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REPORT

Male Menopause

Avoiding andropause with testosterone treatment

By Edward D. Rosick

Menopause, the time in a woman's life of distinct hormonal changes, can be very stressful both on an emotional and physical level. While men feel empathy for their loved ones who are going through this trying period, most men are also inwardly happy they don't have to go through the mood swings, hot flashes, body aches and other effects of declining estrogen and progesterone levels that women face as they enter the fifth and sixth decades of life.^[1] However, just because a man in mid-life does not feel the dramatic changes a woman undergoes doesn't mean that he does not experience hormonal changes.



Andropause—the male menopause

As men reach their 40s, most will start noticing physical and emotional changes. Abdominal fat often takes the place of formally hard muscle, even with regular physical exercise. Eight hours of uninterrupted sleep are less frequent as nocturnal visits to the bathroom to urinate increase in frequency. The thick head of hair that once covered the head becomes gray and thinner. Every-other-night sex may turn into every-other-week sex as both interest and ability to perform decrease. And for men who are in touch with their inner feelings, they may notice that their zest for life has faded away with their libido and hairline.

Many physicians state that these changes in men are an inevitable part of "normal" aging. The idea that there is such a thing as andropause is still thought of as a myth by most mainstream medical doctors. They state that since men don't have a physical signpost (such as the cessation of menstruation seen in women), andropause does not exist. However, even though women have a clear-cut physical demarcation in their lives, other changes of menopause take place over several years. In the case of andropause, it is thought that the majority of physical, mental and emotional changes take place over 10-to-15 years. These changes, which include declines in libido, sexual function, muscle mass and strength, increase in prostate size leading to benign prostatic hypertrophy, along with fatigue and depression, begin around age 40 for most men. It has been estimated by some researchers that today, as many as 25 million American men between 40 and 55 are experiencing signs and symptoms of andropause.

Testosterone—the key to andropause

In women, estrogen and progesterone are the two key hormones that decline during menopause. In men, it is the hormone testosterone that falls most in production as a man ages, and it's thought that this fall is the single most important cause of andropause. Testosterone levels peak in a man at approximately age 30 and then begin a gradual decline.^[2] Some men have low testosterone by age 40. One reason that aging men are not diagnosed as being testosterone deficient is that blood test laboratory reference ranges are age-adjusted to reflect the anticipated reduction in testosterone production. So, when a doctor looks at an aging man's free testosterone blood test result, he often sees it fitting neatly into the standard reference range for a normal aging man. The problem is that normal aging men are expected to have lower testosterone levels, which are far from optimal (youthful) ranges. The optimal testosterone level for most aging males are those of a healthy 21-to-30 year old. Testosterone is vitally important for its anabolic properties, including effects on cholesterol levels, protein breakdown, muscle mass and bone density, and its androgenic effects, including the development and maintenance of male secondary sex characteristics (deep voice, increase in facial and body hair, muscle development) and sexual functions such as libido and erection capability.



Testosterone begins in the brain

While early scientists focused on the testicles as the source of testosterone, medical researchers of today know that the first step in the production of testosterone starts in the brain. This biochemical cascade begins in the part of the brain known as the hypothalamus, which secretes gonadotropin-releasing hormone (GnRH). This hormone then signals the pituitary gland, to make follicle-stimulating hormone (FSH) and lutenizing hormone (LH). Normal levels of FSH prompt the testicles to produce sperm, while LH stimulates the production of testosterone via the Leydig cells in the testicles. While it's been estimated that a man begins life with 700 million Leydig cells, he begins to lose six million of those cells yearly after his twentieth birthday.^[3]

After testosterone is secreted into the bloodstream via the Leydig cells, its fate can follow a few different pathways. Some testosterone attaches to sex hormone binding globulin, or SHBG. Testosterone not bound up with SHBG is known as free testosterone, and it is in this form that it can exert its powerful anabolic and androgenic effects on the human body. Testosterone can also be converted via enzymatic pathways into different hormones. Through the actions of 5-alpha-reductase, an enzyme found in multiple tissues but especially high in the prostate gland, testosterone can be converted into dihydrotestosterone (DHT). Aromatase, an enzyme in skin, fat, bone and brain cells, actually changes testosterone into estrogen. Estrogen (which actually is not just one hormone but several related compounds) has been recently discovered to be important in many physiological functions in men, including maintenance of bone mass and cognitive function.[1]

While some estrogen is essential for health in men, too much of it can be bad, especially when it's in the form of 16-alpha-hydroxyestrone, a breakdown product of estrogen metabolism that has been implicated in cancer. Another estrogen metabolite, 2-hydroxyesterone, is believed to be much less harmful, and in fact, a ratio tilting toward 2-hydroxyesterone is thought to be beneficial.

How testosterone changes in aging men

One change found in aging is in the ratio of free testosterone to testosterone bound to SHBG. In many aging men, especially those who are obese, free testosterone levels drop significantly as the levels of SHBG increase and "bind up" whatever free testosterone is left. As if this news isn't bad enough, there are also steep declines (40% to 75%) in other steroid hormones, including dehydroepiandrosterone (DHEA) and DHEA-sulfate (DHEA-S) seen in men as they age from 20 to 80.[4]



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Testosterone strengthens muscles and bones

One of the most destructive effects of aging is the loss of muscle and bone mass. While the loss of bone mass, or osteoporosis, is now widely recognized as a significant factor in robbing elderly women of their ability to walk, osteoporosis is also a significant health concern for older men. In addition, the loss of muscle tissue, or sarcopenia, is now finally being recognized as a major debilitator of both men and women. In men, both sarcopenia and osteoporosis can be linked to the decline in testosterone and other steroid hormones.



A study of 403 healthy men aged 73-to-94 years, in the *Journal of Endocrinology and Metabolism* examined the hypothesis that the decreases in muscle strength, bone mass and body composition seen in aging males are related to falling testosterone levels.^[5] The researchers measured the men's hormonal levels and ran multiple tests to gauge their body composition, muscle strength and bone mass.

Their findings were that muscle strength and bone mass were at optimal levels in men with the highest levels of free testosterone, leading the authors to state that "a number of clinical problems present in older men may be related to androgen [testosterone] deficiency, including reduced muscle mass, changes in body composition, and loss of BMD [bone mass density]."

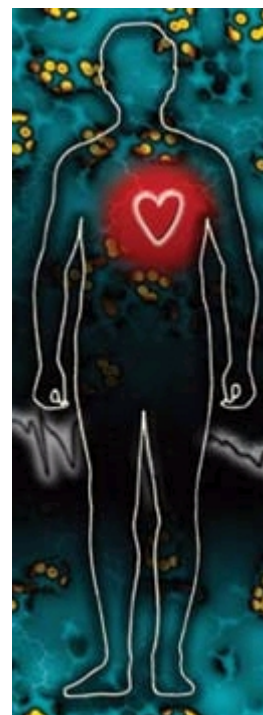
Testosterone—good for your heart and mind

Studies have shown that adequate levels of testosterone are important for maintaining cardiac health and preventing age-related senility. Reports from the oft-cited Rotterdam Study, where researchers examined the association between testosterone levels and cardiac health in 504 men aged 67-to-75, showed that men with higher levels of testosterone had lower levels of coronary artery disease.^[6] As the authors of the study stated, "we found an independent, inverse association between levels of endogenous testosterone and severe aortic atherosclerosis and progression of aortic atherosclerosis in men."

Adequate levels of testosterone are also needed for optimal brain functioning. Multiple studies have confirmed that men who maintain optimal testosterone levels as they age have significantly fewer symptoms of senility compared to men with low levels of testosterone. In a landmark study published in 2002, 407 men aged 50-to-91 were followed for 10 years and were given multiple tests to determine their testosterone levels and cognitive functioning.[7] To quote the authors, "Higher FTI [free testosterone levels] was associated with better scores on visual and verbal memory, visuospatial functioning and visuomotor scanning and a reduced rate of longitudinal decline in visual memory." Furthermore, those randomized, placebo-controlled studies showed that testosterone supplementation improved verbal memory, working memory and visuospatial performance in elderly men.[8-11]

Does testosterone cause prostate cancer?

Ask almost any mainstream physician what causes prostate cancer, the second leading cause of cancer in men, and chances are the answer will be excess testosterone. This is based on research that shows that the removal of a man's testicles (his source of testosterone), either physically or through chemical means, slows (but does not cure) prostate cancer. However, there are a growing number of anti-aging researchers who believe that estrogen and its metabolites, such as 16-alpha-hydroxyesterone, may be more significant in the development of prostate cancer than testosterone. In fact, a recent report made the following statement, which just 10 years ago would have been considering heresy by mainstream medicine: "There is no evidence that exogenous testosterone stimulates the development of severe symptomatic prostate hyperplasia, nor does exogenous testosterone seem to increase the risk of clinically significant prostate cancer."[11]



The concept that estrogen, rather than testosterone, is one of the prime hormonal initiators of prostate cancer is based on the fact that, while testosterone levels are highest in young men, prostate cancer is essentially never seen in this population. It's only in older men, who have lower levels of testosterone but higher levels of estrogen and its breakdown products, that prostate cancer is a significant health threat. Animal studies have shown that male rats treated with testosterone alone showed significantly less prostate growth when compared to animals treated with both testosterone and estrogen.[12] A study published in 1993 showed that men treated with DHT (which cannot convert to estrogen) actually showed a reduction in the size of their prostate with no sign of prostate cancer.[13] A more recent article in the World Journal of Urology sums up the estrogen/ prostate cancer link quite succinctly: "Estrogenic stimulation through estrogen receptor alpha in a milieu of decreasing androgens [testosterone] contributes significantly to the genesis of benign prostatic

hyperplasia, prostate dysplasia, and prostate cancer."[14]

Environmental toxins may affect testosterone

There's evidence that chemicals in the environment known as endocrine disrupters may be causing a decrease in testosterone. Endocrine disrupters interfere with the normal functioning of the endocrine system. Scientists in Britain have done research in rats on the estrogen-mimicking chemical HPTE, which is a metabolite of the commonly used pesticide methoxychlor. These scientists have shown that HPTE causes a decrease in, testosterone production from Leydig cells.[15] Other compounds, such as those found in plastic bottles that hold everything from bottled water to laundry detergent, are man-made mimics of estrogen.[16]

Maintaining optimal health and sexuality

There are multiple ways in which men can combat many of the deleterious effects of aging including andropause. It's vitally important to eat a well-balanced diet full of fresh, organically grown fruits and vegetables to help avoid endocrine-disrupting chemicals. Second, a multivitamin that contains a full range of antioxidants and other essential nutrients should be part of every man's diet, whether he is 20 or 90 years old. Third, engaging in a daily exercise regime and keeping your weight at a lean level is important in aging with vim and vigor intact.



Physical exercise increases testosterone

Regular high-intensity exercise has been shown in multiple studies to contribute to keeping a man's testosterone at optimal levels. A study published in 1999 examined how heavy resistance training in both young (23-to-35 year old) and older (58-to-65 year old) men affected their testosterone levels.

[17] In both the younger and older groups, there was a statistically significant increase in testosterone levels after exercise. A more recent study, again showed that strength training in middle-aged men (44-to-48) caused an increase in their levels of free testosterone.[18]



High-protein diets

It's well known to weightlifters that a diet high in protein is key to adding muscle mass. Unfortunately, many middle-aged and elderly men (and women) probably aren't getting enough protein in their diet to maintain muscle mass and stave off sarcopenia. In fact, a study that looked at the dietary habits of aging Americans came to the conclusion that "the RDA [recommended daily allowance] for protein may not be adequate to completely meet the metabolic and physiological needs of virtually all older people."^[19] Unfortunately for aging men, not getting enough protein may also mean a hit to their testosterone levels. A study found that "diets low in protein in elderly men [40-to-70 years old] may lead to elevated SHBG levels and decreased testosterone availability. The decrease in bioavailable testosterone can then result in declines in sexual function and muscle and red cell mass, and contribute to the loss of bone density."^[20]

Soy and fish oil keep estrogen and SHBG in check

As stated earlier, elderly men often have an increase in unhealthy levels of SHBG and estrogen via activity of the aromatase enzyme, both of which can lead to a decrease in testosterone levels. Two recent studies have shown some natural ways in which men can help tilt the ratio back in favor of

testosterone. In one study of 97 men, 49-to-72 years of age, the researchers showed that men who had high levels of soy intake had lower levels of estradiol (a form of estrogen) when compared to men with lower levels of soy intake.^[21] They postulated that this beneficial inverse relationship could be due to inhibition of the aromatase enzyme by soy and soy-based food products. Another study examined the effects of the essential fatty acids EPA and DHA (which are found in high concentrations in fish) on SHBG levels in men 43-to-88 years of age.^[22] After controlling for other variables, the researchers came to the conclusion that both EPA and DHA decreased levels of SHBG in middle-aged and elderly men.

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Nutrient supplements can boost testosterone

While the above studies emphasize the importance of exercise and proper diet, the judicious use of certain nutrient supplements can also help to augment a man's testosterone levels as he ages. While there's no magic supplement on the market today that can turn a 50-year-old man into his 20-year-old former self, there are some safe, well-studied supplements that every man facing andropause should consider adding to his daily regime.



Zinc—essential for sexual health

One supplement that is essential for maintaining a man's sexual functioning is zinc. This mineral is involved in almost every aspect of male reproduction, including testosterone metabolism, sperm formation and sperm motility. There have been multiple studies on the effectiveness of zinc in treating male infertility due to low testosterone levels.^[23,24] A prime example of the usefulness of zinc was illustrated in a study of 37 infertile men with decreased testosterone levels and associated low sperm counts.^[25] The men were given 60 mg of zinc daily for 45 to 50 days. In 22 patients, testosterone levels significantly increased and mean sperm count rose from 8 to 20 million.

Indole-3-carbinol maintains hormonal balance

Getting an adequate intake of indole-3-carbinol (I3C), either through vegetables like broccoli, brussels sprouts and cabbage or via supplements, may prove helpful in keeping estrogen levels in check and decreasing the risk of prostate cancer. Studies have demonstrated that I3C increases the ratio of 2-hydroxyesterone to 16-alpha-hydroxyesterone, thereby causing a decrease in

“bad” estrogen and an increase in “good” estrogen. For men, this very well might mean a decrease in prostate cancer. In a study done last year that examined the association of prostate cancer risk with estrogen metabolism, the authors stated that “results of this case-control study suggest that the estrogen metabolic pathway favoring 2-hydroxylation over 16-alpha-hydroxylation may reduce risk of clinically evident prostate cancer.”^[26]

DHEA may help keep testosterone at optimal levels

Besides a decline in testosterone levels, there is also a decline seen in dehydroepiandrosterone (DHEA) in aging males. DHEA, a steroid hormone secreted by the adrenal glands in both men and women, is transformed into a variety of important hormones, including estrogen. Several studies have shown that restoring DHEA to youthful levels in older adults increases both physical and mental well being. In a randomized, placebo-controlled trial of 50 mg of DHEA given every night for six months, both male and female patients (aged 40-to-70) who took DHEA had statistically significant improvements in their energy levels, quality of sleep, mood, and ability to handle stress.^[27] Another study measured DHEA levels in 36 men aged 90 to 103 and found that patients who had the highest levels of DHEA had the highest levels of normal daily activities.^[28]



Supplemental testosterone—the key to overcoming andropause?



In any middle-aged man who is experiencing symptoms of andropause, a test of his testosterone levels, both total and free, is essential. If testosterone levels are indeed low, then the use of exogenous, or supplemental, testosterone should be considered. Fortunately, today there are many ways, from gels to patches, that a man with andropause can increase his testosterone levels. And, just as fortunately, there is now a growing body of evidence to lend credence to the idea of supplementing testosterone in older men.

In terms of sexual functioning, testosterone supplementation has been shown in multiple studies to improve both libido and erection capability.^[29-31] Other studies have shown that supplemental testosterone can also alleviate many of the other symptoms of andropause, including depression, loss of energy and LDL cholesterol levels, which are often a marker of

heart disease.^[32,33]

Testosterone supplementation can also help reverse the potentially devastating effects of sarcopenia and osteoporosis. Supplemental testosterone has been shown to increase bone mass of the lumbar spine in elderly men.^[34] A study done in 1995 showed that testosterone given to six men aged 64-to-69 who had low testosterone levels caused a measurable increase in skeletal muscle protein synthesis and strength.^[35] A more recent study examined the effects of testosterone supplementation on 10 men 60-to-78 years in age, in a double-blind trial.^[36] The results showed that testosterone supplementation increased fat-free mass, improved exercise endurance time and improved balance. Until anti-aging researchers finally figure out the secrets of aging, none of us can stop the advance of time, and with it, andropause. However, what we can do is treat ourselves with respect by eating a wholesome, organically based diet, exercising on a regular basis and taking supplements like those discussed above which can stop the hands of time from taking away our vitality and zest for life.



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