy alone or in combination with additional local therapy (e.g. radiation after surgery or cryosurgery).

Finally, hormone therapy is frequently prescribed for men with **metastatic disease**. When prostate cancer spreads beyond its local environment, the first distant sites are usually lymph nodes and then bones. Less often, prostate cancer metastasizes to the organs, such as the liver or lungs, but it is uncommon for prostate cancer to spread to the brain. Androgen deprivation therapy or hormone therapy is thought of as systemic therapy: that is, it kills prostate cancer cells throughout the patient's entire system, regardless of their location. It can treat bone, tissue, lymph nodes, organs, and the prostate gland.

Radiation may be able to treat a localized metastasis, but whether it prevents future metastases is unknown.

What are the types of hormone therapy?

There are four main types of hormone therapy:

1. **Orchiectomy** - Surgical removal of the testicles
2. **LHRH agonists or antagonists** - Medication to stop the testicles from making testosterone
3. **Anti-Androgens** - Medication that prevents cancer cells from using testosterone
4. **Triple Androgen Blockade** – Adding a medication that reduces the production of dihydrotestosterone (DHT).

Orchiectomy removes the testicles but leaves the scrotal sac. Testicles produce the majority of male testosterone, prostate cancer's fuel. Removing the testicles is permanent and irreversible; often, testicular prostheses (artificial testes) can be placed in the scrotal sac for cosmetic purposes to help maintain a more normal appearance.

Permanently removing the testicles makes intermittent hormone therapy difficult and more complicated; intermittent hormone therapy may be advantageous and will be discussed in greater detail later in the booklet. Another problem with bilateral orchiectomy is the psychological effect. Many men may feel distress and a loss of their manhood if they undergo this surgical procedure.

LHRH agonists stop the testicles from making testosterone. It does this by encouraging a continuous message from the brain to produce testosterone that over-stimulates the gonads; they respond to being 'overworked' by switching off. The initial overstimulation is also the reason why some men may experience a spike or 'flare' in their testosterone level before it declines, and why **anti-androgen** drugs like bicalutamide or flutamide (see below) are prescribed for a short period when a man starts LHRH therapy.

LHRH antagonists also stop the testicles from making testosterone but they do not induce the initial overstimulation spike or 'flare' in their testosterone level; thus **anti-androgen** drugs like bicalutamide or flutamide (see below) may not be necessary.

When the LHRH medication is stopped, the testicles usually resume production; how long this takes varies from man to man (and the duration of the therapy) but it can be several months in younger men to a couple of years or not at all in older men.

All the drugs listed in Table 1 stop testicular testosterone production. They are all considered equal. The choice of which drug to use may simply be based on cost and/or convenience.

Knowing your baseline testosterone and monitoring it may also be important. It can tell you whether your cancer is responding to the hormone treatment (hormone sensitive); if your PSA remains high when your testosterone has been lowered, then clearly it is not. If your testosterone remains high despite the usually prescribed drugs, it is possible other medications may be required; perhaps your testosterone producing pathways are not responding as expected.

Generic Name	Trade Name	How is the drug given?	How much drug is given & how often?
Leuprolide Acetate	Lupron®	Injected into the muscle of the buttock	7.5 mg monthly 22.5 mg every 3 months 30 mg every 4 months
Goserelin Acetate	Zoladex®	Injected beneath the skin of the abdomen	3.6 mg monthly 10.8 mg every 3 months
Leuprolide Acetate	Eligard®	Injected beneath the skin of the abdomen	7.5 mg monthly 22.5 mg every 3 months 30 mg every 4 months 45 mg every 6 months
Leuprolide Acetate	Viadur®	Surgically implanted into the upper inner arm	65 mg annually
Triptorelin Pamoate	Trelstar®	Injected into the muscle of the buttock	3.75 mg every 4 weeks 11.25 mg every 12 weeks 22.5 mg every 24 weeks
Degarelix Acetate	Firmagon®	Injected beneath the skin of the abdomen. This drug is an LHRH antagonist, does not cause a spike, and does not require an initial course of anti-androgens.	240 mg initially followed by 80 mg every 4 weeks

Table 1: LHRH Drugs - Medications that stop the testicles from making testosterone.

Anti androgen drugs do not stop the testicles or the adrenal glands from making testosterone; rather they block the cancer cells' ability to use testosterone required for their survival. An anti-androgen from Table 2 is often used in combination with one of the medications listed in Table 1 on a longer term basis than just to counter the 'flare'. This combination therapy is called **Combined Androgen Blockade** and may be prescribed for men with recurrent disease as well as others. Although any of the anti-androgens can be used, bicalutamide is the most frequently used anti-androgen.

Generic Name	Trade Name	How is the drug given?	How much drug is given & how often?
Flutamide	Eulexin®	Oral pills	250 mg three times daily
Bicalutamide	Casodex®	Oral pills	50–150 mg daily depending on situation
Nilutamide	Nilandron®	Oral pills	150 mg daily

Table 2: Anti-androgens—Medications that decrease the cancer cell's ability to use testosterone.

Triple Androgen Blockade adds a third class of hormone drugs known as 5-Alpha Reductase Inhibitors to Combined Androgen Blockade. Five alpha reductase inhibitors are often prescribed for BPH, a benign enlargement of the prostate that can obstruct the urethra and impair urination. The drugs reduce the production of DHT or dihydrotestosterone, the active metabolite of testosterone. UCSF physicians do not generally prescribe Triple Androgen Blockade as it has not been shown to be more efficacious than therapy without a Five Alpha Reductase Inhibitor.

Generic Name	Trade Name	How is the drug given?	How much drug is given & how often?
Finasteride	Proscar®	Oral pills	5 mg daily
Dutasteride	Avodart®	Oral pills	0.5 mg daily

Table 3: 5-Alpha Reductase Inhibitor Drugs—Medications that decrease dihydrotestosterone (DHT)

Starting hormone therapy

If you decide to move forward with hormone therapy, you may still have questions. We have tried to answer some of them:

Am I better off with medical or surgical hormone therapy?

Both options achieve the goal of stopping testicular testosterone production. The recommended treatment for most patients is testosterone lowering medication mainly because it is easily **reversible**. Beginning treatment with the medication will help you avoid a surgical procedure, allow you to keep your testicles, and will provide the option of treating your cancer with **intermittent** hormone therapy.

Should I use the testosterone lowering medication (LHRH analog or antagonist) alone or combine it with the testosterone blocking medications (anti-androgens) listed in Table 2?

At UCSF combined therapy may on occasion be recommended—triple blockade is rarely prescribed.

Many patients begin hormone therapy using a combination of LHRH and anti-androgen drugs to protect against a testosterone flare; the anti-androgen drug is dropped after 15–30 days. Some men may remain on this therapy, or add back the anti-androgens if the PSA does not respond well enough. The final decision may depend on other factors such as side effects or other medical problems. Your health care provider will discuss the best approach for your situation.

Is it possible to use a testosterone blocking drug (anti-androgen) on its own (Table 2) WITHOUT an LHRH agonist or antagonist?

Most of the side effects experienced by men on hormone therapy are caused by low testosterone. Peripheral androgen blockade (PAB) blocks to some degree the use of testosterone by the cancer cells without reducing testosterone levels. Three different PAB options are listed in Table 4; all of these options are still experimental. PAB should not be used on an intermittent basis (see below) and is somewhat inferior to testosterone lowering therapy with an LHRH agonist, but may be considered for some patients. Your health care provider will discuss whether or not PAB is an appropriate option for you.

Generic Name	Trade Name	How much drug is given & how often?
High Dose bicalutamide	High Dose Casodex®	150 mg orally daily
Finasteride and Flutamide	Proscar® and Eulexin®	5 mg orally daily 250 mg orally three times daily
Dutasteride and Bicalutamide	Avodart® and Casodex®	0.5 mg orally daily 50 mg orally daily

Table 4: Types of peripheral androgen blockade (PAB).

Intermittent hormone therapy

Intermittent hormone therapy is widely used in men undergoing hormone treatment for prostate cancer. Testosterone lowering drugs are prescribed for a period of time, usually 9–12 months, and then stopped. The patient is then placed on a temporary time off hormones, hopefully reducing some of the side effects of the hormone therapy. During this 9–12 month treatment period, the PSA hopefully declines to undetectable, and testosterone falls to castrate levels (less than 20 ng/dl). After the medication is stopped, the PSA usually starts to climb as testosterone levels increase. The level and rate of PSA increase depends very much on how quickly the testosterone returns, and that varies

greatly from man to man depending on many factors including age, and the duration of hormone therapy; younger men often see a faster return. The time off hormones may last a few months to a couple of years or more in some men.

Clearly knowing your baseline PSA is important, as is regular monitoring of your PSA.

The most appropriate interval for PSA testing will depend on your circumstances, but does not need to be more often than once a month. For most men quarterly tests are sufficient although your doctor may indicate monthly tests. While you should receive reminders from your health care provider, make a note of your test dates in your own calendar.

When your PSA returns to a pre-determined number (Table 5) the medication is restarted for another 9–12 months. This on and off cycle is continued for as long as the PSA responds, signifying the cancer appears to be under control. The main reasons for intermittent rather than continuous treatment include:

- Improved quality of life for the patient—shorter medicated spans may avoid many of the side effects, especially the ‘quality of life’ responses like fatigue, loss of libido, and hot flushes.
- Reduced risk of medical co-morbidities (side effects)
- The theoretical possibility of an extended life for the hormone therapy drugs—in most men the drugs lose their effectiveness over a period of time. There are many reasons for this but essentially the prostate cancer cells want to survive and figure a way to sustain themselves without external sources of testosterone.

Intermittent hormone therapy may not be appropriate in all situations. Your health care provider can discuss with you whether or not intermittent therapy is recommended for you.

If your PSA when starting hormone therapy is:	You will restart hormone therapy when your PSA is approximately:	Example:
Less than or equal to 10	50% of your starting PSA	If your starting PSA is 6, then treatment would be restarted when the PSA climbs back up to 3.
Greater than 10	Between 5 and 10	If your starting PSA is 16, then treatment would be restarted when the PSA is between 5 and 10.

Table 5: UCSF guidelines for when to restart hormonal therapy on intermittent androgen deprivation.

Side Effects of Hormonal Therapy and How to Deal With Them

The majority of side effects from hormone therapy are related to decreased levels of testosterone. The top three most commonly reported side effects are fatigue, hot flashes, and sexual changes including decreased libido and diminished erectile functioning.

Many of the side effects discussed are experienced over time. Men treated for 8 months or fewer are far less likely to experience many of the issues listed below, although some, like hot flashes and sexual side effects, manifest within the first four to six weeks. Most of these side effects are usually temporary and reversible; they will usually diminish or disappear when the therapy is stopped.

Perhaps the most important thing to keep in mind when undertaking hormone therapy and coping with its effects is: **BE ACTIVE!** And be active in **all** areas of your life—Physically (with exercise, active sports, household chores); Intellectually (with games, stimulating reading, discussion groups, general problem solving); Socially (seeing friends, going to meetings, getting out with loved ones); Sexually (work with your partner and seek out sexual stimulation, even if you are significantly affected by a loss of sexual interest and inability to have an erection). This may be hard to do for those men who do experience serious energy loss, or difficulty concentrating, or greatly lessened sexual interest. But try to push yourself as much as you can, and enlist the help of loved ones, friends, and other supports to keep going.

It is important to remember that not all men will experience all side effects. There is also a large variation from man to man in their severity.

Lifestyle

- **Hot flashes**—are common and vary greatly in frequency, intensity and duration among individuals. They are often the first to present and some men find them less bothersome over time.

Remedy: Hot flashes can be treated with different medications like venlafaxine or megestrol (Effexor® & Megace® respectively), but most men tolerate them well enough to find treatment unnecessary. There is some evidence that suggest that decreasing alcohol and caffeine intake may help.

- **Decrease in libido**—The large majority of men on hormone therapy experience some decrease in sexual desire and erectile dysfunction, from minimal to almost total. For men who are recovering their sexual function after surgery or radiation this can be dismaying but there is a significant difference; while ED from such treatments is often a result of nerve and blood vessel trauma, loss of testosterone reduces libido rather than the physical ability to perform. It may also take some months to impact, and some 10% of men do not experience significant decline.

Remedy: Working cooperatively with your partner to accommodate the changes resulting from hormone therapy can help you remain sexually active. The old saying, “Use it or lose it!” very much applies here. The lessened interest in sex may lead to a man avoiding sexual activity; in such cases, use whatever helps arouse and maintain your sexual interest. Pick up a copy of *Your Health Matters: Managing Impotence—A Patient Guide* for a complete and thorough discussion. www.urology.ucsf.edu/patientGuides/pdf/Manage_Impotence.pdf

- **Depression, mood changes, anxiety and irritability**—low testosterone does impact brain chemistry and may result in being “more emotional”. For men who have never experienced depression this can be traumatic, but bear in mind it is largely a chemical rather than a social or psychological response to your illness.

Remedy: Depending on severity, there are many anti-depressant and anti-anxiety drugs. They work in different way for each person so it may take more than one try to find the drug that works best for you...don't give up. For some men, exercise can be a practical and easy access solution; it is known to stimulate the brain chemistry to produce some of the enzymes that may be lacking. Seek out counseling and support groups, both of which can be very helpful, and ask those around you to be tolerant.

Physical

- **Fatigue**—Fatigue can be caused by low testosterone levels. Other causes include anemia caused by a reduction in red blood cells as a result of very low testosterone levels. Fatigue can also result from loss of muscle mass as well as loss of brain function from low testosterone. Again, there is a great deal of variability among men as to how fatigue is experienced.

Remedy: Regular physical activity and exercise! This is not only critical in dealing with these side effects, but is also very important in developing a feeling of well-being, reducing depression, maintaining an effective diet, and reducing the risk of cardiovascular disease. Just walking for half an hour three times a week can provide some positive benefit. Pick up a copy of *Your Health Matters: Cancer and Exercise*, and if you are a UCSF patient make an appointment with the Exercise Counselor (see *UCSF Resources*).

- **Reduced muscle mass, and/or weight gain**—loss of testosterone results in a slower metabolism as well as less androgens to feed muscle mass. Weight gain is often around the belly.

Remedy: Regular physical activity and exercise! This is not only critical in dealing with these side effects, but is also very important in developing a feeling of well-being, reducing depression, and reducing the risk of cardiovascular disease. Just walking for half an hour three times a week can provide some positive benefit. Pick up a copy of *Your Health Matters: Cancer and Exercise*, and if you are a UCSF patient, make an appointment with the Exercise Counselor (see *UCSF Resources*).

- **Breast enlargement**—also known as gynecomastia along with nipple tenderness &/or sensitivity caused by a hormone imbalance that results in a more dominant role for estrogen in a man's body. It is more associated with anti-androgen drugs than with the LHRH medications.

Remedy: Regular weight resistant chest exercises are recommended—start light with two or three sets of 8–12 reps three times a week; if you have never lifted before, be sure to seek supervision initially. A single dose of radiation to the breasts at the start of treatment can also be preventative.

- **Increased appetite**—many men find increased appetite is an immediate response to the LHRH agonists. This only increases the tendency to put on weight mentioned above.

Remedy: If you have not already done so, changing to a prostate healthy diet is essential—in one sentence, that means reducing your intake of animal protein; for more detail see the sister *Your Health Matters: Prostate Cancer and Nutrition* www.urology.ucsf.edu/patientGuides/pdf/uroOnc/Nutrition_Prostate.pdf. When hungry, keep healthy snacks around to munch—carrots and celery work well. Exercise is always helpful too.

- **Brain Functions**—extended hormone treatment may result in a loss of concentration, clarity of thought and memory; this side effect is comparable to ‘chemo brain’, and attributable to a combination of fatigue, anemia and depression all of which may be associated with hormone therapy.

Remedy: Keep your brain active during treatment! If you are not actively employed, then use your brain with word games, card games online, Sudoku puzzles or similar brainteasers. Making lists, writing reminders and alarm reminders can all help. Exercise is definitely a brain stimulus too promoting the production of certain brain enzymes that counter these side effects.

- **Hair Loss & Gain**—Loss of testosterone results in loss of body hair over time. Men on shorter treatments may see little difference but longer treatments lead to loss of hair on your arms, legs, underarms and genital area; facial hair may grow more slowly too. Conversely, hair on your head grows in thicker.

Remedy: No practical solutions to this one, but growth restarts as you rebuild testosterone ... as does hair loss on your head!

- **Genital Shrinkage**—some men may experience shrinkage of their penis or testicles caused by reduced testosterone.

Remedy: If this distresses you and/ or your partner, counsel with your physician and consider counseling. Pick up a copy of *Your Health Matters: Managing Impotence—A Patient Guide* www.urology.ucsf.edu/patientGuides/pdf/Manage_Impotence.pdf for a complete and thorough discussion.

Medical

- **Bone Loss/ Osteoporosis**—Osteoporosis is a thinning of the bones caused by a loss of calcium that is a direct effect of lowered testosterone. Men who are on hormone therapy for more than 12 months, are older or smokers are at much higher risk for developing this condition. Osteoporosis is diagnosed by a bone density imaging (DEXA) test. If you expect to be on hormone therapy for longer than 12 months, consult with your physician about having a bone density test to establish your baseline bone mineral density prior to starting on long-term hormone therapy. A follow-up test should be done at least every two years.

Remedy: A class of medications called bisphosphonates can effectively treat or even reverse osteoporosis, if a significant reduction in bone density is found. An oral medication, such as Fosamax®, is taken once a week, while medications such as zoledronic acid (Zometa®) infusion are given every 3-6 weeks or at longer intervals. A recently approved medicine, denomusab, is

injected subcutaneously, and is less traumatic on the kidneys than infused medication. If you are prescribed either zoledronic acid or denosumab, you will likely also be placed on Calcium supplements and Vitamin D supplements. Periodic monitoring of calcium, phosphate, and for Zometa®, kidney function with a creatinine blood test will be undertaken.

Vitamin D3 should be monitored periodically; before each shot if you are receiving LHRH at 3–6 month intervals. Your doctor may recommend supplements according to your levels. Regular weight-bearing exercise is recommended, and in particular weight resistance exercise at least three times weekly. If you have not lifted weights before, supervision is strongly advised initially. Pick up a copy of *Your Health Matters: Cancer and Exercise*, and if you are a UCSF patient make an appointment with the Exercise Counselor (see UCSF Resources).

- **Anemia**—while generally quite mild, longer term hormone therapy may result in a reduction of your red blood cells. This can contribute to fatigue, but is unlikely to occur within the first 12 months.

Remedy: Iron supplements may, but are unlikely to help since iron deficiency is not the cause.

- **Abnormal liver function**—Very rarely, in less than 5% of patients the oral anti-androgens can irritate the liver, resulting in an increase in “liver function tests”. This typically happens early on in the use of anti-androgens, but can happen after years of use with no side effects. Blood tests evaluating liver function are simple to do, and should be done after the first month of therapy, and every 3 months thereafter. Typically, these test abnormalities are detected long before there are any symptoms, and discontinuation of the medicine almost always results in normalization of the liver tests. Switching to another anti-androgen is often successful.

Remedy: Ask your doctor to check your liver functions (ALT & AST) every 3 months. Reduce alcohol and acetaminophen (such as Tylenol) intake, and discuss alternative hormone medications with your physician.

- **Diarrhea** caused by anti-androgens, primarily flutamide—again relatively less frequent.

Remedy: This is occasionally severe enough to require discontinuing the medication. Sometimes, switching to another anti-androgen can alleviate the problem.

- **Elevated blood pressure**—anxiety from your diagnosis may increase your blood pressure, and hormone therapy can also raise it.

Remedy: Monitor your blood pressure for the first few weeks after starting hormone therapy. If it increases and/or remains high, consult with your physician. There are several blood pressure medicines that can be taken alone or in combination.

- **Cardiovascular disease**—Recent analyses have shown that hormone therapy may slightly raise the risk of heart attack and stroke. Not surprisingly, that risk appears to be highest for those who already have other risk factors such as such as high blood pressure or high cholesterol. Studies also suggest that high belly fat increases your risk.

Remedy: Make sure you know your cholesterol and blood pressure and that you inform your primary care physician that you are on hormone therapy. There are many excellent statin drugs that can help control your cholesterol. Lifestyle changes in nutrition, exercise and stress management are all within your control; a heart healthy diet, plenty of appropriate exercise and

practicing relaxation technique will all reduce your risk. Make an appointment with a nutrition counselor—at UCSF this is provided free (see *UCSF Resources*) and pick up a copy of *Your Health Matters: Prostate Cancer and Nutrition*; remember, a prostate healthy diet is a heart healthy diet! www.urology.ucsf.edu/patientGuides/pdf/uroOnc/Nutrition_Prostate.pdf

If you know you are high risk before commencing hormone therapy, be sure to discuss this with your physician. Your physician as well as the UCSF Cancer Resource Center can make helpful suggestions.

- **Diabetes**—Lack of testosterone is known to increase blood sugar levels. If you are diabetic this may require some adjustment to how you manage your disease; if you are not diabetic, be aware your blood sugar may increase.

Remedy: If diabetic, be sure to consult with your primary care physician or specialist to determine if you need to adjust your disease management. If not diabetic, monitor your blood sugar levels by testing every 3 months when you get your hormone shot. For everyone, exercise and a healthy diet with whole grains and fiber help control your sugar and glucose levels.

- **Erectile Dysfunction**—Hormone therapy reduces libido and induces ED but not through impact on the erectile nerves. Nonetheless, hormone therapy is usually used in conjunction with other treatments that may impair the nerves causing ED.

Remedy: ED drugs such as Viagra, Cialis and Levitra do not work as well for hormone therapy. Other solutions such as penile injections, pump, and prosthesis may be appropriate; consult with your physician. Pick up a copy of UCSF Health Matters Pamphlet, *Managing Impotence—A Patient Guide* (www.urology.ucsf.edu/patientGuides/pdf/Manage_Impotence.pdf) for a complete and thorough discussion.

Your local prostate cancer support group can be an excellent source for information and psychological support in addressing the side effects of hormone therapy. UsTOO (www.ustoo.org), American Cancer Society Man-to-Man (www.cancer.org), and the California Prostate Cancer Coalition (www.prostatecalif.org) will guide you to your local support group.

Other Considerations

Hormone therapy has a finite life for most men. Sooner or later the hormone therapy will probably stop working—for some men that can take 10, 15 or even 20 years or even longer; for others it can happen within a matter of months. Much current prostate cancer research is focused on discovering why this happens and on new treatments for advanced prostate cancer. There are several exciting new developments with many more in the pipeline of clinical trials.

Indications that this may be happening:

- Continuous hormone therapy—The continued rise of the PSA while you are on the hormone therapy and if testosterone levels remain low, is the main indicator of declining effectiveness.

- Intermittent hormone therapy—Potential indicators that the treatment is becoming less effective are: it takes longer for the PSA to get down to undetectable when the hormone therapy is restarted; the PSA no longer gets down to undetectable at its lowest point; or, PSA rises quicker when medication is ceased, so the duration of the ‘off’ cycle is shorter.

Should the hormone therapy be stopped at this point?

Not necessarily. The conversion of the cancer to a hormone independent form is usually a more gradual process, and some of the cancer will continue to respond to the standard treatment. In general LHRH agonists are not stopped.

There are a large number of therapies for patients with prostate cancer that is growing despite low testosterone levels. UCSF is a leading center for these and other therapies. Your doctor can discuss these with you.

UCSF Resources

If you are a UCSF patient, there are excellent resources available.

Familiarize yourself with the UCSF Ida Friend Cancer Resource Center (CRC) (415-885-3693) located on the lobby level at UCSF Mount Zion Cancer Center at 1600 Divisadero. CRC has many excellent programs, lectures, and a place to sit if waiting for treatment. It boasts an excellent library as well as a good selection of many pamphlets in the UCSF Health Matters series. You can sign up for their monthly e-mail newsletter to keep you informed.

Two excellent programs are worth singling out. As a UCSF patient you can receive a free one-on-one nutrition counseling session; speak to your doctor or nurse practitioner to make an appointment with our dietician. There are also excellent and informative monthly lectures on Nutrition and Prostate Cancer open to all patients and their families; the CRC will provide you with the dates. Similarly as a UCSF patient you can see an exercise counselor who can assess your exercise capacity, help formulate a program, direct you to classes and follow up with your progress; call 415-514-6430 to make your appointment.

The UCSF Symptom Management Service is available to help you manage many of the side effects you may encounter. They have programs to assist with pain management, stress management and much more. Speak to your doctor or nurse practitioner for a referral.

Glossary of Terms

Adrenal Glands: A pair of glands located near the kidneys that are responsible for producing multiple steroids and hormones, including testosterone.

Androgens: Hormones associated with male physical and sexual characteristics. The principal androgen is testosterone; the principal female hormone is estrogen.

Anti-Androgens: A class of drugs that blocks the uptake of testosterone by the cancer cell.

Bone Scan: A bone scan is a radiological test used to look for cancer in the bones

BPH: Benign prostate hyperplasia or an enlargement of the prostate is neither cancerous or necessarily a precursor to prostate cancer. It can however have similar side effects, like an increase in PSA and/or difficulties in urinating. The 5-Alpha reductase drugs (*Table 3*) are used to treat BPH.

Brachytherapy: A treatment where radioactive material is inserted into &/or near the prostate.

CT Scan: The Computed Tomography Scan, also known as CATscan, is a test used to look for cancer in the lymph nodes and organs.

Erection: The state of the penis when it becomes engorged with blood resulting in a firm erect position.

External Beam Radiation: The use of high-energy x-rays or heavy particles (protons) aimed from outside the body to treat a cancer.

Gleason Grade & Score: This a grading system to determine the aggressive level of a man's prostate cancer. Biopsy samples are examined under a microscope by the pathologist. The largest and second largest concentrations are graded on a rank of 1–5 based on how variant the cells appear to normal cells; the two numbers are then added together. Low grades of 1 & 2 are rarely used.

GnRH Agonists (also called LHRH agonists): Gonadotropin releasing hormone agonists stimulate the hypothalamus to shut down the production of testosterone by the testes.

Hypothalamus: A regulatory center located in the brain. One of its functions is to secrete hormones as part of a cascade of events that ultimately results in the production of testosterone.

Locally Advanced Prostate Cancer: The cancer is outside, or suspected to be outside, the prostate gland but still in the neighborhood of the prostate; seminal vesicles and/ or local lymph nodes may be involved.

Libido: The desire for sexual activity.

Lymph Nodes or Glands: Small, bean shaped collections of tissue located along the channels of the lymphatic system that may trap infectious organisms or cancer cells. Those closest to the prostate capsule are located in the groin and if involved with cancer, suggest the cancer has metastasized.

Metastatic Disease: The process by which cancer cells are transported from an original site of disease to a new location where a similar cancerous lesion develops.

MRI: MRI is an abbreviation for "magnetic resonance imaging." This technology allows a detailed image to be created of the internal parts of the human body. An MRI machine uses a strong magnetic force and sophisticated software to create a picture of the body part in question, in this case the prostate.

MRSI: Magnetic Resonance Spectroscopy Imaging is an MRI test using an endorectal probe analyzing chemical composition to determine the presence of cancer. It can be used to assess metabolic activity in the prostate, further defining the degree of cancer.

Orchiectomy: The surgical removal of the testicles.

Pituitary Gland: A gland that exerts a controlling or regulatory influence on other glands, such as the adrenal gland.

Prostate: A muscular and glandular body that surrounds the male urethra and produces fluid that combines with semen to form the ejaculate.

PSA: Prostate specific antigen is a substance produced by all prostate cells whether healthy or diseased; it is measured with a simple blood test. For men diagnosed with prostate cancer, PSA can be used as a cancer marker to determine the success of treatment. Higher PSA levels may suggest the existence of more prostate cells; for diagnosed men these are usually assumed to be cancerous cells.

Radical Prostatectomy: The surgical removal of the prostate gland.

Serologic Progression: The state of having a rising PSA after prostatectomy and/or radiation, but no metastatic disease on scans

Testicles: Two bodies of glandular tissue that reside in the scrotum and produce testosterone and sperm.

Testosterone: A male hormone produced by the testicles that is responsible for inducing and maintaining male secondary sex characteristics. The adrenal glands also produce a small amount of testosterone in both males and females.

Prepared by UCSF Health Care Professionals and Advocates

Notes:
