THE INSTITUTE OF NUTRITIONAL MEDICINE & CARDIOVASCULAR RESEARCH

MALE HORMONES AND AGING

Too Much Estrogen

As men age past age 40, hormonal changes occur that perceptibly inhibit physical, sexual, and cognitive function. The outward appearance of a typical middle-aged male shows increased abdominal fat and shrinkage of muscle mass, a hallmark effect of hormone imbalance (94-97, 271).1 Loss of a feeling of well-being, sometimes manifesting as depression, is a common psychological complication of hormone imbalance. Until recently, these changes were attributed to "growing old," and men were expected to accept the fact that their bodies were entering into a long degenerative process that would someday result in death.

A remarkable amount of data has been compiled indicating that many of the diseases that middle-aged men begin experiencing, including depression, fatigue, abdominal weight gain, alterations in mood and cognition, decreased libido, erectile dysfunction, prostate disease, and heart disease are directly related to hormone imbalances that are correctable with currently available drug and nutrient therapies. The onset of these symptoms usually appears in the early 50s, although with smokers the onset is significantly earlier (290-293).

To the patient's detriment, conventional doctors are increasingly prescribing drugs to treat depression, elevated cholesterol, angina, and a host of other diseases that might be caused by an underlying hormone imbalance.

If doctors checked their male patients' blood levels of estrogen, testosterone, thyroid, and DHEA (instead of prescribing drugs to treat symptoms), they might be surprised to learn that many problems could be eliminated by adjusting hormone levels to fit the profile of a healthy 21-year-old male.

Few physicians are familiar with the hormone blood tests that should be ordered for men, nor do they have the experience required to properly adjust hormones to reverse the degenerative changes that begin in midlife. This protocol will provide the patient and physician with the information necessary to safely modulate hormone levels for the purpose of preventing and treating many of the common diseases associated with growing older.

The most significant hormone imbalance in aging men is a decrease in free testosterone, while estrogen levels remain the same or increase precipitously. As men grow older, they experience a variety of disorders relating to the dual effects of having too little testosterone and excess estrogen. The result is a testosterone-estrogen imbalance that directly causes many of the debilitating health problems associated with normal aging (1-12, 28)

One cause of hormone imbalance in men is that their testosterone is increasingly converted to estrogen. One report showed that estrogen levels of the average 54-year-old man are higher than those of the average 59-year-old woman (1, 5, 13-18, 48).

The reason that testosterone replacement therapy does not work by itself for many men is that exogenously administered testosterone may convert (aromatize) into even more estrogen, thus potentially worsening the hormone imbalance problem in aging males (i.e., too much estrogen and not enough free testosterone) (21, 26). Although there are studies that show that testosterone replacement therapy does not increase estrogen beyond normal reference ranges, we will show later how the standard laboratory reference ranges do not adequately address the issue of estrogen overload (4, 8, 9, 17, 22-25, 27, 29-32).

Estrogen is an essential hormone for men, but too much of it causes a wide range of health problems. The most dangerous acute effect of excess estrogen and too little testosterone is an increased risk of heart attack or stroke (39-43, 261-270). High levels of estrogen have been implicated as a cause of benign prostatic hypertrophy (BPH) (35-44, 46, 47). One mechanism by which nettle root extract works is to block the binding of growth-stimulating estrogen to prostate cells (42-44, 48-50).

When there is too little testosterone present, estrogen attaches to testosterone cell receptor sites throughout the body and creates many problems in aging men. In youth, low amounts of estrogen are used to turn off the powerful cell-stimulating effects of testosterone. As estrogen levels increase with age, testosterone cell stimulation may be locked in the "off" position, thus reducing sexual arousal and sensation and causing the loss of libido so common in aging men (94, 99, 259).

High serum levels of estrogen also trick the brain into thinking that enough testosterone is being produced, further slowing the natural production of testosterone. This happens when estrogen saturates testosterone receptors in the hypothalamus region of the brain. The saturated hypothalamus then stops sending out a hormone to the pituitary gland to stimulate secretion of luteinizing hormone that the gonads require to produce testosterone. High estrogen can thus shut down the normal testicular production of testosterone (1, 53, 54, 271-277).

One further complication of excess estrogen is that it increases the body's production of sex hormone-binding globulin (SHBG). SHBG binds free testosterone in the blood and makes it unavailable to cell receptor sites (51, 52, 55, 56).

Based on the multiple deleterious effects of excess estrogen in men, aggressive action should be taken to reduce estrogen to a safe range if a blood test reveals elevated levels. We will discuss the appropriate blood tests and steps that can be taken to lower estrogen levels later in this protocol.

THE CRITICAL IMPORTANCE OF FREE TESTOSTERONE

Testosterone is much more than a sex hormone. There are testosterone receptor sites in cells throughout the body, most notably in the brain and heart (60-180). Youthful protein synthesis for maintaining muscle mass and bone formation requires testosterone (67, 69, 81). Testosterone improves oxygen uptake throughout the body, helps control blood sugar, regulates cholesterol, and maintains immune surveillance (82, 83). The body requires testosterone to maintain youthful cardiac output and neurological function (58, 65). Testosterone is also a critical hormone in the maintenance of healthy bone density (59, 66, 67, 84-86), muscle mass, and red blood cell production (67, 69, 91-93, 98).

Of critical concern to psychiatrists are studies showing that men with depression have lower levels of testosterone than do control subjects. For some men, elevating free testosterone levels could prove to be an effective antidepressant therapy. There is a basis for free testosterone levels being measured in men with depression and for replacement therapy being initiated if free testosterone levels are low normal or below normal.

Testosterone is one of the most misunderstood hormones. Body builders tarnished the reputation of testosterone by putting large amounts of synthetic testosterone drugs into their young bodies. Synthetic testosterone abuse can produce detrimental effects (34), but this has nothing to do with the benefits a man over age 40 can enjoy by properly restoring his natural testosterone to a youthful level.

Conventional doctors have not recommended tes-tosterone replacement therapy because of an erroneous concern that testosterone causes prostate cancer. As we will later show, fear of prostate cancer is not a scientifically valid reason to avoid testosterone modulation therapy.

Another concern that skeptical physicians have about prescribing testosterone replacement therapy is that some poorly conducted studies showed it to be ineffective in the long-term treatment of aging. These studies indicate anti-aging benefits when testosterone is given, but the effects often wear off. What physicians fail to appreciate is that exogenously administered testosterone can convert to estrogen in the body. The higher estrogen levels may negate the benefits of the exogenously administered testosterone. The solution to the estrogen-overload problem is to block the conversion of testosterone to estrogen in the body.

Numerous studies show that maintaining youthful levels of free testosterone can enable the aging man to restore strength, stamina, cognition, heart function, sexuality, and outlook on life, that is, to alleviate depression. A study in Drugs and Aging (1999) suggested that androgen therapy can result in polycythemia (increased numbers of red blood cells) causing an increase in blood viscosity and risk of clotting (303). For many aging men, however, borderline anemia is a greater concern than red blood cell overproduction. When men are deprived of testosterone during prostate cancer therapy, anemia frequently manifests. Life Extension has not seen cases in which polycythemia developed in men taking enough tes-tosterone to restore physiological youthful ranges.

In other words, too much testosterone could cause problems, but replacing testosterone to that of a healthy 21-year-old should not produce the side effects that some doctors are unduly concerned about. As you will read in the section entitled "Testosterone and the Heart," it appears that testosterone replacement therapy provides significant beneficial effects against cardiovascular disease.

Why Testosterone Levels Decline

Testosterone production begins in the brain. When the hypothalamus detects a deficiency of testosterone in the blood, it secretes a hormone called gonadotrophin-releasing hormone to the pituitary gland. This prompts the pituitary to secrete luteinizing hormone (LH), which then prompts the Leydig cells in the testes to produce testosterone.

In some men, the testes lose their ability to produce testosterone, no matter how much LH is being produced. This type of testosterone deficiency is diagnosed when blood tests show high levels of LH and low levels of testosterone. In other words, the pituitary gland is telling the testes (by secreting LH) to produce testosterone, but the testes have lost their functional ability. So the pituitary gland vainly continues to secrete LH because there is not enough tes-tosterone in the blood to provide a feedback mechanism that would tell the pituitary to shut down. In other cases, the hypothalamus, or pituitary gland, fails to produce sufficient amounts of LH, thus preventing healthy testes from secreting testosterone. Blood testing can determine whether sufficient amounts of LH are being secreted by the pituitary gland and help determine the appropriate therapeutic approach. If serum (blood) testosterone levels are very low, it is important to diagnose the cause, but no matter what the underlying problem, therapies exist today to safely restore testosterone to youthful levels in any man (who does not already have prostate cancer).

As indicated earlier, a major problem that aging men face is not low production of testosterone, but excessive conversion of testosterone to estrogen. Specific therapies to suppress excess estrogen and boost free testosterone back to youthful physiological levels will be discussed later.

The Effects of Testosterone on Libido

Sexual stimulation and erection begin in the brain when neuronal testosterone-receptor sites are prompted to ignite a cascade of biochemical events that involve testosterone-receptor sites in the nerves, blood vessels, and muscles. Free testosterone promotes sexual desire and then facilitates performance, sensation, and the ultimate degree of fulfillment.

Without adequate levels of free testosterone, the quality of a man's sex life is adversely affected and the genitals atrophy. When free testosterone is restored, positive changes can be expected in the structure and function of the sex organs. (It should be noted that

sexual dysfunction can be caused by other factors unrelated to hormone imbalance. An example of such a factor is arteriosclerotic blockage of the penile arteries.)

The genital-pelvic region is packed with testosterone receptors that are ultra-sensitive to free testosterone-induced sexual stimulation. Clinical studies using tes-tosterone injections, creams, or patches have often failed to provide a long-lasting, libido-enhancing effect in aging men. We now know why. The testosterone can be converted to estrogen. The estrogen is then taken up by testosterone receptor sites in cells throughout the body. When an estrogen molecule occupies a testosterone receptor site on a cell membrane, it blocks the ability of serum testosterone to induce a healthy hormonal signal. It does not matter how much serum free testosterone is available if excess estrogen is competing for the same cellular receptor sites.

Estrogen can also increase the production of SHBG, which binds the active free testosterone into an inactive "bound testosterone." Bound testosterone cannot be picked up by testosterone receptors on cell membranes. For testosterone to produce long-lasting, libido-enhancing effects, it must be kept in the "free" form (not bound to SHBG) in the bloodstream. It is also necessary to suppress excess estrogen because this hormone can compete for testosterone receptor sites in the sex centers of the brain and the genitals.

Restoring youthful hormone balance can have a significant impact on male sexuality (99-102).

Testosterone and the Heart

Normal aging results in the gradual weakening of the heart, even in the absence of significant coronary artery disease. If nothing else kills the elderly male, his heart just stops beating at some point.

Testosterone is a muscle-building hormone, and there are many testosterone-receptor sites in the heart (57). The weakening of the heart muscle can sometimes be attributed to testosterone deficiency (103-108).

Testosterone is not only responsible for maintaining heart muscle protein synthesis, it is also a promoter of coronary artery dilation (109-113) and helps to maintain healthy cholesterol levels (81-114).

There are an ever-increasing number of studies indicating an association between high testosterone and low cardiovascular disease rates in men. In the majority of patients, symptoms and EKG measurements improve when low testosterone levels are corrected. One study showed that blood flow to the heart improved 68.8% in those receiving testosterone therapy. In China, doctors are successfully treating angina with testosterone therapy (9, 115, 116).

The following list represents the negative effects of low testosterone on cardiovascular disease:

Cholesterol, fibrinogen, triglycerides, and insulin levels increase

Coronary artery elasticity diminishes (30-33)

Blood pressure rises

Human growth hormone (HGH) declines (weakening the heart muscle)

Abdominal fat increases (increasing the risk of heart attack)

Those with cardiovascular disease should have their blood tested for free testosterone and estrogen. Some men (with full cooperation from their physicians) may be able to stop taking expensive drugs to stimulate cardiac output, lower cholesterol, and keep blood pressure under control if they correct a testosterone deficit or a testosterone-estrogen imbalance. A compelling study of 1100 men showed that those with serum dehydroepiandrosterone-sulfate (DHEA-S) in the lowest quarter < 1.6 mcg/mL) were significantly more likely to incur symptoms of heart disease (295), and in a review of several studies, other authors have confirmed this association (296). Dehydroepiandrosterone (DHEA) is produced by the adrenal gland and is a precursor hormone for the manufacture of testosterone (see the DHEA Replacement Therapy protocol).

Despite numerous studies substantiating the beneficial effects of testosterone therapy in treating heart disease, conventional cardiologists continue to overlook the important role this hormone plays in keeping their cardiac patients alive (9, 30, 31, 77, 93, 111-113, 115, 116, 261-270).

Testosterone and the Prostate Gland

Many doctors will tell you that testosterone causes prostate disease. The published scientific literature indicates otherwise.

As readers of Life Extension Magazine learned in late 1997, estrogen has been identified as a primary culprit in the development of benign prostatic hyperplasia (BPH). Estrogen has been shown to bind to SHBG in the prostate gland and cause the proliferation of epithelial cells in the prostate (124, 182-184). This is corroborated by the fact that as men develop benign prostate enlargement, their levels of free testosterone plummet, although their estrogen levels remain the same or are rising. As previously discussed, aging men tend to convert their testosterone into estrogen. The published evidence

shows that higher serum levels of testosterone are not a risk factor for developing benign prostate disease (8, 36, 41, 117-137).

The major concern that has kept men from restoring their testosterone to youthful levels is the fear of prostate cancer. The theory is that since most prostate cancer cell lines need testosterone to proliferate, it is better not to replace the testosterone that is lost with aging. The problem with this theory is that most men who develop prostate cancer have low levels of tes-tosterone, and the majority of published studies show that serum testosterone levels do not affect one's risk for contracting prostate cancer.

Because there is such a strong perception that any augmentation of testosterone can increase the risk of prostate cancer, we did a MEDLINE search on all the published studies relating to serum testosterone and prostate cancer. The abstracts at the end of this protocol provide quotations from the published literature as it relates to the issue of whether testosterone causes prostate disease. Of the 27 MEDLINE studies found, five studies indicated that men with higher testosterone levels had a greater incidence of prostate cancer, whereas 21 studies showed that testosterone was not a risk factor and one study was considered neutral. Before starting a testosterone replacement program, men should have a serum PSA test and a digital rectal exam to rule out prostate cancer. Nothing is risk free. A small minority of men with low testosterone and prostate cancer will not have an elevated PSA or palpable lesion detectable by digital rectal exam. If these men use supplemental testosterone, they risk an acute flare-up in their disease state. That is why PSA monitoring is so important every 30-45 days during the first 6 months of any type of testosterone augmentation therapy. If an underlying prostate cancer is detected because of testosterone therapy, it is usually treatable by nonsurgical means.

Please remember that testosterone does not cause acute prostate cancer, but if you have existing prostate cancer and do not know it, testosterone administration is likely to boost PSA sharply and provide your doctor with a quick diagnosis of prostate cancer (and an opportunity for very early treatment). We acknowledge that some aging men will not want to take this risk.

As stated above, the MEDLINE score was 21 to 5 against the theory that testosterone plays a role in the development of prostate cancer. None of these studies took into account the prostate cancer prevention effects for men who take lycopene, selenium, and vitamins A and E, nor did they factor in possible prostate disease preventives such as saw palmetto, nettle, soy, and pygeum (42-44, 145-170, 172).

In the book, Maximize Your Vitality & Potency, a persuasive case is made that testosterone and DHEA actually protect against the development of both benign and malignant prostate disease. Dr. Wright also points out that natural therapies, such as saw palmetto, nettle, and pygeum, provide a considerable degree of protection against the alleged negative effects that higher levels of testosterone might have on the prostate gland.

We eagerly await the results of more studies, but the fear of developing prostate cancer in the future should not be a reason to deprive your body today of the life-saving and life-enhancing benefits of restoring a youthful hormone balance.

Once a man has prostate cancer, testosterone therapy cannot be recommended because most prostate cancer cells use testosterone as a growth promoter. Regrettably, this denies prostate cancer patients the wonderful benefits of testosterone therapy. Men with severe BPH should approach testosterone replacement cautiously. It would be prudent for those with BPH who are taking testosterone replacement therapy to also use the drug Proscar (finasteride) to inhibit 5-alpha-reductase levels, thereby suppressing the formation of dihydrotestosterone (DHT) (171-182). DHT is 10 times more potent than testosterone in promoting prostate growth, and suppressing DHT is a proven therapy in treating benign prostate enlargement. Saw palmetto extract suppresses some DHT in the prostate gland, but its effectiveness in alleviating symptoms of BPH probably has more to do with its:

blocking of alpha-adrenergic receptor sites on the sphincter muscle surrounding the urethra. (This is how the drug Hytrin works.)

inhibition of estrogen binding to prostate cells (such as nettle)

inhibition of the enzyme 3-ketosteroid (which causes the binding of DHT to prostate cells)

anti-inflammatory effect on the prostate

Note: Men with severe BPH may also consider using the drug Arimidex (0.5 mg twice a week) to suppress excess levels of estrogen. Estrogen can worsen BPH and supplemental testosterone can elevate estrogen if an aromatase-inhibiting drug such as Arimidex is not used.

It is unfortunate that many people still think that restoring testosterone to youthful levels will increase the risk of prostate disease. This misconception has kept many men from availing themselves of this life-enhancing and life-saving hormone.

Although it is clear that excess estrogen causes benign prostate enlargement, the evidence for excess estrogen's role in the development of prostate cancer is uncertain (8, 41, 117-134, 182-217, 236). Some studies show that elevated estrogen is associated with increased prostate cancer risk, while other studies contradict this finding. For more information on testosterone, estrogen, and the prostate gland, refer to the February 1999 issue of Life Extension Magazine (182-217, 306).

Testosterone and Depression

A consistent finding in the scientific literature is that testosterone replacement therapy produces an increased feeling of well-being. Published studies show that low testoster-

one correlates with symptoms of depression and other psychological disorders (94-97, 272).

A common side effect of prescription antidepressant drugs is the suppression of libido. Those with depression either accept this drug-induced reduction in quality of life, or get off the antidepressant drugs so they can at least have a somewhat normal sex life. If more psychiatrists tested their patients' blood for free testosterone and prescribed natural testosterone therapies to those with low free testosterone, the need for libido-suppressing antidepressant drugs could be reduced or eliminated. As previously described, tes-tosterone replacement often enhances libido, the opposite effect of most prescription antidepressants.

One study showed that patients with major depression experienced improvement that was equal to that achieved with standard antidepressant drugs (97).

Androderm is one of several natural testosterone-replacement therapies that can be prescribed by doctors. A 12-month clinical trial using this FDA-approved drug resulted in a statistically significant reduction in the depression score (6.9 before versus 3.9 after). Also noted were highly significant decreases in fatigue: from 79% before the patch to only 10% after 12 months (218).

According to Jonathan Wright, M.D., co-author of Maximize Your Vitality & Potency, the following effects have been reported in response to low testosterone levels (305):

Loss of ability to concentrate

Moodiness and emotionality

Touchiness and irritability

Great timidity

Feeling weak

Inner unrest

Memory failure

Reduced intellectual agility

Passive attitudes

General tiredness

Reduced interest in surroundings

Hypochondria

The above feelings can all be clinical symptoms of depression, and testosterone replacement therapy has been shown to alleviate these conditions. Testosterone thus has exciting therapeutic potential in the treatment of depression in men.

Testosterone and Mental Decline

Evidence indicates that low levels of testosterone may contribute to memory impairment and increase the vulnerability of the brain to Alzheimer's and related disorders. Beta-amyloid, a peptide that may accumulate in certain regions of the aging brain, is implicated in the development of Alzheimer's disease. Researchers have found that testosterone exerts neuroprotective benefits from the effects of toxic beta-amyloid. An article published in Brain Research describes a study in which cultured neurons were exposed to beta-amyloid in the presence of testosterone. The resulting toxicity from beta-amyloid was significantly reduced by testosterone through a rapid estrogen-independent mechanism (317).

Other researchers have explored the mechanism by which testosterone may exert its protective effect in Alzheimer's disease. Their research in animals shows that testosterone decreases the secretion of harmful beta-amyloid and increases the secretion of the non-amyloidogenic APP fragment, sbetaAPPalpha, indicating that testosterone supplementation in elderly men may be beneficial in the treatment of Alzheimer's (318, 319).

Another published study examined the neuroprotective effects of estradiol, testosterone, epi-testosterone, and methyl-testosterone in neurons induced to undergo apoptosis by serum deprivation. Physiologic concentrations of testosterone were found to be neuroprotective, similar to estradiol. Methyl-testosterone showed an effect that was delayed in time, suggesting that a metabolite may be the active agent. Epi-testosterone showed a slight neuroprotective effect but not through the androgen receptor. The authors concluded that androgens may be of therapeutic value against Alzheimer's disease in aging males (302).

Researchers in Oxford, England found that lower levels of testosterone were present in men with Alz-heimer's as opposed to controls. These results were independent of confounding factors such as age, body mass index, education, smoking, alcohol abuse, and endocrine therapy. The authors recommended further studies to determine whether low levels of total tes-tosterone precede or follow the onset of Alzheimer's disease.

Testosterone and Aging

We know that many of the degenerative diseases of aging in men, such as Type-II diabetes, osteoporosis, and cardiovascular disease, are related to a testosterone deficiency. We also know that common characteristics of middle age and older age, such as depression, abdominal fat deposition, muscle atrophy, low energy, and cognitive decline, are also associated with less than optimal levels of free testosterone (58, 219)

A consistent pattern that deals with fundamental aging shows that low testosterone causes excess production of a dangerous hormone called cortisol. Some antiaging experts call cortisol a "death hormone" because of the multiple degenerative effects that it produces. Some of these effects are immune dysfunction, brain cell injury, and arterial wall damage.

A group of scientists conducted two double-blind studies in which they administered supplemental testosterone to groups of aging men and observed the typical responses of lower levels of cholesterol, glucose, and triglycerides, reductions in blood pressure, and decreased abdominal fat mass. The scientists showed that excess cortisol suppressed testosterone and growth hormone production and that the administration of testosterone acted as a "shield" against the overproduction of cortisol in the adrenal gland. Another study published in 1999 on testosterone and atherosclerosis in men showed a statistically significant correlation between low testosterone and excess serum insulin. It was noted that an elevated estradiol to testosterone ratio is connected with insulin resistance.

It is important to point out that testosterone is an anabolic (or protein building) hormone while cortisol is a catabolic hormone that breaks down proteins in the body. Normal aging consists of a progressive decrease in free testosterone with a marked increase in cortisol. As men age past 40, cortisol begins to dominate, and the catabolic effects associated with growing older begin to dominate.

These findings have significant implications in the battle to maintain youthful hormone balance for the purpose of staving off normal aging and its associated degenerative diseases.

THE TESTOSTERONE DOCTOR

Eugene Shippen, M.D. (co-author of The Testosterone Syndrome, 1998) provided extensive evidence documenting the pathology of the testosterone deficiency syndrome in men. Some excerpts follow from a lecture presented by Dr. Shippen at the American Academy for Anti-Aging Medicine Conference in December 1998:

First, testosterone is not just a "sex hormone." It should be seen as a "total body hormone," affecting every cell in the body. The changes seen in aging, such as the loss of lean body mass, the decline in energy, strength, and stamina, unexplained depression, and decrease in sexual sensation and performance, are all directly related to testosterone deficiency. Degenerative diseases such as heart disease, stroke, diabetes, arthritis, osteoporosis, and hypertension are all directly or indirectly linked to testosterone decline (220-223). Secondly, testosterone also functions as a pro-hormone. Local tissue conversion to estrogens, dihydrotestosterone (DHT), or other active metabolites plays an important part in cellular physiology.

Excess estrogen seems to be the culprit in prostate enlargement. Low testosterone levels are in fact associated with more aggressive prostate cancer (201, 205, 224-229). While fear of prostate cancer keeps many men from testosterone replacement, it is in fact testosterone deficiency that leads to the pathology that favors the development of prostate cancer.

Testosterone improves cellular bioenergetics. It acts as a cellular energizer. Since testosterone increases the metabolic rate and aerobic metabolism, it also dramatically improves glucose metabolism and lowers insulin resistance (76, 80, 230).

Another myth is that testosterone is bad for the heart. Actually, low testosterone correlates with heart disease more reliably than does high cholesterol (19, 231). Testosterone is the most powerful cardiovascular protector for men. Testosterone strengthens the heart muscle (232); there are more testosterone receptors in the heart than in any other muscle. Testosterone lowers LDL cholesterol and total cholesterol (69, 81, 111) and improves every cardiac risk factor. It has been shown to improve or eliminate arrhythmia and angina (9, 106, 113-115, 233, 266). Testosterone replacement is the most underutilized important treatment for heart disease.

Testosterone shines as a blood thinner, preventing blood clots (32). Testosterone also helps prevent colon cancer (235, 236).

Previous research on testosterone used the wrong form of replacement. Injections result in initial excess of testosterone, with conversion of excess to estrogens. Likewise, total testosterone is often measured instead of free testosterone, the bioavailable form. Some studies do not last long enough to show improvement. For instance, it may take six months to a year before the genital tissue fully recovers from atrophy caused by testosterone deficiency, and potency is restored.

Physicians urgently need to be educated about the benefits of testosterone and the delicate balance between androgens (testosterone) and estrogens. Each individual has his or her own pattern of hormone balance; this indicates that hormone replacement should be individualized and carefully monitored.

OBESITY AND HORMONE IMBALANCE

A consistent finding in the scientific literature is that obese men have low testosterone and very high estrogen levels. Central or visceral obesity ("pot belly") is recognized as a risk factor for cardiovascular disease and Type-II diabetes. Research has shed light on subtle hormone imbalances of borderline character in obese men that often fall within the normal laboratory reference range. Boosting tes-tosterone levels seems to decrease the abdominal fat mass, reverse glucose intolerance, and reduce lipoprotein abnormalities in the serum. Further analysis has also disclosed a regulatory role for testosterone in counteracting visceral fat accumulation. Epidemiological data demonstrate that relatively low tes-tosterone levels are a risk factor for development of visceral obesity (7, 237).

One study showed that serum estrone and estradiol were elevated twofold in one group of morbidly obese men. Fat cells synthesize the aromatase enzyme, causing male hormones to convert to estrogens (278). Fat tissues, especially in the abdomen, have been shown to literally "aromatize" testosterone and its precursor hormones into potent estrogens (80, 237-242).

Eating high-fat foods may reduce free testosterone levels according to one study that measured serum levels of sex steroid hormones after ingestion of different types of food. High-protein and high-carbohydrate meals had no effect on serum hormone levels, but a fat-containing meal reduced free testosterone levels for 4 hours (243).

Obese men have testosterone deficiency caused by the production of excess aromatase enzyme in fat cells and also from the fat they consume in their diet. The resulting hormone imbalance (too much estrogen and not enough free testosterone) in obese men partially explains why so many are impotent and have a wide range of premature degenerative diseases (45).

FACTORS CAUSING THE ESTROGEN-TESTOSTERONE IMBALANCE IN MEN

If your blood tests reveal high estrogen and low tes-tosterone, here are the common factors involved:

Excess "Aromatase" Enzyme. As men age, they produce larger quantities of an enzyme called aromatase. The aromatase enzyme converts testosterone into estrogen in the body (17, 240, 241, 244, 245). Inhibiting the aromatase enzyme results in a significant decline in estrogen levels while often boosting free testosterone to youthful levels. Therefore, an agent designated as an "aromatase inhibitor" may be of special value to aging men who have excess estrogen.

Liver Enzymatic Activity. A healthy liver eliminates surplus estrogen and sex hormone-binding globulin. Aging, alcohol, and certain drugs impair liver function and can be a major cause of hormone imbalance in aging men. Heavy alcohol intake increases estrogen in men and women (54, 246, 285).

Obesity. Fat cells create aromatase enzyme and especially contribute to the buildup of abdominal fat (241, 242). Low testosterone allows the formation of abdominal fat (47, 239, 248), which then causes more aromatase enzyme formation and thus even lower levels of testosterone and higher estrogen (by aromatizing testosterone into estrogen). It is especially important for overweight men to consider hormone modulation therapy.

Zinc Deficiency. Zinc is a natural aromatase enzyme inhibitor (247). Since most Life Extension Foundation members consume adequate amounts of zinc (30-90 mg a day), elevated estrogen in Foundation members is often caused by factors other than zinc deficiency.

Lifestyle Changes. Lifestyle changes (such as reducing alcohol intake) can produce a dramatic improvement in the estrogen-testosterone balance, but many people need to use aromatase-inhibiting agents to lower estrogen and to improve their liver function to remove excess SHBG. Aromatase converts testosterone into estrogen and can indirectly increase SHBG. SHBG binds to free testosterone and prevents it from exerting its biochemical effects in the body.