HORMONE BALANCE

FOR MEN

What Your Doctor
May *Not* Tell You
About Prostate Health
and Natural Hormone
Supplementation

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INTRODUCTION

The first thing that must be said about male hormone balance is that we don't know nearly as much about it as we do women's hormone balance. Information coming from both conventional and alternative medicine is fraught with misunderstandings and misinterpretations of how male hormones work, and how prostate problems occur. There is little good clinical information available about treating men with bio-identical (i.e. natural) hormones, because so few clinicians truly understand how to give physiologic doses (the same as a healthy body would make), and how to create balance.

This booklet is also not meant to be an exhaustive look at all of the drugs and other treatments related to prostate enlargement and prostate cancer. It is an overall look at how male hormones and biochemistry work, how problems are created in the prostate gland, and what might be done to treat them. In general, this is an explanation of my theory of how the proper use of supplemental hormones in men can create optimal health, and conversely, how hormone imbalances can create ill health and disease.

At the heart of the misunderstandings about male hormones is the work done by Charles Huggins, M.D., a surgeon who, back in 1941, observed that surgical castration in a few men with prostate cancer seemed to improve their survival a bit, compared to non-castrated men. In another study involving eight men with advanced prostate cancer with metastases, he observed that, after the men received bull-derived testosterone, serum alkaline phosphatase levels rose a bit in three of them. From this alone, Dr. Huggins concluded that testosterone increased growth of prostate cancer metastases.

Dr. Huggins went on to other surgical ablation research ventures including surgical removal of ovaries and of the adrenal glands, all without much success. Eventually, in 1963, Dr. Huggins was awarded the Nobel Prize, at which time he recapped his claim that testosterone caused prostate cancer. Despite forty years of testosterone treatment failure and mounting evidence that estradiol dominance and testosterone depletion are important factors in causing prostate cancer, most physicians still cling to Dr. Huggins' mindset that it is testosterone that stimulates prostate cancer. It is time to move on. Dr. Huggins was an adventurous researcher and may have deserved some sort of award, but his notions regarding testosterone were wrong. For science to advance, clear thinking is required. Calling castration "androgen suppression" is not clear thinking, when estrogen and progesterone suppression are also involved. But more about that later.

The bottom line is that we're still in an era of experimentation with regard to creating natural hormone balance in men and treating prostate problems. We know a lot, but there may be subtleties in treatment and individual variations in biochemistry that require approaches that we haven't recognized yet. This makes it important for men using supplemental hormones to take full responsibility for any hormone treatment: to become as educated as possible; to keep up with research on the subject; to track symptoms carefully; to get regular saliva hormone level tests; and if at all possible to work with a health care professional who can help with all of the above.

CHAPTER 1

The Mechanics of Male Hormones

The anatomy and biochemistry of the human male is simultaneously robust and delicate; men can maintain the ability to manufacture sperm, get erections and father children throughout their lives. At the same time, a slight enlargement of the prostate gland in the wrong spot can wreak havoc with the entire system.

The prostate gland is chestnut-sized, sitting below the bladder and above the root of the penis (see diagrams). The urethra, which carries urine out of the body, on exiting the bladder, passes through the center of the prostate gland before passing through the length of the penis. The "back" or posterior side of the prostate gland can be easily palpated by a finger placed in the rectum. There is a sphincter, or valve, at the top of the prostate, and another at the base. These sphincters control urine flow. When urinating, both sphincters open. When ejaculating , the top sphincter closes and only the bottom sphincter opens. Certain drugs, such as some antidepressants, glaucoma drugs, and belladonna-type drugs confuse the action of the sphincters, sometimes causing semen to be ejaculated upwards into the bladder. Stress and diabetes also can cause inappropriate sphincter action.

The prostate gland contains bundles of tubules that secrete fluid (semen) for carrying sperm for ejaculation. The sperm arrive from the testes (testicles) and are stored in two seminal vesicles attached near the base of the prostate gland. Each ejaculation may use about 50 percent of the sperm stored in the seminal vesicles. The fluid made by the prostate gland comprises about 30 percent of the semen. Each ejaculation contains 300,000 to 400,000 sperm.

Sperm is produced more or less continually by the Sertoli cells of the testes, an action that is mediated by two pituitary (a gland in the brain) hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH). Sperm collect in the epididymis for maturation, and then are carried up to the seminal vesicles to await future ejaculation. The movement of the sperm to the seminal vesicles is passive, meaning that it is moved by tiny hair-like cilia within a tube known as the vas deferens, to spare the limited supply of fuel each sperm carries.

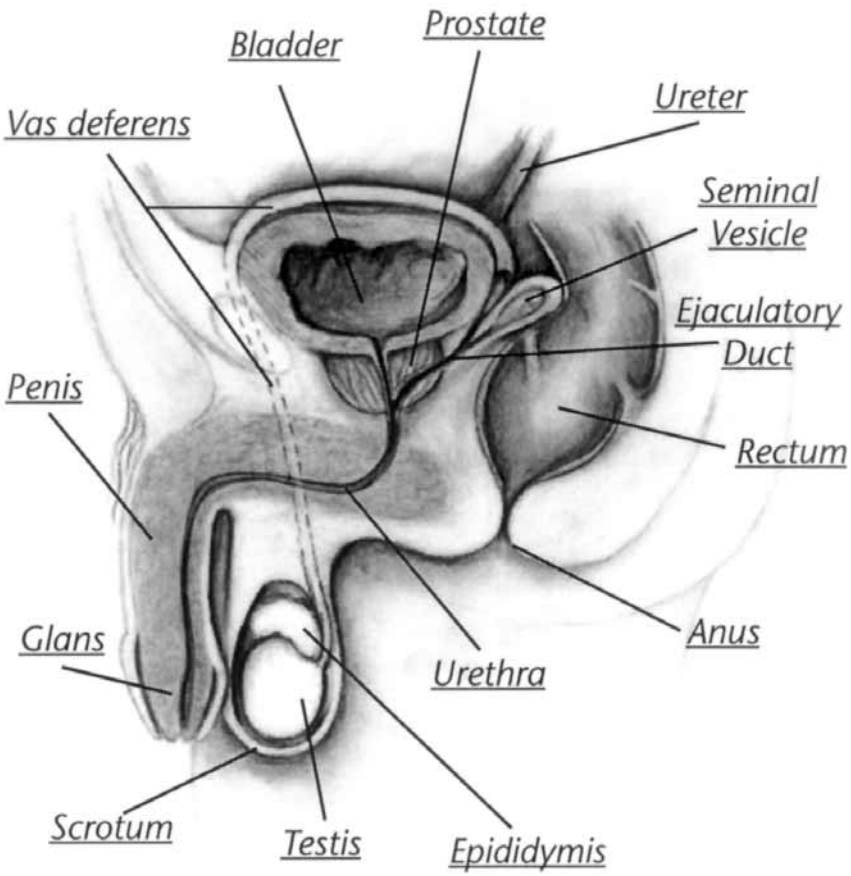
Their work starts after ejaculation, as they travel through the vagina, past the cervix, up through the uterus and out along the Fallopian tubes to their possible rendezvous with an ovum. Each is

propelled by the whipping action of its flagellum or tail. Their path is random and, innately, they pull away when they bump into anything. The outer coat of the ovum is thick and sticky, so that when sperm bump into it, they become entrapped. Sooner or later, the ovum coat opens and accepts one sperm, after which all the others fall away.

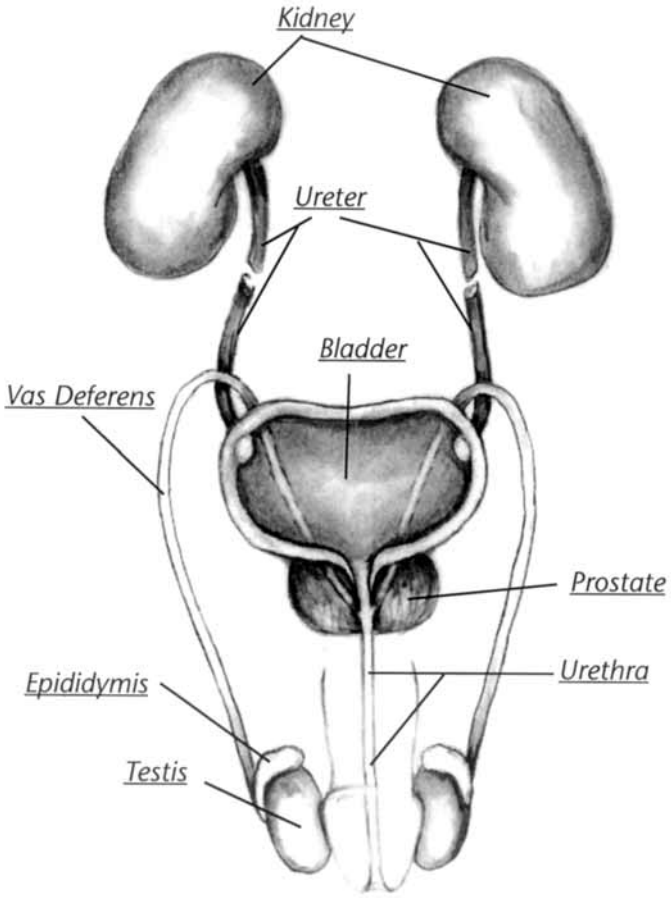
The ovum quickly destroys the sperm except for its 23 single strands of DNA, which are saved to become aligned with the ovum's DNA strands, making a full complement of DNA for the now-fertilized ovum. All ova carry the X chromosome. The sperm carrying an X chromosome creates females, and the sperm carrying the Y chromosome creates males.

The metabolic actions of the prostate gland are determined in large part by hormones, especially estradiol, progesterone, and testosterone, which are made by the testes. These, in turn, are mediated by pituitary hormones, especially FSH and LH, just as ovarian function in women is. Both the prostate gland and the uterus develop from the same embryonic cells, and both respond to the same hormones—estradiol, progesterone, and testosterone. In the same manner, both the ovaries and the testes develop from the same embryonic cells. A fertilized ovum with XX chromosomes develops ovaries and an uterus, while the fertilized ovum with XY chromosomes develops testes and a prostate gland.

Side View of Reproductive System



Front View of Urinary & Reproductive System Pathways



CHAPTER 2

The Mechanics of Prostate Enlargement and Prostate Cancer

The prostate gland participates in many of the mechanics of discharging urine as well as creating and discharging semen. It is very sensitive to the effects, both good and bad, of the sex hormones. One of the most common problems experienced by aging men is prostate enlargement. Whether or not prostate enlargement has an effect on urination and ejaculation depends more on where the enlargement is than how big it is.

Prostate Enlargement or BPH

If you're a man over the age of 50 who's not sleeping well, chances are good it's because you've got prostate problems that require visits to the bathroom a couple of times a night. It's estimated that benign prostate disease affects over 40 percent of American men by age 50 and over 70 percent by age 60. The most common symptom is trouble with urination. Such men may have increased urinary frequency (hence getting up at night), their urine flow may be decreased in force or rate, they may have urinary urgency, and they may feel that they haven't emptied the bladder (a sign of urinary retention), especially after drinking coffee. Urinary retention also makes them more susceptible to urinary tract infections.

When such men consult with their doctor, he will usually examine the prostate gland through the rectum (a digital exam) and diagnose the problem as BPH, an acronym meaning benign prostate hypertrophy (enlarged cells in the prostate gland) or hyperplasia (enlarged by an increase in the number of cells in the gland). The two meanings of BPH are used interchangeably. BPH, like most conditions, varies in how it manifests itself. In some men, the obstruction of urine flow is due to prostate tissue overgrowth and the gland will be definitely enlarged. In others, however, the obstruction is due to smooth muscle contraction of the urinary sphincters in the prostate gland, causing the same urinary problems without much prostate enlargement. In some men, the problem is mixed. Since either or both of these two conditions (cell proliferation or urethral constriction) lead to the same or similar urination problems, it is sometimes difficult to determine which or both of these two problems exists.

In the prostate (and in hair follicles) is an enzyme (5-alpha-reductase) that converts testosterone into dihydrotestosterone (DHT). Higher DHT levels in hair follicles is a primary cause of male pattern

Some Non-Drug Treatments for BPH

Certain botanicals have been found to be of benefit in treating prostate disease, though their mechanisms of action are still unclear. These botanicals, and a few others like them, deserve further research. Many products for the prostate found at health food stores contain various combinations of these ingredients.

- Saw Palmetto berry extract: Studies indicate that it inhibits 5-alpha-reductase and it may block DHT from binding to prostatic androgen receptors; reduces prostatic edema (swelling), inhibits estradiol and antagonizes alpha-adrenergic receptors.
- Nettle root: May inhibit aromatase, reducing conversion of androgens to estrogen.
- Antioxidants, such as vitamin E, lycopene (found in cooked tomatoes), and vitamin C.
- Polyphenols (e.g., catechins, found in green tea.)
- Ellagic acid (found in nuts and raspberries) may trigger beneficial apoptosis.
- Zinc (low zinc levels correlate with increased prostate disease). Be sure to get extra copper if you're taking zinc for longer than a few weeks.

baldness. DHT stimulates proliferation of prostate cells, more so than testosterone does, enlarging the prostate gland and narrowing the urethral channel, leading to urination problems. Further, has been speculated that elevated DHT is the cause of prostate cancer.

Inhibiting this conversion of testosterone to DHT is often a treatment goal for men with BPH. While there are pharmaceutical drugs to inhibit 5-alpha-reductase (e.g., Proscar, finisteride), it is better to use saw palmetto berry extract or progesterone, both of which inhibit 5 alpha-reductase and are safer than the pharmaceutical drugs.

In BPH where obstruction is due to smooth muscle contraction of the urinary sphincters, conventional medicine often uses drugs such as alpha-1-selective adrenoreceptor blocking agents (e.g., Hytrin, terazosin hydrochloride) which are also used for treating hypertension. The problem with these drugs is that the dose necessary to relax the urethral sphincter muscles is sometimes high enough to cause hypotension (low blood pressure) and fainting (syncope).

Another conventional medical treatment for BPH is transurethral resection of the prostate (TURP), the surgical coring-out of the urine passageway through the prostate, quite often resulting in undesirable dribbling problems.

Finasteride and Prostate Problems

Finasteride is a synthetic compound that inhibits the enzyme 5α-reductase, thus inhibiting the conversion of testosterone to dihydrotestosterone (DHT). It is marketed as Propecia for male pattern baldness in doses of 1 mg per day, and as Proscar in doses of 5 mg per day for the purpose of reducing the levels of DHT, thus reducing prostate enlargement. It has been found to reduce prostate size and urinary retention.

Since conventional wisdom implicates androgens in prostate cancer, it is not surprising that a Prostate Cancer Prevention Trial (PSPT) was initiated in the early 1990s to test the hypothesis that finasteride might prevent prostate cancer. The seven-year trial involved more than 18,000 men aged 55 or over, randomly assigned to

finasteride 5 mg per day or placebo, and was published in the July 17th, 2003, issue of the *New England Journal of Medicine*. The men were monitored annually with a PSA test (more about that shortly) and a digital (rectal) prostate exam. If the PSA level rose above 4.0 ng per ml or if the digital exam was abnormal, a prostate biopsy was done. At the end of the trial all men without previous biopsy were biopsied.

The results were certainly interesting. The lifetime risk of diagnosed prostate cancer in men in the U.S. is estimated to be 16.7 percent. (The risk of death from prostate cancer is 3.6 percent; this amounts to 28,900 expected prostate cancer deaths in 2003). In this trial, prostate cancer was detected in 18.4 percent in the finasteride group, and 24.4 percent in the placebo group, indicating a 28 percent reduction in prevalence over the seven-year period. Likewise, there was a difference in median prostate volume of 25.5 cm3 in the finasteride group and 33.6 cm3 in the placebo group.

Initially this looks like a slam dunk in favor of finasteride. But such is not the case. The lower rate of prostate cancer diagnosis in the finasteride group is deceiving. Most of them were small localized lesions that probably had no clinical significance. More important, the rate of high-grade cancers (6.5 percent) in the finasteride group was actually higher than that (5.1 percent) in the placebo group. Editorialist Peter T. Scardino, M.D., speculates that finasteride, in reducing prostate hyperplasia, might reduce PSA levels, thus delaying diagnosis. Thus, finasteride is not recommended for prevention of prostate cancer.

What about relief of urinary symptoms? Yes, finasteride did that, but at the expense of more problems of sexual dysfunction. No points gained for finasteride.

What I find interesting is that nowhere in the "comments" section of the study did either the authors or the editorialist consider alternatives such as saw palmetto berry extract, lycopene, or hormone balancing with progesterone and testosterone. Both saw palmetto berry extract and progesterone inhibit 5α-reductase and reduce symptoms of benign prostate hyperplasia just as well as finasteride. Neither did the authors or editorialist consider the fact that androgen blockade is essentially ineffective against prostate cancer, or that prostate cancer occurs more often in men with low testosterone than in men with higher testosterone levels. It is simple laziness to state that the higher incidence of prostate cancer in older men is due to aging. Cancer, like any other disease, must have a metabolic cause.

How does conventional medicine ignore the fact that, at the age of highest testosterone levels (age 18 or so), prostate cancer rarely, if ever, occurs? Prostate cancer occurs because testosterone and progesterone levels fall with age and estradiol levels rise, leading to estrogen dominance in older men. The same mechanism that causes breast and endometrial cancer in women, causes prostate cancer in men. It is time to set finasteride aside and turn to proper hormone balancing in men as well as in women.

Prostate Cancer

Prostate problems are the fastest-growing health concern among men in Westernized countries, and the rate of prostate cancer is increasing steadily. I believe it is time to reanalyze our underlying hypotheses concerning prostate cancer. The present treatments are based on a war metaphor—find the abnormal cells and obliterate them with radiation or surgical removal, or by drastically reducing hormone levels. Even estrogen is being used to treat prostate cancer! Little thought is given to the underlying metabolic causes

The Underlying Metabolic Imbalances that Lead to Prostate Cancer

GENERAL

- Metabolic acidosis
- Trans-fatty acids
- Lack of essential Omega-3 fatty acids
- Excessive exposure to toxins
- Insufficient daytime sun exposure = Vitamin D deficiency and mitochondrial inhibition
- Thyroid deficiency may underlie many other deficiencies and oxidative damages

SPECIFIC TO PROSTATE CANCER

- Estrogen dominance
- Testosterone deficiency
- Use it or lose it (regular sexual activity is thought to be helpful)
- Zinc deficiency
- Insufficient nighttime sleep = Melatonin deficiency → Estrogen dominance

that change normal cells into cancer cells. As with any disease, once the cause is identified, successful prevention and treatment strategies emerge.

The incidence of prostate cancer increases with age. The majority of men in the U.S. will acquire prostate cancer if they live beyond 65. It is a slow-growing cancer (more rapidly growing in younger men, however). For men over 65, the doubling time of a prostate cancer nodule is usually about 5 years. Compare this with the doubling time of a breast cancer nodule, which is about 3 to 4 months. If left untreated, prostate cancer tends to eventually metastasize to bones.

The initiation of normal cells turning into cancer cells is the same for both the breast or uterus and the prostate gland. In these organs, cancer initiation is due primarily to estrogen dominance combined with lifestyle factors and/or toxic insults that predispose estrogen to become oxidized. In women, the important factor is the ratio between progesterone (P) and estradiol (E2) when measured by saliva testing. A healthy P/E2 ratio in women is 200 to 300 to 1. Cancer of the breast and/or in the uterus most often occurs in women with a P/E2 ratio of less than 200 to 1. According to Dr. David Zava of ZRT, who has amassed a database of tens of thousands of saliva samples and questionnaires, these cancers occur very rarely in women with a healthy P/E2 ratio.

In men, estrogen gradually rises with age, while saliva levels of progesterone and testosterone gradually fall with age. Thus, with aging, estrogen dominance occurs. Estrogen levels are particularly apt to increase in aging men who are overweight because fat cells convert testosterone and androstenedione into estrogens, which then stimulates prostate growth. Thus, the more fat a man carries on his body, the higher his estradiol levels are likely to be. Regular exposure to xenoestrogens such as pesticides by, for example, spraying in the home or garden, only adds to the problem.

Even if a middle-aged man's testosterone levels are normal, if his estradiol levels are high he can have estrogen dominance symptoms such as weight gain, larger-than-normal breasts, gall bladder problems, anxiety and insomnia, and prostate enlargement that leads to urinary problems.

Some research indicates that BPH and prostate cancer correlate with higher levels of sex hormone binding globulin (SHBG). As a result, some have hypothesized that SHBG may play a role in the cause of BPH and of prostate cancer. SHBG is the binding hormone for estradiol. Excessive levels of estradiol activate the liver to make more SHBG. Thus, it is likely that the elevated SHBG is merely a marker for excessive estradiol. Testosterone binds to both SHBG and simple albumin. It is like a hitchhiker who doesn't care whether he catches a ride with a cattle car or rides the rails. The albumin binding is less secure, however, and the testosterone is more likely to become "free" of it. Therefore, serum (or plasma) levels of testosterone tend to run somewhat more parallel to saliva levels than, say, serum and saliva levels of progesterone. However, the only sure method of measuring "free" testosterone is saliva testing.

All disease comes from metabolic imbalance. When the underlying metabolic imbalance is corrected, the disease goes away. If you fail to keep up the correction for the underlying metabolic imbalance (i.e., revert to whatever it was that created the metabolic imbalance in the first place), the disease will come back. This is called preventive medicine. Cancer is no different—it is caused by an underlying metabolic imbalance that turns normal cells into cancer cells.

CHAPTER 3

Estrogen Dominance and Prostate Problems

The mechanism by which estradiol causes breast, uterine, and prostate cancer has been established by researchers such as Ercole Cavalieri, Ph.D., director of the Eppley Institute for Research in Cancer at the University of Nebraska. One of the metabolites or byproducts of estradiol and estrone is a catechol estrogen-3,4-quinone that is a destructive depurinating DNA adduct. What that means is the estrogen-3,4 quinone molecule is destructive to both adenine and guanine, the two purines, which along with the two pyrimidines, cytosine and thymine, make up the four nitrogenous bases of DNA. This destruction of the DNA causes gene mutations that can lead to cancer. Most other estrogen metabolites are generally methylated in the liver and safely excreted.

Professor Cavalieri has discovered that the metabolite's damage to adenine is slow and can be corrected by healthy repair mechanisms, whereas the damage to guanine is rapid and unlikely to be repairable. The mutated gene leads directly to cancer. This mechanism of gene mutations is the primary cause of most cancers of the breast, the endometrium (uterus), and prostate.

Dr. Cavalieri was a major participant in a March 1998 National Cancer Institute symposium in which over 20 speakers from leading cancer research centers around the world reported on their breast cancer and/or prostate cancer research and the role of estrogen. All the evidence implicated estrogen as a major cause of both breast *and* prostate cancer. These reports are available as NCI Monograph #27, from the Oxford University Press (800-852-7323).

As far as nutrition goes, the formation of this destructive metabolite of estradiol and estrone, as found by Dr. Cavalieri, is found most often in people who eat more trans fatty acids (e.g. hydrogenated oils), fewer of the "good" fats (e.g. olive oil, fish oil), and less of the sulfur-containing amino acids (beans, garlic, onions, broccoli, cauliflower, cabbage).

Hormonally, the best protection against this type of gene mutation involves good physiologic levels of both progesterone and testosterone. Stress increases cortisol levels, which will make the body somewhat resistant to using its other hormones, and also increases oxidation, which is at the heart of how the DNA damage is caused by these estrogen metabolites.

Estrogen dominance activates the oncogene Bcl-2, whereas progesterone and testosterone activate the protector gene, p53. In laboratory cultures of breast cancer cells, endometrial cancer cells, and prostate cancer cells, their proliferation is increased by Bcl-2, and prevented by p53. The same mechanism applies to all these types of cancer.

If you'd like a more detailed biochemical description of how estrogens damage DNA, please read my book, *What Your Doctor May Not Tell You About Breast Cancer*.

Two studies published in the *American Journal of Pathology* in 1999 show that estrogen increases prostate cancer, and that progesterone receptors in the prostate are more abundant in cases of more aggressive prostate cancer. Misinterpretation of this type of result is common. Conventional interpretation suggests that this might indicate that progesterone causes the more aggressive breast and prostate cancers. The truth is that progesterone receptors are made by estrogen. The higher the estradiol/progesterone ratio, the greater are the number of progesterone receptors that will emerge. This is the tissue's effort to restore proper progesterone function in situations where estrogen dominance is present. Thus, increase of progesterone receptors is evidence of estrogen dominance, and *not* evidence that progesterone increases the risk of cancer.

There are also some theories that estrogen and testosterone hit the same receptors in the hypothalamus, the area of the brain that regulates hormone level feedback mechanisms. Thus, when estrogen levels are high, the brain may be getting the message that testosterone is high, and actually reducing testosterone production by the testes.

What Causes Estrogen Dominance

The conclusion is that estrogen dominance is responsible for more cancers of the breast, prostate and endometrium than any other cause. Estrogen dominance has many causes but several are more common than others. In men they include insulin resistance, stress, and early (especially embryonic, during early life in the womb) exposure to petrochemical toxins (called xenoestrogens) such as pesticides, emulsifiers, and toxic chemicals that out-gas from certain plastics and adhesives (such as carpeting) that are common in the environment.

Researchers at the National Cancer Institute assessed the relationship between insulin resistance and prostate cancer risk. They found that men with the highest insulin resistance had an increased risk of prostate cancer compared to men with the best insulin sensitivity. When men with the highest tertile of insulin resistance and waist-to-hip ratio were combined, their risk of prostate cancer increased to an odds ratio of 8.21. These associations were independent of total caloric intake, serum levels of insulin-like growth factors, sex hormones and sex hormone binding globulin.

As we know from breast cancer research, insulin resistance leads to estrogen dominance and an increased risk of breast cancer. It seems to be that the same pattern occurs in prostate cancer. If saliva tests had been used more in prostate cancer research, I suspect that the association between insulin resistance, estrogen dominance, and prostate cancer would be apparent.

Progesterone helps by restoring normal inhibition of 5-alpha-reductase, thus preventing testosterone from changing into dihydrotestosterone (DHT), which stimulates proliferation of prostate cells.

Progesterone not only stimulates the action of the cancer-preventive gene, p53, but also maintains testosterone, which is a direct antagonist of estradiol.

You may have noticed that aging men tend to develop breasts. This is a clear sign of estrogen dominance. It is a sign that the man is low in progesterone and testosterone. All studies show that estradiol in men rises gradually with age. Therefore, the ratio of progesterone and testosterone to estradiol falls, producing estrogen dominance.

Damage in the Womb

There are over 70,000 petrochemicals now in our environment, and very few of them have been tested for their toxicity.

The hallmark of these not-found-in-nature compounds is that embryonic cells undergoing differentiation are extremely sensitive to them. This is especially true of developing ovaries and testes in embryos at about day 18 to day 23 of human embryo life. The damage is not detected until later in life, such as middle age. Read *Our Stolen Future*, by Theo Colborn, Ph.D., and her fellow scientists who have demonstrated this toxicity in many forms of wildlife. Humans are part of the same web of nature.

In humans, the damage results in progesterone deficiency and early miscarriages in women by age 30; deficient sperm production in men by age 35, and the increase in both breast cancer and prostate cancer that has become epidemic in industrialized countries.

Causes of Hormone Imbalance

A man's prostate gland is very sensitive to the hormonal changes that occur around middle age (e.g. declining testosterone and progesterone, rising estrogen). The prostate is also very sensitive to inflammation. A Swedish study published in the *Lancet* (June 2, 2001) indicated that fish oils, which help reduce inflammation, can help reduce the risk of prostate cancer. The researchers found that feeding omega-3 oils (found in fish) to animals inhibited prostate cancer. Scientists at the Karolinska Institute in Stockholm decided to see if this applied to humans, and looked at the dietary habits of 3,100 pairs of male twins who had been filling out various health questionnaires for 34 years. They found that men who ate three or four servings of fish a week had half the risk of getting prostate cancer and a third of the risk of dying from it, as compared to men who ate little to no fish. Men who ate one or two servings of fish a week did about half as well as those who ate it frequently.

Omega-3 oils are also good for your brain, your heart and your joints. If you aren't going to be eating fish three or four times a week, consider taking a fish oil supplement if your prostate, brain, heart, and joints seem to be in need of some extra help. I also recommend reading the excellent book *The Omega-3 Connection* (Simon & Schuster 2001) by Harvard Professor Andrew L. Stoll, M.D. Dr. Stoll has had great success treating various forms of depression with omega-3 oils.

Causes of Estrogen Dominance

The following factors may directly or indirectly cause or contribute to estrogen dominance:

- Insulin resistance and obesity (brought about by excess sugars and refined starches)
- Trans fatty acids (as in pastries and highly processed foods)
- Chronic stress (excess cortisol)
- Sleep deprivation
- Working nights under bright lights and trying to sleep in the daytime (the melatonin effect)
- Fluoridated water and toothpaste
- Environmental xenoestrogens
- Cigarette smoking
- Zinc deficiency
- Testosterone deficiency
- Progesterone deficiency
- Sedentary life style
- Cadmium toxicity
- Lack of sulfur-containing amino acids and glutamine
- Lack of good antioxidants
- Lack of good exercise
- Magnesium deficiency
- Liver dysfunction (and the use of drugs that impair liver function)
- Polluted air
- Hypothyroidism
- All of these are correctable. When Israel banned food contaminated with xeno-estrogen (pesticides), the incidence of breast cancer dropped over 15 percent within 6 years. We could do the same (and actually much better) for prostate cancer. Given what is already known, it should be possible to reduce the incidence of prostate cancer by 90 percent.

CHAPTER 4

The Role of Testosterone

Testosterone is our most important anabolic hormone, meaning that it helps cells create energy from the food we eat, builds stronger bones and muscles, and is needed by the brain for normal brain function. Considerable new evidence exists to show that prostate cancer is more likely to occur in men with high estradiol and low testosterone levels. Testosterone is primarily made in the testes, although small amounts are also made in the adrenal glands. Testosterone is responsible for the characteristically male body hair, muscle development and deep voice. From about age 40 on, testosterone levels drop at the rate of about one percent per year.

Although testosterone does play a role in male libido, it isn't just a sex hormone. Maintaining sufficient levels of the hormone can lower LDL cholesterol, triglycerides and fibrinogen, raise HDL cholesterol and human growth hormone (HGH), lower blood pressure, normalize abnormal heart rhythms and angina, improve insulin resistance, build muscle and decrease body fat. Testosterone deficiency is associated with a higher risk of heart disease and depression. There are more testosterone receptors in the heart than in any other muscle in the body. Testosterone also builds bone, improves wound healing, improves oxygen uptake, and improves immune system function.

Excess testosterone can cause acne, headaches, anxiety, irritability and even rage (thus the expression "testy"). Because excess testosterone spills over and becomes estrogen, it can cause water retention, breast enlargement, prostate enlargement, atrophy of the genitals, decrease in libido, and cancer. It's possible that the misconception that testosterone causes prostate cancer has been perpetuated by conventional medicine's routine use of grossly excessive doses of testosterone and the potent synthetic testosterones.

The Testosterone Fiasco

As I mentioned in the introduction, in 1941, Dr. Charles Huggins showed that castration (orchiectomy) slowed the progression of prostate cancer. Castration removes much of one's testosterone production. He unfortunately assumed that the reduction of testosterone levels was the operative agent for his beneficial results. He failed to consider that castration also removes one's estrogen production.

Thus, it is likely that the estrogen reduction was the real operative agent. Despite these faulty assumptions, Dr. Huggins was given the Nobel Prize for his research. As a result, conventional medicine came to believe that testosterone was the culprit in causing prostate cancer. The prevention and treatment of prostate cancer focused on either removing the prostate gland or reducing testosterone, or both. Techniques were found to castrate men surgically or chemically, as in Lupron, for example. Other doctors opted for radiation. In all of these treatments, all sex hormone production by the testes is stopped or arrested, and undesirable side effects are common. The sad fact is that survival of men with prostate cancer has not improved with these treatments. Further drugs (e.g., flutamide) were developed to block all testosterone receptors (called total androgen blockade), thus eliminating the testosterone effect completely. It is now conceded that survival time is not affected; the men so treated instead developed depression, dementia, and diarrhea before dying right on time.

How did this fiasco come about? A number of different factors are involved. Consider the following.

- Dr. Huggins, in 1941, had no good means for establishing the extent or grade of the prostate cancer of his patients. Therefore, it suggests that the patients he chose to undergo orchiectomy may have had earlier or lower grade prostate cancer than the control patients.
- Many of the earlier prostate cancer studies did not measure estrogen or progesterone levels. They often measured only the testosterone levels. It is the balance between progesterone and testosterone with estradiol that is key to the effects of the hormones. The range of so-called normal hormone levels is so broad that estrogen dominance can occur even if all the hormones are still in these “normal” ranges.
- The vast majority of early prostate cancer studies used serum levels instead of saliva levels when measuring hormone levels in men (and women). This is a mistake since serum testing does not discriminate between total “free” and protein-bound hormone. It is the “free” hormone that is bio-active, whereas the protein-bound hormone is not bio-active. Thus, serum tests are generally irrelevant since they can not tell you how much of the “free” hormone is present. This means that the thousands of studies done with serum hormone testing are essentially irrelevant.
- Since the doubling time of prostate cancer growth is quite slow compared to breast cancer, doctors are often seduced into thinking that their treatments are working when, in fact, such patients, who are generally older men, die from other causes rather than from their cancer. During the slow latency period of prostate cancer cell growth, conventional medicine claims to be preventing or, at least, slowing the progression of cancer growth. When metastases eventually develop, this is attributed (without any good evidence) to the cancer becoming insensitive to their treatment of testosterone blockade.
- PSA testing is big business and very profitable to doctors and pharmaceutical companies. The PSA test is used to frighten patients into having expensive treatments, regardless of their futility. Treating patients with androgen blockade is very profitable, also, despite its futility. The income derived from these ventures serves as positive reinforcement for continuing these forms of treatment, despite their futility. The example of Pavlov's dogs comes to mind.

- Pharmaceutical companies are very clever in their advertisements to doctors. When confronted by difficult treatment problems, doctors tend to be overly optimistic and gullible about believing the advertisements.
- Doctors tend to be very busy with other problems in their practice, and have little time or energy to read all the literature themselves. They therefore rely on supposed authorities to tell them what to do. They like to believe in authorities because it saves the time from having to study to seek out the best treatment options.
- Doctors' main avenue of learning (besides visiting "reps" from the pharmaceutical industry) is the CME (Continuing Medical Education) seminars. He/she must attend at least 50 hours of accredited CME seminars every three years. He does not know that accreditation is determined by an AMA panel made up of doctors representing pharmaceutical companies, or that virtually all of the speakers represent pharmaceutical companies. The doctor rarely hears of alternative effective treatments. Pharmaceutical-sponsored seminars are often more convenient and low-cost or free, whereas the unaccredited alternative seminars usually require a little travel and there is a cost for attending.
- Doctors fear the consequences of malpractice. Since the definition of malpractice is deviation from the norm of the local medical community (and not the question of whether one's treatment is good or bad), the doctor seeks protection by doing what other doctors in the community are doing for their patients. This atmosphere of needing protection against malpractice has the effect of extra unnecessary tests and conforming to standard modes of practice.

Therefore, change in medicine is gradual. While it is true that change comes when brave doctors go against the grain to find better modes of practice, each individual doctor is a bit apprehensive about being the non-conforming one to lead the change, regardless of the benefits it might bring to the health of his/her patients.

These factors of conventional medicine are, I believe, delaying true progress in medicine.

Testosterone and Estrogen

The same things that cause breast cancer, cause prostate cancer. It is highly unlikely that testosterone is the cause of prostate cancer. The highest testosterone levels in males are made during one's late teens, at a time when no one gets prostate cancer. Conversely, men's prostate cancer risk rises when their testosterone and progesterone have fallen, and estradiol has risen. How do conventional doctors ignore this fact? One physician thought that perhaps young men have some sort of strength in fighting off cancer, and this strength is lost somehow in older age. To this I suggest that this greater strength in younger men might derive from their good levels of testosterone and progesterone, both of which are our major anabolic (energy-providing) hormones.

Back in the 1950s, when I was in medical school, it was reported by the University of Chicago, as I recall, that researchers trying to create prostate cancer cell skin implants in mice found that pre-treating the mice with testosterone prevented successful implantation. If the cancer cells were implanted and allowed to "take," and then the testosterone was added, the implants stopped growing and failed to

thrive. This is potent evidence that testosterone inhibits prostate cancer cell growth and development. But all this dropped off our radar screens in the rush to castrate men with prostate cancer.

Testosterone is a direct antagonist to estradiol. Women develop full breasts because their estradiol effect is stronger than their testosterone effect. Men make estradiol, but throughout most of the young and middle adult life they make more testosterone, sufficient to block female breast development. Testosterone is the major masculinizing hormone and estradiol is the major feminizing hormone. The ratio of testosterone to estradiol (T/E2) is the major operant factor.

The relationship of estradiol to progesterone is more like Yin and Yang. They are designed to work together by balancing their mutually opposing properties to produce the optimal hormone benefit to both men and women. Unopposed estradiol can be lethal. Progesterone is necessary to prevent potent undesirable side effects of unopposed estradiol. Thus, the ratio of progesterone to estradiol (the P/E2 ratio) is also very important. Optimal protection against estradiol-induced cancer occurs when the saliva progesterone level is 200 to 300 times that of saliva estradiol level.

CHAPTER 5

The PSA Factor

Like breast cancer, very little real progress has been made in the treatment of prostate enlargement and prostate cancer. Yes, there are many new types of treatments available, but aside from surgery to remove a cancer that hasn't metastasized yet, not one treatment has been convincingly shown to significantly prolong life or reduce the numbers of men who are dying of prostate cancer. In fact, the *Journal of the American Medical Association* (*JAMA*) of June 28, 2000, carried an article comparing treatment recommendations by radiation oncologists and urologists for men with moderately well differentiated, localized prostate cancer and greater than a 10-year life expectancy based on age. In such cases, 92 percent of urologists recommended radical prostatectomy (removal of the prostate gland), whereas 72 percent of radiation oncologists recommended radiation treatments. An accompanying editorial points out that the treatment advice is determined by the services the doctor provides rather than by any clear-cut evidence of the superiority of either treatment, or even whether or not either treatment is any better than watchful waiting.

The PSA Count

One of the biggest areas of misunderstanding in prostate cancer has been the PSA count. Prostate specific antigen (PSA) is produced within the prostate gland and within breast tissue. (Therefore the phrase PSA is not correct, since it is not specific to the prostate.) The function of PSA is finally becoming clarified—when abnormal crowding of normal cells in the prostate occurs, the cells produce more PSA, which inhibits angiogenesis of its neighboring cells. Angiogenesis is the growth of blood vessels leading to a cancer tumor. Think of it as developing supply lines to feed an army. Since cancer cells grow more rapidly than normal cells, they tend to crowd against normal cells. One of the hallmarks of cancer cells is that they will induce angiogenesis that will increase the flow of blood to them. The anti-angiogenesis function of PSA is a defense against abnormally growing cells in the prostate. Firm massage of normal prostate cells will increase PSA levels in the prostate. Thus, PSA is a marker for increased crowding of normal prostate cells.

Unfortunately, conventional medicine uses PSA levels as a marker for prostate cancer. However, most "occult" prostate cancer occurs without elevating the PSA level. Some people even think that PSA elevation is bad and should be reduced. An example is the company that produced a drug called PCSpes which inhibits PSA production and causes breast development. In the past, I have challenged that company to produce evidence that using the drug will lower the mortality or extend the survival of men using the drug. No such evidence exists, to my knowledge. This is an example of blaming the messenger rather than understanding the message. Recently PCSpes, supposedly an herbal product, was found to contain a mixture of pharmaceutical drugs and was taken off the market.

Conventional doctors often use PSA levels to determine treatment options. The facts are that prostate cancer patients in countries who have abandoned PSA tests have the same or better survival rates as countries that use PSA tests. In Sweden, for example, physicians rarely screen for prostate cancer or use radical therapies, choosing watchful waiting instead. Despite this, mortality rates for prostate cancer have declined in Sweden. In the U.K., prostate cancer mortality rates are similar to the U.S. even though PSA screening is not routinely performed. In older men, when most prostate cancer occurs, the cancer is slow-growing and early intervention may be of little consequence. An interesting study by researchers in British Columbia examined the relation between changes in prostate cancer incidence (equivalent to PSA screening) and subsequent changes in mortality in regions using common treatment recommendations. They found no association between the intensity of PSA screening and subsequent decreases in prostate cancer mortality.

Further, good references show that men early in the course of their prostate cancer generally have low testosterone levels and little or no elevation of PSA.

As men age, their testosterone and progesterone levels fall. These are the two hormones known to be anabolic—meaning that they produce energy, rather than using up energy, such as estrogen and insulin do. With the fall of testosterone and progesterone, cellular energy wanes. Only the cancer cell, with its ability to create angiogenesis, retains its high energy. When a testosterone-deficient man has his testosterone restored, normal cells then have more energy and, thus, can produce more PSA. This is why PSA tends to rise a bit when testosterone is restored. The PSA is a defense factor and the increased PSA inhibits angiogenesis of the cancer cells. If one's PSA rises a bit after the testosterone is brought up to normal physiological levels of a younger man, it is not a sign that the cancer is growing, but, instead, is a sign that the normal cells have become stronger in fighting against the cancer cells.

Maintaining good levels of both progesterone and testosterone should be the goal of men for preventing, and for treating, prostate cancer.

CHAPTER 6

Restoring Hormone Balance

The crux of the present confusion about men's hormones is the matter of achieving hormone balance. Hormone balance refers not to absolute concentrations of any given hormone, but to the ratio of one hormone with another.

The concept of testosterone (or androgen) deficiency is now common in medical and lay literature. Unfortunately, most researchers and authors do not yet understand the importance of saliva testing and, therefore, their diagnostic steps are inept and dosage suggestions are unnecessarily high. The makers of Androgel (a transdermal testosterone now being highly promoted), recommend starting doses of 5 mg/day up to 100 mg/day. From my experience, I find these doses to be hugely excessive and not physiological, and therefore I cannot recommend them.

General Guidelines for Achieving Hormone Balance

Give hormones only to those people who need them. This may sound simplistic but conventional medicine has for years been giving potent sex hormones to women without proving that they are truly deficient in them. No one would give insulin to anybody without proving that they need it. The same should be true for any hormone, including testosterone.

Use only bio-identical (natural, human) hormone rather than synthetic hormones. For years conventional medicine used not-found-in-nature synthetic testosterones (e.g. methyl testosterone) both for supplementation and in research. The results of giving these toxic substances to humans were predictably disastrous, and the results of using them in research were predictably confusing.

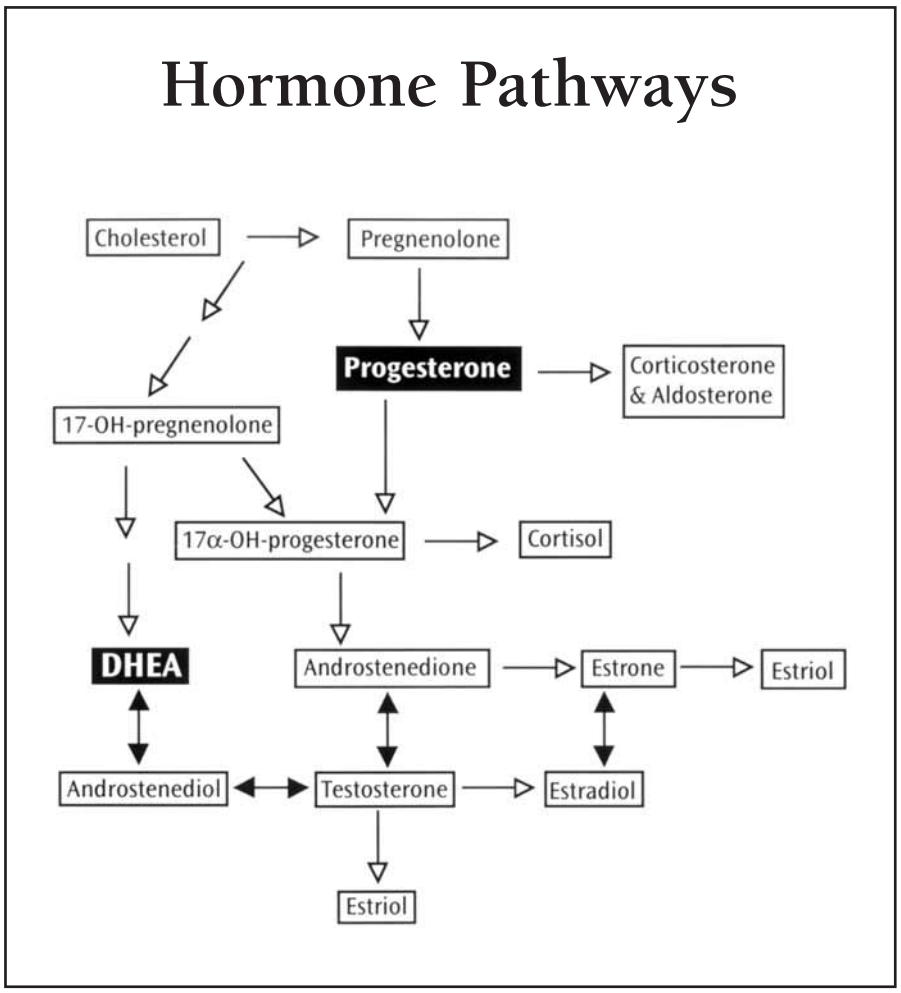
Use dosages that create normal physiologic levels. Without using saliva testing, this is practically impossible. Until doctors understand the failure of serum testing, they will continue overdosing their patients.

Summary of Expected Benefits of Hormone Balance in Men

— Progesterone inhibits 5-alpha-reductase, an enzyme that otherwise would convert testosterone into dihydrotestosterone (DHT) that is thought to cause prostate hypertrophy (enlargement).

Progesterone thus helps maintain normal testosterone levels and inhibits production of DHT. Progesterone is also an anabolic (energy-raising) hormone.

— Testosterone is our most potent anabolic hormone, and thus very important to metabolism throughout the body. Testosterone is also a direct antagonist of estradiol. The balance of testosterone versus estradiol = balance between masculinity and femininity. Maintaining a good T/E2 ratio reduces risk of prostate cancer.



— Both progesterone and testosterone promote the p53 gene that leads to normal healthy cell apoptosis (normal cell death), important to cancer prevention. Estradiol, on the other hand, promotes the Bcl-2 gene, a known oncogene that inhibits apoptosis and causes cancer. Thus, maintaining the proper ratio of these hormones to estradiol is important in preventing and treating prostate cancer.

Hormone Levels and Dosing

The goal of hormone balancing in men is to reestablish healthy ratios between estradiol, progesterone, and testosterone.

In men over 60, typical saliva hormone levels are:
Estradiol at 2.0 to 2.7 pg/ml
Progesterone at 20 to 30 pg/ml
Testosterone at 20-30 pg/ml
(Testosterone levels in men aged 30 to 35 are 200 to 300 pg/ml. This level of testosterone does not hurt these 30 to 35 year old men, and it will not hurt men who are 65 to 70 years old.)

To restore hormone balance we're looking for:

Saliva progesterone levels that are 200 to 300 times that of estradiol or around 400 pg/ml (in a two-ounce jar or tube of cream containing 960 mg of progesterone, this would be a bit less than 1/8 tsp of cream daily).

The ratio of saliva testosterone to estradiol should be about 200 to 300 to 1.

The saliva testosterone level should be approximately 200 to 300 pg/ml. Creams with the proper testosterone content are not readily available, so ask your doctor to write a prescription for the cream, then take it to a compounding pharmacist. It is essential that the pharmacist use real testosterone, and not one of the synthetic versions such as methyltestosterone.

General dosages for men deficient in progesterone and/or testosterone:

Transdermal progesterone . . . . . 5 to 8 mg/day

Transdermal testosterone . . . . . 1 to 2 mg/day

I have seen remarkable benefits and no side effects in men who use hormones this way. The low doses used attest to the excellent absorption of these hormones when applied transdermally (via creams, through the skin). Though retired, I keep in contact with a number of my patients with prostate cancer that I had treated with diet, antioxidants, progesterone and testosterone (as described above) and these men, now 16 years later, remain in good health, without having to resort to surgery or chemotherapy.

Dosages for individuals can vary depending on absorption and excretion kinetics. It is wise to re-test saliva levels after 2 to 3 months of transdermal hormone use. When testing for the effect of transdermally applied hormone, it is wise to standardize the time between dosing and the time of saliva collection. I recommend saliva collection be done 10 hours after application of the hormone. In this manner, serial testing will be more informative and reliable.

Androstenedione

This steroid hormone is a precursor to testosterone and estrogens, and it can theoretically act as a DHEA precursor. Secreted from the adrenals and the testes into the circulation, it has its own jobs to do before being converted into other hormones in the liver.

Androstenedione is a popular supplement for bodybuilders, who use it to boost their testosterone levels, increase muscle mass and decrease the length of time needed to recover from hard workouts. Many of the positive effects of supplemental testosterone–including enhanced energy, libido, and sense of well-being–have also been attributed to androstenedione.

Although baseball superstar Mark McGwire popularized the use of the male hormone androstenedione as a performance-enhancing supplement, its use is fraught with uncertainty created by individual biochemistry and even daily variations in metabolism. Sometimes androstenedione may be converted to testosterone, and sometimes it may be converted to estrogen. For this reason I do not recommend its use, particularly in men with hormonal imbalances.

DHEA

DHEA, or dehydroepiandrosterone, is a steroid hormone made in the adrenal glands, which make over 150 different hormones. The amount of DHEA is greater than any other of the steroid hormones. All but five percent of it is bound to sulfur molecules (DHEA-S), making it more soluble in blood plasma and providing us with ample reserves to draw from. We know that DHEA is important for the maintenance of health, but a complete understanding of its specific actions has so far eluded researchers.

Between the ages of twenty and twenty-five, DHEA production peaks. Men produce more than women, but both sexes make about two percent less every year after the age of twenty-five. By the time a man reaches the age of fifty, DHEA levels can be quite low. The decline in DHEA levels over time tends to parallel what is called "aging." Indeed, some people claim that aging is due to the decline of DHEA, whereas other researchers consider DHEA to be merely a marker for aging, but not its cause.

DHEA has weak androgenic properties and is considered to help with protein-building. The results of giving oral DHEA to people with low levels are rather spotty. Some seem to experience a boost in energy, ability to adapt to stress, feelings of well-being, and sex drive. Some researchers credit it with boosting immune function. However, it is not easy to separate these claims of benefit from placebo effects.

DHEA seems to have more benefits and fewer risks for men than women, which may be due to the fact that it converts to either testosterone or estrogen before excretion. In this process, it follows the path of least resistance: it will become testosterone in people with low testosterone, or estrogen in people with low estrogen levels. Thus, the ultimate effects of DHEA supplementation, if any, are difficult to predict.

If your DHEA levels are *low* (the normal range for middle-aged men is quite broad), taking enough to restore mid-normal levels may be beneficial, but keep in mind that an excess of DHEA could be harmful. If you decide to use it, keep a close watch on your overall hormone balance levels, testing every six months or so.

The recommended dose of DHEA for men is 10 to 25 mg a day. If you have your DHEA levels checked with a blood test, remember that DHEA-S is the relatively inactive form. Saliva DHEA testing is a more accurate measurement of the active DHEA in the blood.

There's still more that we don't know about DHEA than we do know, but if saliva hormone tests indicate a deficiency, then modest supplementation may be worth a try.

Vitamins, Minerals and Diet

In addition to creating hormone balance, it is wise to supplement 20 to 30 mg of zinc daily. Zinc is a potent antioxidant, and an aromatase inhibitor. Zinc levels are especially high in prostate tissue.

I also recommend supplementary anti-oxidant vitamins (vitamins C, A, and E), the mineral selenium in doses of 60 to 120 mcg per day, and in older men, vitamin D in doses of 400 mg daily. A number of recent studies have shown that adequate vitamin D levels may help prevent prostate cancer.

As I explained in earlier chapters, the diet should contain a minimum of sugar, refined starches, trans-fatty acids (especially bakery products), milk, fluoride and feed-lot beef. Diet should emphasize fresh, unprocessed, in-season vegetables of all kinds, fresh fruit, nuts, seeds, whole grains, eggs, cheese, deep ocean fish, organic meat and chicken, and good drinking water.

RESOURCES

WEB SITES

The Official Web Site of John R. Lee, M.D (www.JohnLeeMD.com). Although Dr. Lee died in October 2003, his work lives on in his best-selling books, his audio and video tapes. This web site offers all of these materials and a wealth of additional information about natural hormones, from "Frequently Asked Questions" for beginners, to biochemistry for experts.

John Lee M.D. Solutions (www.ProgesterAll.com). Besides offering books, newsletters, and tapes from Dr. Lee, this site features ProgesterAll, a balancing cream that contains 20 milligrams of USP Natural Progesterone per quarter teaspoon of cream. ProgesterAll is the same formula that Dr. Lee and his family have used for the past decade. It is the only cream that is authorized by the Lee family to have Dr. Lee's name on it.

HORMONE TESTING SERVICES

The Official Web Site of John R. Lee, M.D (www.JohnLeeMD.com) offers state-of-the-art hormone testing services from its web site. To learn about or purchase these services, click on the "Hormone Tests" tab on the home page.

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HOW TO FIND A HEALTH CARE PROFESSIONAL IN YOUR AREA WHO PRACTICES ALTERNATIVE MEDICINE

Of course there's no guarantee that any given individual you might contact is knowledgeable, competent and will work in partnership with you, but these resources will give you a good jump start on your search. One of the best sources of information is your local health food store. You can also look in your yellow pages under "physicians." Those who practice alternative medicine often advertise themselves as wholistic or holistic physicians.

Dr. Lee's web site (www.JohnLeeMD.com) has a section called Resources that has a page entitled "Find a Doctor Who Uses Natural Hormones". This page provides links to directories of physicians who are open to alternative therapies, including natural hormones.

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