

ANDROPAUSE

Male Menopause

Male Hormones and Aging

As men age past year 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. 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 concentration, 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. These symptoms usually start around age 40-50, although with smokers the onset is significantly earlier.

At times to the patient's detriment, 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 35-year-old male.

Too Much Estrogen

The most significant hormone imbalance in aging men is a decrease in free testosterone, while estrogen levels remain the same or increase. As men grow older, they experience a variety of symptoms from 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 .

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. 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).

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. High levels of estrogen have been implicated as a cause of benign prostatic hypertrophy (BPH). 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.

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.

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. Youthful protein synthesis for maintaining muscle mass and bone formation requires testosterone. Testosterone improves oxygen uptake throughout the body, helps control blood sugar, regulates cholesterol, and maintains immune surveillance. The body requires testosterone to maintain youthful cardiac output and neurological function. Testosterone is also a critical hormone in the maintenance of healthy bone density, muscle mass, and red blood cell production.

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, 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.

Many doctors do not recommend testosterone 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, i.e., 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

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risk of clotting. 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. Polycythemia is rare in men replacing testosterone to physiological youthful ranges. If this problem should occur a visit once or twice a year to the Red Cross to donate blood solves the problem.

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 to do so. The pituitary gland vainly continues to secrete LH because there is not enough testosterone 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 have prostate cancer).

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 testosterone 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 sex hormone-binding globulin (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.

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. The weakening of the heart muscle can sometimes be attributed to testosterone deficiency. Testosterone is not only responsible for maintaining heart muscle protein synthesis, it is also a promoter of coronary artery dilation and helps to maintain healthy cholesterol levels.

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.

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

- Cholesterol, fibrinogen, triglycerides, and insulin levels increase
- Blood pressure rises
- Coronary artery elasticity diminishes
- Human growth hormone (HGH) declines (weakening heart muscle).
- Abdominal fat increases (increasing the risk of heart attack).

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.

Testosterone and the Prostate Gland

Many doctors will tell you that testosterone causes prostate disease. The published scientific literature indicates otherwise. Estrogen has been identified as a primary culprit in the development of benign prostate hypertrophy (BPH). Estrogen has been shown to bind to SHBG in the prostate gland and cause the proliferation of epithelial cells in the prostate. This is corroborated by the fact that as men develop benign prostate enlargement, their levels of free testosterone plummet, while their estrogen levels remain the same or are rising. As previously discussed, aging men tend to convert their testosterone into estrogen. The published evidence

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shows that serum levels of testosterone are not a risk factor for developing benign prostate disease.

The major concern that has kept men from restoring their testosterone to youthful levels is 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 testosterone, and the majority of published studies show that serum testosterone levels do not affect one's risk for contracting prostate cancer.

Since 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, 5 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 1 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 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 non-surgical 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). In Dr. Jonathan Wright's 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 benign prostatic hyperplasia (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). DHT is ten 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 saw palmetto's effectiveness in alleviating symptoms of BPH are probably related to other hormone effects.

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.

While 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. Some studies show that elevated estrogen is associated with increased prostate cancer risk, while other studies contradict this finding.

Testosterone and Depression

A consistent finding in the scientific literature is that testosterone replacement therapy produces an increased feeling of well-being. As stated earlier, newly published studies show that low testosterone correlates with symptoms of depression and other psychological disorders.

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 doctors 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, testosterone replacement often enhances libido, the opposite effect of most prescription antidepressants. At least one study showed that patients with major depression experienced improvement that was equal to that achieved with standard antidepressant drugs.

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 vs. 3.9 after). Also noted were highly significant decreases in fatigue: from 79% before the patch to only 10% after 12 months.

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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
- Memory failure
- General tiredness
- Reduced intellectual agility
- 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

New 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. Researchers have found that testosterone exerts neuroprotective benefits from the effects of toxic beta-amyloid.

Researchers in Oxford, England found that lower levels of testosterone were present in men with Alzheimer'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 testosterone 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.

A consistent pattern that deals with fundamental aging shows that low testosterone causes excess production of a dangerous hormone called cortisol. Some anti-aging experts call cortisol a "death

hormone" because of the multiple degenerative effects 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 on testosterone and atherosclerosis in men showed a statistically significant positive correlation between testosterone and 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.

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. New findings have shed light on subtle hormone imbalances of borderline character in obese men and often fall within the normal laboratory reference range. Boosting testosterone 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. Longitudinal epidemiological data demonstrate that relatively low testosterone levels are a risk factor for development of visceral obesity.

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

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.

The fact that most aging men have too much estrogen does not mean it is acceptable for a man to have low estrogen. Estrogen is used by men to maintain bone density, and abnormally low estrogen levels may increase the risk for prostate cancer and osteoporosis. The objective is to achieve hormone balance, not to create sky-high testosterone levels without enough estrogen.

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Forms of Testosterone

Testosterone can be made into pills, injections, rub-on gels, sublingual tablets, patches and suppositories. In general, hormones should not be taken in pill form because of an effect called ‘first-pass phenomenon’ by the liver. When a medication is taken orally, it first goes through the liver where a significant portion of it is de-activated. It can also be transformed into other compounds, which may have harmful effects. These problems can be avoided by using rub-on gels, sublingual(under-the tongue) tablets, patches or injections.

Getting Started

The evaluation for Hormone Replacement includes a complete physical exam and measurement of current hormone levels. With this information, a precise HRT program can be designed around your body’s needs. After starting therapy, hormone levels will be measured periodically to ensure that your hormone levels remain in the ‘youthful’ range.

More Information

The best source for actual case histories of men who successfully used hormone modulation is Dr. Eugene Shippen's book entitled *The Testosterone Syndrome* (260). Dr. Shippen provides many interesting details too numerous to be covered in this concise protocol. Another book, *Maximize Your Vitality & Potency*, by Dr. Jonathan Wright also contains historical and more technical data about the benefits of testosterone that are, again, too numerous to include in this protocol.

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**Portions of this protocol have been excerpted from The Life Extension Foundation’s “Male Hormone Modulation Therapy Protocol”*