

Male Hormone Restoration

As men age, they begin to experience changes in their bodies. Abdominal fat increases and muscle mass decreases. They also experience a distressing decline in their sex drive. At the same time, the risk of serious health conditions such as depression and heart disease rises. While most conventional physicians (and some members of the lay media) dismiss these woes as signs of “natural aging,” there is often an underlying and identifiable cause of these symptoms—the gradual decline of important sex hormones, especially testosterone.

Too often, men who have problems related to a low testosterone level are advised to treat only the symptoms of their conditions (such as taking antidepressant and/or cholesterol-lowering drugs). Fortunately, progressive physicians, along with the Life Extension Foundation, now recognize the connection between hormones and the diseases of aging. Restoration of youthful hormone levels is associated with optimal sexual function, energy, and vitality, while declining hormone levels correlate with many age-related conditions, including high blood pressure, atherosclerosis, diabetes, loss of muscle and bone mass, and fatigue (Shores MM et al 2004).

FACTORS THAT AFFECT TESTOSTERONE LEVELS

Testosterone, which is abundantly produced during puberty, is responsible for the development of secondary sexual characteristics and has profound effects throughout the body. Testosterone receptors are found in virtually all body tissues, so levels of testosterone affect the function of most organ systems. For example, testosterone causes growth of facial and body hair in skin cells, increased fiber size and strength in muscle cells, and maturation of the external genitalia. The effects of testosterone on the central nervous system are also well-known (Okun MS et al 2004). Testosterone governs such behaviors as aggression, risk taking, and territoriality. It is now recognized as an important factor in mitigating depression (King JA et al 2005).

As with all sex hormones, testosterone is part of a cascade that begins with cholesterol, the building block for hormones. Pregnenolone, the “master hormone,” is produced directly from cholesterol. In turn, dehydroepiandrosterone (DHEA; a precursor to testosterone), testosterone (and its metabolites), and estrogen (and its metabolites) are produced from pregnenolone. Both testosterone and estrogen are produced by enzymatic reactions from DHEA. This ubiquitous molecule is the steroid found in highest quantities in humans. Changes in the supply of DHEA (and/or changes in the levels of the enzymes that convert DHEA to the sex hormones) can have powerful effects on sex hormone-dependent systems.

As men age, a number of changes occur that reduce the testosterone level available to the body and that alter the ratio between testosterone and the chief female hormone, estrogen. This condition is now referred to as partial androgen deficiency of aging men (Harman SM 2005).

One of the most important factors that affect testosterone levels of aging men is an enzyme called aromatase, which is found in fat tissue. This enzyme is responsible for converting testosterone into estrogen, thus altering the ratio of estrogen to testosterone (Steiner MS et al 2003). Men who have excessive body fat, especially abdominal fat, are likely to have increased estrogen levels caused by aromatase activity and a dramatically increased estrogen level compared to testosterone. An increased estrogen level has been linked, in turn, to a host of disorders, including decreased insulin sensitivity and blood glucose problems. Some studies suggest that there is an association between a low testosterone level, insulin resistance, an elevated estrogen level, and increased body fat in aging men (Phillips GB 1993).

This relationship between low testosterone and obesity has been described as the hypogonadal/obesity cycle. In this cycle, a low testosterone level leads to an increase in abdominal fat, which leads to increased aromatase activity, which leads to further conversion of testosterone to estradiol, which further reduces testosterone and increases the tendency toward abdominal fat (Cohen PG 1999).

The effect of sex hormones on tissues is also affected by the level of sex hormone-binding globulin (SHBG). Sex hormones circulate in the bloodstream in very small quantities as free molecules. The bulk of sex hormones are bound to SHBG, which is a specialized carrier protein (Nankin HR et al 1986). Hormones bound to carrier molecules are inactive, so the amount of SHBG has an important impact on the degree to which tissues respond to sex hormone levels (Misao R et al 1999; Zmuda JM et al 1993; Dambe JE et al 1983; Van Look PF et al 1981). Nutritional status and the levels of other hormones are among the factors that determine levels of SHBG.

Aging men who have an androgen deficiency experience both an increase in aromatase activity and an elevation in SHBG production. The net result is to increase the ratio of estrogen to testosterone and lower the total testosterone level (Killinger DW et

al 1987; Kley HK et al 1980a,b). Finally, it is important that aging men also strive for optimal liver function. The liver is responsible for removing excess estrogen and SHBG, so any compromise in liver function (such as that caused by heavy alcohol consumption, for example) can exacerbate hormonal imbalances.

EFFECTS OF AGE-RELATED DECLINE IN TESTOSTERONE LEVELS

The exact causes of the age-related reduction in testosterone levels is not known; it is probably the result of a combination of factors, including increased body fat (and therefore increased aromatase activity), oxidative damage to tissues responsible for the production of testosterone, and declining levels of precursor molecules such as DHEA. The results of the decline, however, are strikingly apparent.

Nervous system effects. Low testosterone levels have been associated with depression and other psychological disorders (Barrett-Connor E et al 1999b; Rabkin JG et al 1999; Schweiger U et al 1999; Seidman SN et al 1999; Moger WH 1980). In addition, many conventional antidepressants suppress libido. Some experts recommend that patients whose reduced libido is caused by taking antidepressants undergo testing to have their testosterone levels checked—and that they get supplemental treatment if necessary. Others suggest that testosterone therapy might reduce the need for the antidepressants themselves (Goldstat R et al 2003; Morley JE 2003). Feelings of well-being are often reported with testosterone treatment (Carnahan RM et al 2004; Dunning TL et al 2004; Orengo CA et al 2004; Wright JV et al 1999).

Cognition and alertness are also governed in part by testosterone's effects on the central nervous system (Cherrier MM et al 2004; Cherrier MM et al 2001; Janowsky JS et al 2000). Low testosterone levels have been shown to correlate with lower scores on various psychometric tests (Moffat SD et al 2002; Barrett-Connor E et al 1999a; Janowsky JS et al 1994). Similar effects have been reported in men taking androgen-deprivation therapy for prostate cancer (Salminen EK et al 2004). Testosterone's ability to protect nerve cells against a variety of toxins, including oxidative stress (Ahlbom E et al 2001) and the Alzheimer's protein beta-amyloid (Zhang Y et al 2004; Hammond J et al 2001), may explain the low testosterone levels found in men who have neurodegenerative diseases (Hogervorst E et al 2004; Okun MS et al 2004; Ready RE et al 2004).

Sexual enjoyment and function. Falling levels of free testosterone diminish sexual desire, as well as pleasure and performance in sexual activity. There is evidence that, in men with low free testosterone levels, replacement therapy can improve sexual function (Tenover JL 1998; Anderson RA et al 1992; Ahmed SR et al 1988; Davidson JM et al 1982).

Cardiovascular disease and metabolic syndrome. There is a clear relationship between low levels of testosterone and increased incidence of cardiovascular disease, particularly as testosterone level relates to metabolic syndrome (Dobrzycki S et al 2003; Hak AE et al 2002; Zhao SP et al 1998; Jeppesen LL et al 1996). Metabolic syndrome is the combination of abdominal obesity, high blood pressure, insulin resistance, and lipid disorders in the same person. This condition is associated with a high risk of cardiovascular disease. Studies have shown that testosterone administration (500 milligrams [mg] of intramuscular injections) in middle-aged, obese men was able to increase insulin sensitivity (Marin P et al 1992a). These results were confirmed in another study in which testosterone treatment led to reduced insulin resistance (Marin P et al 1992b). Later studies also showed that testosterone administration is helpful in the context of metabolic syndrome (Bhasin S 2003; Boyanov MA et al 2003).

The musculoskeletal system. Bone integrity depends upon a balance between bone formation and bone resorption, which are controlled by multiple factors including estrogen and testosterone (Rucker D et al 2004; Tok EC et al 2004; Valimaki VV et al 2004). One clinical trial has demonstrated that testosterone increases bone mineral density in elderly men (van den Beld AW et al 2000). Testosterone supplementation also has a positive effect on muscle metabolism and strength (Herbst KL et al 2004). The effect is undiminished with age, although older men have a greater incidence of adverse effects.

THE IMPORTANCE OF HORMONE TESTING

When testosterone levels are measured, it is critical to determine the levels of both free and total testosterone to understand the cause of any observed symptoms of deficiency or excess (Pardridge WM 1986).

The Life Extension Foundation believes that a comprehensive battery of tests, along with a careful physical examination, is helpful in detecting hormonal imbalances in aging men. If testing is conducted, it is important to remember that blood levels of both free and total testosterone vary widely among individuals, making it difficult to establish a general threshold for treatment. However, levels are quite consistent within individuals, so it is helpful for men to have multiple tests over time to determine trends and individual thresholds for treatment.

It is also important to note that so-called normal levels of testosterone for older men reflect averages in the current population. The Life Extension Foundation believes that most aging men would prefer not to accept the loss of youthful vigor as normal. Instead, we suggest that a more valid optimal range for all men would be in the upper one-third of the range for men aged 21 to 49 years, and that any supplementation should aim to restore hormone levels to that range.

Finally, during the initial testing, it is imperative to also test estrogen levels. Many of the unwanted effects of male hormone imbalance are actually caused by an elevated estrogen level relative to testosterone level (the estrogen/testosterone ratio).

Using Hormone Replacement Wisely

If a man chooses to pursue hormone testing with the intention of using testosterone supplementation (available orally or as an injection, implant, or skin patch), he should keep several facts and precautions in mind (Rhoden EL et al 2004; Schaeffer EM et al 2004):

- The patterns and trends over time of multiple hormone levels (such as free testosterone, total testosterone, and estrogen) determine the specific hormone replacements required.
- It is not safe to use large amounts of testosterone in any form.
- Hormone replacement should not be initiated without comprehensive testing.
- Because of the risk of worsening prostate cancer, careful screening for prostate cancer, including a digital rectal examination and prostate specific antigen (PSA) screening, must be done before starting any hormone replacement program.
- Certain conditions are contraindications to hormone replacement (Ebert T et al 2005). Prostate cancer, in particular, can be made worse by increasing available testosterone.
- A man who is contemplating taking hormone replacement, whether through a prescription or through supplements, should work closely with a qualified physician to plan a rationale approach to treatment and continued monitoring and screening.

TESTOSTERONE THERAPIES

Synthetic anabolic steroids. Synthetic anabolic steroids sold in the form of patches, creams, pellets, and tablets are chemically different from the testosterone made by the body and do not accomplish the same effect as natural testosterone. These drugs are aimed primarily at the musculoskeletal system and are known to have myriad toxic side effects, including causing serious heart and kidney complications. They are sometimes abused by athletes and bodybuilders who want to build muscle mass. A few of the synthetic testosterone drugs that men should avoid using on a long-term basis are methyltestosterone, danazol, oxandrolone, testosterone propionate, cyclopentanepropionate, and enanthate.

Testosterone patches, creams, pellets and tablets. Scientists learned decades ago how to make the identical testosterone that a man's body produces. However, because natural testosterone could not be patented, drug companies developed all kinds of synthetic testosterone analogues. Currently available recommended natural testosterone drugs include testosterone transdermal patches and testosterone creams, pellets, and sublingual tablets.

Both synthetic testosterone and natural testosterone require a prescription. A physician should prescribe testosterone only after a man's blood tests have verified that he has a testosterone deficiency.

Alternative physicians usually prescribe testosterone creams (available at compounding pharmacies). Conventional physicians are more likely to prescribe testosterone patches. All forms of natural testosterone are the same and all will markedly increase free testosterone in the blood and saliva.

Testosterone and Cholesterol

Millions of aging men have the dual conditions of low testosterone and high cholesterol. Conventional physicians prescribe cholesterol-lowering drugs to reduce cholesterol when in fact the age-related rise in cholesterol may simply be the body's way of increasing hormone levels by supplying the raw materials from which hormones are made (Dzugas SA et al 2002). Researchers at the Life Extension Foundation have successfully treated high cholesterol levels through a program of bioidentical hormones that restores these hormones to youthful levels, reducing the body's need to make excess cholesterol. While this approach has received almost no attention outside of alternative health circles, it may prove to be the link between high cholesterol and hormone-related disorders of aging.

NATURAL APPROACHES TO BOOST TESTOSTERONE AND SUPPRESS ESTROGEN

Nutrients function by increasing testosterone availability, often by affecting testosterone's interaction with SHBG or by decreasing its aromatization (conversion) into estrogen. Natural supplements can complement hormone replacement therapy. For people who choose not to (or should not) use hormone replacement therapy, nutrients can be a vital part of a comprehensive program to reduce the impact of aging on the systems of sex hormone production, regulation, and metabolism. Nutritional therapy also has a role in preventing diseases of the male reproductive tract, such as prostate cancer and benign prostatic hyperplasia (BPH). More specific information on these diseases can be found in the chapters "Prostate Cancer" and "Benign Prostatic Hyperplasia."

The following is a list of nutrients that are part of the Life Extension Foundation's comprehensive male hormone modulation program:

Zinc. Zinc is related to testosterone levels. In one animal study, rats subjected to an acute swimming test were either supplemented with zinc or placebo. The study showed that zinc supplementation led to significant increases in testosterone levels and may help in athletic performance (Kaya O et al 2006). Among humans, zinc supplementation in a group of male wrestlers prevented the depletion of testosterone after exertion (Kilic M et al 2006). Additional studies have suggested that zinc is important to the synthesis of testosterone (Ali H et al 2005).

Chrysin. A bioflavonoid called chrysin has shown potential as a natural aromatase inhibitor (Kellis JT Jr et al 1984). Chrysin can be extracted from various plants and is found in high concentrations in honey. Bodybuilders have used it as a testosterone-boosting supplement because, by inhibiting the aromatase enzyme, less testosterone is converted into estrogen. Although chrysin is a known inhibitor of aromatase, in one study it did not result in the expected increase in testosterone levels (Gambelunghe C et al 2003). This may be because of poor intestinal absorption of chrysin (Walle UK et al 1999). The Life Extension Foundation has identified a novel supplement called piperine that increases the bioavailability of chrysin.

Carnitine. Carnitine is an amino acid derivative that may be more active than testosterone in aging men who have sexual dysfunction and depression caused by an androgen deficiency (Cavallini G et al 2004). Both testosterone and carnitine improve sexual desire, sexual satisfaction, and nocturnal penile tumescence, but carnitine is more effective than testosterone in improving erectile function, nocturnal penile tumescence, orgasm, and general sexual well-being. Carnitine was better than testosterone at treating depression (Cavallini G et al 2004).

Muira puama. Muira puama is a South American folk medicine derived from a shrub, *Ptychopetalum olacoides*, which grows in the Amazon region of Brazil. Also called marapuama and "potency wood," it is considered an aphrodisiac and an effective treatment of impotence. Because of its purported libido-enhancing properties, muira puama has been the subject of two published clinical studies by Dr Jacques Waynberg, an eminent medical sexologist and author of 10 books on the subject.

The first study, conducted at the Institute of Sexology in Paris under Dr Waynberg's supervision, consisted of examining the effect of muira puama on 262 men who complained of lack of sexual desire or inability to attain or maintain erection. After receiving 1.5 grams (g)/day of muira puama for 2 weeks, 62 percent of the patients with loss of libido rated the treatment as having a dynamic effect, and 52 percent of patients with erectile dysfunction rated the treatment as beneficial (Wright JV et al 1999).

Dr Waynberg's second study, entitled "Male Sexual Asthenia," focused on sexual difficulties associated with asthenia, a deficiency state characterized by fatigue and loss of strength, both symptoms of a testosterone deficiency. The study population consisted of 100 men older than 18 years who complained of impotence and/or loss of libido. A total of 94 men completed the study, and their conditions were evaluated. Muira puama treatment led to significantly increased frequency of intercourse for 66 percent. Of the 46 men who complained of loss of desire, 70 percent reported intensification of libido. The stability of erection during intercourse was restored in 55 percent of patients, and 66 percent of men reported a reduction in fatigue. Other reported beneficial effects included improvement in sleep and morning erections (Waynberg J 1990).

Cruciferous vegetables. Cruciferous vegetables, such as broccoli and cauliflower, contain isothiocyanates and glucosinolates, which act as antioxidants and potent inducers of phase 2 proteins believed to suppress prostate cancer formation (Kris-Etherton PM et al 2002; Talalay P et al 2001).

Quercetin. Wine contains antioxidant polyphenols and quercetin. One study showed that red wine inhibited aromatase. The study attributed this effect to the quercetin and other ingredients (Eng ET et al 2002). In human colon cancer cells, quercetin has been shown to inhibit local synthesis of estrogen by inhibiting aromatase (Fiorelli G et al 1999).

Saw palmetto and nettle extracts. These two supplements are commonly used to reduce symptoms of BPH. In Europe, saw palmetto (*Serenoa repens*) has been used extensively as a drug for some time. Saw palmetto's clinical benefits for prostate enlargement include:

- Reduced nocturnal urinary urgency (Boyle P et al 2004).
- Increased urinary flow rate (Boyle P et al 2004; Gerber GS et al 2004).
- Decreased residual urine volume in the bladder (Giannakopoulos X et al 2002).
- Reduced discomfort from urination symptoms (Giannakopoulos X et al 2002; Wilt T et al 2002).

In fact, results of treatment with saw palmetto compare favorably with the prescription drug finasteride, with far fewer adverse effects (Wilt T et al 2002). Similarly, another study compared saw palmetto extract to the prescription drug tamsulosin for 1 year. After the treatment period was over, the symptoms of the patients in both groups had improved, and their PSA scores remained stable. However, the size of the prostate gland decreased only in the group taking saw palmetto, and sexual dysfunction was more common in the group taking tamsulosin. Overall, saw palmetto produced a superior response after only 3 months of treatment, and

maintained its superiority (Debruyne F et al 2002). Finally, in a meta-analysis of saw palmetto, researchers found there was an average reduction of 5 points in the International Prostate Symptoms Score (IPSS) across all studies (Boyle P et al 2004).

As with most supplements, it is important to be sure that you are buying the highest quality supplement possible. In the case of saw palmetto, that means supercritical, standardized extracts. Supercritical fluid extraction technology produces an extract of extraordinary purity while leaving behind no solvent residues on the product. The first medicinal herb to benefit from large-scale supercritical fluid extraction was saw palmetto.

While a large number of studies document the benefits of saw palmetto by itself, European physicians frequently prescribe saw palmetto extract that is combined with additional herbs that interfere with other factors involved in prostate enlargement, including nettle root.

Nettle root extract may provide a unique mechanism for increasing levels of free testosterone by binding to SHBG, the globulin that inactivates sex hormones, therefore potentially increasing the amount of unbound, free testosterone (Lichius JJ et al 1997; Schottner M et al 1997; Gansser D et al 1995; Hryb DJ et al 1995; Hirano T et al 1994). Nettle root extract is used extensively, either in combination with saw palmetto or by itself, for relief of BPH symptoms.

In 2005, researchers conducted a randomized, double-blind, placebo-controlled, crossover study of nettle root extract. This is the gold standard of clinical trial formats and is used to rigorously test pharmaceutical drugs before they gain market approval. Almost 600 patients were enrolled in this trial for up to 18 months. At the end of the study, 81 percent of the treated patients experienced significant relief of their symptoms and significant reductions in their IPSS compared with only 16 percent of the control subjects. After the 18-month follow-up, only those patients who continued with the therapy experienced any benefits (Safarinejad MR 2005).

These results were confirmed in another study that examined the effect of saw palmetto combined with nettle root extract on men. Once again, this was a double-blind, placebo-controlled study. In this case, the reduction in IPSS was “clearly superior” among men receiving saw palmetto and nettle root extract, compared to men receiving placebo (Lopatkin N et al 2005).

Nettle root extract has also shown an affinity for SHBG (Hryb DJ et al 1995). SHBG is closely related to levels of free testosterone and estrogen; most of these hormones travel through the bloodstream “bound” to SHBG. Any testosterone that is unbound to SHBG is referred to as free testosterone. Studies have shown that men with BPH have elevated levels of SHBG in their prostate gland (Jiang H et al 2004); thus, any nutrient that reduces SHBG levels may also be able to reduce BPH.

Antioxidants. One reason testosterone production may decline is because of oxidative damage directed at the tissues that synthesize testosterone. A Chinese study examined the role of antioxidants in male hormone imbalance or partial androgen deficiency of aging men. The article’s authors note that antioxidants (including vitamin A, vitamin E, zinc, and selenium) all support testosterone production (He F et al 2005).

A WORD ABOUT TESTOSTERONE AND PROSTATE DISEASE

For more than 50 years, it has been thought that men should avoid testosterone replacement therapy because testosterone increases the risk of prostate disease, including BPH and prostate cancer. A look at the published literature, however, reveals that this long-standing belief is actually a myth.

In fact, a review of studies on the National Institutes of Health database reveals that high testosterone levels are not associated with increased risk of prostate cancer and, conversely, that low testosterone levels are not protective against prostate cancer (Morgentaler A 2006). In one study (with a 7-year follow-up) of more than 500 men, high levels of androgens were associated with a decreased risk of aggressive prostate cancer, while there was no change in the risk of nonaggressive prostate cancer. Overall, levels of any steroid hormones (except estrogen) had no correlation to the risk of prostate cancer (Severi G et al 2006).

Elevated estrogen levels, however, are frequently associated with BPH. As readers of Life Extension magazine learned in late 1997, estrogen has been identified as a factor behind the enlargement of the prostate gland that affects so many older men. Compared to younger males, older males have much more estradiol (a potent form of estrogen) than free testosterone because of aromatase activity. These rising estrogen and declining androgen levels are even more sharply defined in the prostate gland. With aging, estrogen levels increase significantly in the prostate gland. Estrogen levels in prostate gland tissues rise even higher in men who have BPH (Shibata Y et al 2000; Gann PH et al 1995; Krieg M et al 1993).

Based on research, high levels of testosterone are not implicated in an increased risk of developing either prostate cancer or BPH. However, among men who already have these conditions, testosterone replacement therapy will likely cause increased disease activity. For these reasons, it is important that men who are considering hormone replacement therapy undergo frequent screening for prostate cancer (with PSA testing and digital rectal exams). If cancerous cells are present in the prostate, testosterone therapy will likely produce a spike in PSA levels that will lead to a diagnosis of prostate cancer.

Once a man actually has prostate cancer, testosterone therapy cannot be recommended because most prostate cancer cells use testosterone to promote the growth of the cancerous cells. Similarly, men with BPH should approach testosterone replacement cautiously. It may be prudent for men with BPH who are undergoing testosterone replacement therapy to also use a 5-alpha-reductase inhibitor (such as finasteride or dutasteride). These drugs inhibit the synthesis of dihydrotestosterone (DHT), a metabolite of testosterone that causes BPH. 5-Alpha-reductase inhibitors are a standard part of prescription therapy for BPH. For more information on natural ways to suppress BPH, please see the chapter on Benign Prostatic Hyperplasia.

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

Hormone therapy for aging men can be a complicated topic. While many books talk about the dangers of low testosterone levels, there are few sources that can help men safely embark on a program of testosterone replacement therapy. The Life Extension Foundation offers a step-by-step program to safely restore youthful hormone levels in aging men.

Step One: Testing

It is critical that men undergo comprehensive medical testing before embarking on a hormone modulation program. First, a baseline blood PSA must be taken to rule out existing prostate cancer. (For more information, please see the chapter on Prostate Cancer.) Then free and total testosterone and estradiol tests are needed to make sure that too much testosterone is not being converted into estrogen. If estrogen levels are too high, the use of aromatase inhibitors can keep testosterone from converting into estrogen in the body. Follow-up testing for estrogen, testosterone, and PSA are needed to rule out prostate cancer and fine-tune your program. Additional tests that should be considered include:

- Complete blood cell count and chemistry profile to include liver and kidney function, glucose, minerals, lipids, and thyroid-stimulating hormone (TSH)
- DHEA
- Homocysteine
- Luteinizing hormone (LH) (optional)
- SHBG (optional)

Blood for these tests may be drawn at your physician's office or directly at a laboratory in your area. Information about ordering these tests on your own may be obtained by calling 1-800-208-3444. These tests will yield crucial information that can help you design a program tailored to your unique situation.

Step Two: Interpreting the Results

Free testosterone. Most conventional physicians accept testosterone levels that are far too low. Normal ranges usually reflect population averages among men of a particular age. This assumes, however, that decreasing hormone levels are acceptable and normal. The Life Extension Foundation recommends that men strive for a free testosterone level that is in the upper one-third range for men aged 21 to 49 years. These ranges can be found in the Blood Testing appendix at the back of this book.

There are five basic reasons that free testosterone levels may be low:

- Too much testosterone is being converted to estrogen through the activity of aromatase, and/or the liver is failing to remove excess estrogen, possibly because of heavy alcohol intake.
- Too much free testosterone is being bound by SHBG. This would be especially apparent if a man's total testosterone level is in the high normal range but his free testosterone level is low.
- The pituitary gland, which controls testosterone production through the production of LH, is not secreting enough LH to stimulate gonadal production of testosterone. In this case, total testosterone would be low.
- The testicles (gonads) have lost their ability to produce testosterone, despite adequate amounts of LH. In this case, the level of LH would be high despite a low testosterone level.
- DHEA level is abnormally low.

Estrogen. Estrogen (measured as estradiol) should be kept at 30 picograms per milliliter (pg/mL) or lower. If a man's estrogen level is more than 30 pg/mL, it should be reduced by using aromatase-inhibiting drugs or nutrients. If a man's estrogen level is elevated, it could be associated with:

- Increased aromatase activity, often caused by increased abdominal fat.
- Heavy alcohol intake. An animal study has shown that high alcohol intake results in increased aromatization and decreases the ability of the liver to clear excess estrogen (Purohit V 2000). In men, heavy alcohol intake has been shown to boost estrogen levels within the liver, possibly as a protective mechanism, resulting in the "feminization" of the liver (Colantoni A et al 2002).

Total testosterone. The Life Extension Foundation believes that direct testing for free testosterone is the best way to test for testosterone activity, as free testosterone is active testosterone and consists of only 1 to 2 percent of total testosterone. However, some men have their total testosterone measured also.

Step Three: Correcting Abnormal Levels

Ultimately, the ideal program will depend on the results of various tests. Below are some of the common scenarios and solutions to correct hormone imbalances.

Low Free Testosterone, High Estradiol, Mid Total Testosterone

This situation suggests excessive aromatase activity, which converts free testosterone to estrogen. Inhibition of aromatase and reduction in aromatase-containing tissue (fat) is indicated. Suggestions include:

- Take the following supplements:
 - **Zinc**—50 milligrams (mg)/day
 - **Acetyl-L-carnitine**—1000 to 2000 mg/day
 - **Muir puama**—850 mg/day
 - **Chrysin**—1500 mg/day
 - **Piperine**—10 mg/day to enhance absorption of chrysin
 - **Quercetin**—500 to 1000 mg/day
- Lose weight to reduce aromatase activity.
- Reduce or eliminate alcohol to enable the liver to better remove excess estrogen.
- Review all current medications to see if they are interfering with healthy liver function. Common medications that affect liver function are nonsteroidal anti-inflammatory drugs (NSAIDs) such as naproxen, ibuprofen, acetaminophen, and aspirin; the statin class of cholesterol-lowering drugs; some heart medications; some blood pressure-lowering medications; and some antidepressants. Drugs being prescribed to treat the symptoms of testosterone deficiency (such as the statins and certain antidepressants) may actually aggravate the testosterone deficit, thus making the cholesterol problem or depression worse. However, do not discontinue any prescription medicine without consulting your physician.
- If all of the above fail to increase free testosterone and lower excess estradiol, consider discussing with your physician the use of the aromatase inhibitor anastrozole at the very low dose of 0.5 mg twice per week.

Low Free Testosterone, Low Estrogen, High Total Testosterone

This situation suggests excessive SHBG levels, making testosterone unavailable to target tissues. Suggestions include:

- Inhibit aromatase by following some of the recommendations in the previous section. Many of the same factors are involved in excess SHBG activity.
- Take the following supplements:
 - **Saw palmetto extract**—320 mg/day
 - **Nettle root extract**—240 mg/day
 - **Cruciferous vegetable extract**—400 mg/day
 - **DHEA**—15 to 75 mg/day, followed by blood tests in 3 to 6 weeks

Low Free Testosterone, Low Estrogen, Low Testosterone

This situation suggests low production of testosterone, with resultant low conversion to estrogen. Suggestions include:

- Use testosterone patches, pellets, or cream. Do not use testosterone injections or tablets. If tests reveal low levels of LH, ask your physician about the possibility of using human chorionic gonadotropin (HCG). HCG function is similar to LH function, and HCG can restart gonadal production of LH.
- Take 15 to 75 mg/day of DHEA.

General Nutrients to Boost Testosterone

A number of nutrients have been studied for their ability to boost testosterone and/or treat conditions such as erectile dysfunction and loss of libido. This nutrient group includes antioxidants, which may function by reducing oxidative damage to testosterone-producing tissues.

- **Selenium**—200 micrograms (mcg)/day
- **Vitamin A**—5000 International Units (IU)/day
- **Vitamin E**—400 IU/day with at least 200 mg of gamma-tocopherol

PRODUCT AVAILABILITY

All the nutrients and supplements discussed in this section are available through the Life Extension Foundation Buyers Club, Inc. For ordering information, call anytime toll-free 1-800-544-4440, or visit us online at www.LifeExtension.com.

The blood tests discussed in this section are available through Life Extension National Diagnostics, Inc. For ordering information, call anytime toll-free 1-800-208-3444, or visit us online at www.LifeExtension.com.

MALE HORMONE RESTORATION SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Acetyl-L-Carnitine

- Acetyl-L-carnitine can cause gastrointestinal symptoms such as nausea and diarrhea.

Chrysin

- Do not take chrysin if you have prostate cancer.
- Chrysin can increase the effects of aromatase inhibitors such as aminoglutethimide, anastrozole and letrozole.

DHEA

- Do not take DHEA if you could be pregnant, are breastfeeding, or could have prostate, breast, uterine, or ovarian cancer.
- DHEA can cause androgenic effects in woman such as acne, deepening of the voice, facial hair growth and hair loss.

Piperine

- Piperine can inhibit drugs such as: propranolol, theophylline, phenytoin, sulfadiazene, rifampicin, isoniazid, ethambutol, pyrazinamide and dapsona that are metabolized by cytochrome P450 enzymes.

Quercetin

- Quercetin can cause headache, mild tingling of the extremities, and gastrointestinal symptoms such as nausea.

Saw Palmetto

- Consult your doctor before taking saw palmetto if you have any form of cancer that is stimulated by hormones.

Selenium

- High doses of selenium (1000 micrograms or more daily) for prolonged periods may cause adverse reactions.
- High doses of selenium taken for prolonged periods may cause chronic selenium poisoning. Symptoms include loss of hair and nails or brittle hair and nails.
- Selenium can cause rash, breath that smells like garlic, fatigue, irritability, and nausea and vomiting.

Vitamin A

- Do not take vitamin A if you have hypervitaminosis A.
- Do not take vitamin A if you take retinoids or retinoid analogues (such as acitretin, all-trans-retinoic acid, bexarotene, tretinate, and isotretinoin). Vitamin A can add to the toxicity of these drugs.
- Do not take large amounts of vitamin A. Taking large amounts of vitamin A may cause acute or chronic toxicity. Early signs and symptoms of chronic toxicity include dry, rough skin; cracked lips; sparse, coarse hair; and loss of hair from the eyebrows. Later signs and symptoms of toxicity include irritability, headache, pseudotumor cerebri (benign intracranial hypertension), elevated serum liver enzymes, reversible noncirrhotic portal high blood pressure, fibrosis and cirrhosis of the liver, and death from liver failure.

Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.
- Discontinue using vitamin E 1 month before any surgical procedure.

Zinc

- High doses of zinc (above 30 milligrams daily) can cause adverse reactions.
- Zinc can cause a metallic taste, headache, drowsiness, and gastrointestinal symptoms such as nausea and diarrhea.
- High doses of zinc can lead to copper deficiency and hypochromic microcytic anemia secondary to zinc-induced copper deficiency.
- High doses of zinc may suppress the immune system.

For more information see the Safety Appendix

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