

LE Magazine July 2008

## REPORT

### Optimizing Testosterone Levels in Aging Men

By Paul D. Navar, MD

By the age of 80, a man's testosterone level may only be 20% of what it was in his youth. This decline in testosterone occurs gradually, starting as early as his mid-30s, and can result in an increased risk of life-threatening illnesses such as obesity, diabetes, and heart disease.

Testosterone deficiency can also lead to a number of disturbing symptoms, including loss of stamina and lean muscle mass, reduced libido, anxiety, depression, and cognitive decline. Known as the andropause, these changes are the male equivalent of female menopause. Unlike menopause, however, the drop in testosterone is so gradual that the symptoms of andropause appear over a longer period of time and are often ignored for a while or are attributed to "getting older."



The good news is that many symptoms of testosterone deficiency can be reversed by restoring youthful testosterone levels in a variety of ways. Millions of men are now using testosterone-building supplements and even testosterone itself for this reason.

#### RECOGNITION OF AN INCREASINGLY PREVALENT PROBLEM

Testosterone is the primary male sex hormone that is vital for sustaining proper erectile function and libido. It is also critically involved in building muscle, burning fat, and supporting endothelial function, energy level, mood, immune function, and bone density.

Millions of men in the United States suffer from the effects of low testosterone levels. This population of testosterone deficient men will only grow in the future, as the number of aging American men increases.<sup>1</sup>

Low testosterone is associated with increased morbidity and mortality. A recent study found that men with lower testosterone levels were more likely to die from cardiovascular disease and all causes compared with men who had higher levels. The authors concluded that low testosterone may be a predictive marker for those at high risk of cardiovascular disease.<sup>2</sup> Another review from the Baylor College of Medicine reported that there is a higher prevalence of depression, coronary heart disease, osteoporosis, fracture rates, frailty, and even dementia with low testosterone states.<sup>3</sup>

You might now be asking yourself these questions—Why hasn't my doctor discussed these risks with me and why haven't I been tested for low testosterone levels? Why am I just hearing about this?

#### TESTOSTERONE SUPPLEMENTS — AN UNDESERVED SHADY PAST

The medical community has been slow to recognize the consequences of low testosterone levels in aging males and, in fact, wrongly believes that restoring youthful levels of testosterone is dangerous and unwarranted. Back in the mid-1900s, some drug companies sold a synthetic and chemically altered testosterone called methyltestosterone. They pawned this chemical off as real testosterone, even though it does not naturally exist in the human body. After several years on the market, some men taking this particular chemical developed liver cancer.<sup>4,5</sup> "Testosterone therapy" was then declared to be dangerous, and research on testosterone fell by the wayside.

While testosterone is a member of the group of compounds known as “anabolic steroids,” it is different and less potent than the illegal synthetic compounds that have been taken in excessive doses and abused. Beginning in the late 1980s, overambitious and unscrupulous professional athletes began taking illegal anabolic steroids to gain an unfair competitive edge. Unfortunately, this abuse has wrongly clouded the important health benefits of prescribing testosterone therapy to correct its decline associated with aging and other diseases. In response to the sports abuse issue, federal law has made testosterone a controlled substance just like narcotics and amphetamines. Illegal-use penalties can be severe for any doctor who improperly prescribes anabolic steroids. Although this has made some doctors reluctant to prescribe testosterone, medical prescribing of the hormone jumped by 50% in four years from 2001 to a total of 2.3 million prescriptions in 2005.<sup>6</sup> Some physicians do therefore appear to be increasingly recognizing the consequences of low testosterone levels in aging males.



## EVOLVING OPINIONS ON TESTOSTERONE REPLACEMENT

In November 2003, the Institute of Medicine declared that “existing scientific **evidence does not justify claims that testosterone treatments can relieve or prevent certain age-related problems in men.**” Most age-management physicians today strongly disagree with that statement. There are hundreds of studies in the medical literature showing the health benefits and safety of testosterone therapy.

In 2007, Drs. Miner and Seftel published a review of the medical literature on testosterone since the 2003 Institute of Medicine Report.<sup>7</sup> The summary of their article states: “**Recent studies have demonstrated that hypogonadism [low testosterone] in men may be more prevalent than previously thought, is strongly associated with metabolic syndrome, and may be a risk factor for type 2 diabetes and cardio-vascular disease. Clinical studies have shown that testosterone replacement therapy in hypogonadal men improves metabolic syndrome indicators and cardiovascular risk factors. Maintaining testosterone concentrations in the normal range has been shown to contribute to bone health, lean muscle mass, and physical and sexual function, suggesting that testosterone replacement therapy may help to prevent frailty in older men. Based on current knowledge, testosterone replacement therapy is unlikely to pose major health risks in patients without prostate cancer and may offer substantial health benefits.**”

## TESTOSTERONE AND CARDIOVASCULAR HEALTH

Let’s take a closer look at what the medical literature says about the specific benefits of testosterone restoration. Many studies have shown an association between low testosterone levels and a higher prevalence of coronary artery disease<sup>8-10</sup> and aortic atherosclerosis.<sup>10</sup> Lower testosterone levels are also associated with reduced pumping ability of the heart.<sup>9</sup>

Recent studies suggest that testosterone-replacement may improve the symptoms of coronary artery disease. A placebo-controlled crossover study in men with ischemic heart disease and low testosterone levels reported that exercise time and the time to development of ischemic changes on a treadmill test were both increased with testosterone-replacement therapy.<sup>11</sup> Another placebo-controlled study found that 12 weeks of oral testosterone-replacement therapy improved the ability of the brachial artery to dilate in men with coronary artery disease,<sup>12</sup> suggesting an improvement in endothelial function. These and other medical studies provide mounting evidence of the clinical benefits of testosterone-replacement therapy in men with coronary artery disease.



## TESTOSTERONE AND INSULIN RESISTANCE/ DIABETES

Type 2 diabetes is reaching epidemic proportions in America today. Likewise, metabolic syndrome—a condition marked by insulin resistance that dramatically increases the risk of heart disease and diabetes—is becoming increasingly more prevalent.

Growing research suggests that low testosterone levels may be intimately linked with insulin resistance and its related conditions of metabolic syndrome and diabetes.<sup>13,14</sup> Recent research suggests that between 20% and 64% of men with diabetes have low testosterone levels; older men appear to be particularly susceptible.<sup>15</sup> Likewise, low serum testosterone is common among men with metabolic syndrome, and some scientists have proposed that low testosterone might serve as a prognostic tool for early detection of the condition.<sup>14</sup>

Restoring testosterone to youthful ranges may confer a wide array of benefits to men affected by type 2 diabetes. The reported benefits of testosterone administration in these men include improved glucose homeostasis (balanced sugar levels), reduction in abdominal fat, and improved erectile function.<sup>16</sup> Likewise, scientists believe that testosterone replenishment may help reverse some of the key biochemical abnormalities that underlie metabolic syndrome, such as insulin resistance and central obesity.<sup>14,15</sup>

## WHAT YOU NEED TO KNOW: OPTIMIZING TESTOSTERONE LEVELS IN AGING MEN

- Testosterone, the chief male hormone, is essential for libido and erectile function, and plays a crucial role in mood, energy, bone health, and body composition.
- Testosterone levels decline with age, usually beginning in a man's mid-30s. Diminishing testosterone levels have been linked with disorders such as depression, fatigue, obesity, and cognitive decline.
- Low testosterone levels increase the risk of coronary heart disease as well as all-cause and cardiac mortality.
- Restoring testosterone to youthful levels offers men a wealth of health benefits, including benefits for heart health, body composition, mood, and memory.
- Bioidentical testosterone has not been found to have adverse effects on the healthy prostate gland—in fact, it may help improve prostate symptoms in men with low-normal testosterone levels. Testosterone therapy is contraindicated in men with prostate cancer.
- Regular blood testing can help you and your physician decide if testosterone therapy is right for you. Optimizing testosterone levels requires a multi-pronged approach that includes optimal diet, proper nutrition, nutritional supplements, exercise, and bioidentical testosterone, if necessary.

### TESTOSTERONE AND BODY COMPOSITION

With the obesity epidemic raging and its tremendous impact on the overall health of our nation's population, integrative physicians are particularly interested in the role testosterone plays in body composition. Testosterone appears to affect fat cell metabolism and fat loss in several ways through:

- Inhibiting fat storage by blocking a key enzyme called lipoprotein lipase that is necessary for the uptake of fat into the body's fat cells. When fat cells are exposed to testosterone in a test tube, the activity of lipoprotein lipase is dramatically reduced.
- Stimulating fat burning by increasing the number of certain receptors on the fat-cell membrane that release stored fat.<sup>17</sup>
- Increasing insulin sensitivity and improving lipid and insulin metabolism, while enhancing growth of muscle fibers and decreasing fat deposits.

All of these effects benefit body composition by promoting lean body mass and reducing fat mass.<sup>18,19</sup>

In a landmark study out of Sweden in 1991, researchers gave a group of overweight men supplemental testosterone for six weeks.<sup>20</sup> After this time, they found the activity of the fat-storage enzyme lipoprotein lipase to be dramatically reduced in abdominal fat tissue. Waist and hip circumference also decreased in 9 of the 11 men.

Furthermore, a recent review highlights numerous placebo-controlled trials that have demonstrated both significant increases in lean body mass and decreases in fat mass after varying courses of testosterone supplementation in older men.<sup>21</sup> In these studies, the greatest favorable changes in body composition were seen in participants with low baseline testosterone levels who received testosterone therapy for a period in excess of 12 months.



### TESTOSTERONE AND THE PROSTATE

A common misconception among physicians is that testosterone administration adversely affects the normal prostate. This idea is not supported by the medical literature. A 2002 study indicates that testosterone is actually beneficial for the prostate gland in the vast majority of cases. In this study, researchers looked at multiple parameters, including prostate volume, prostate-specific antigen (PSA) levels, and lower urinary tract symptoms in a group of men with low or low-normal testosterone levels.<sup>22</sup> Of the 207 men studied, 187 responded favorably to testosterone treatment. These positive responders all showed improvement in almost every parameter measured: their prostate glands all decreased in size, PSA was lower, and urinary symptoms such as frequency, urgency, dribbling, and getting up at night to urinate all improved.

In a separate recent study that looked at a similar group of men, the authors observed that *“No treatment-related change was observed in prostate histology, tissue biomarkers, gene expression, or cancer incidence or severity. Treatment-related changes in prostate volume, serum PSA, voiding symptoms, and urinary flow were minor.”*<sup>23</sup>

On the question of whether testosterone therapy causes prostate cancer, the answer clearly appears to be no. In a landmark review article published in 2004 in the New England Journal of Medicine, the authors report *“there appears to be no compelling evidence at present to suggest that men with higher testosterone levels are at greater risk of prostate cancer or that treating men who have hypogonadism [low testosterone] with exogenous androgens increases this risk.”*<sup>24</sup> However, since testosterone stimulates cell growth, it is possible that it can accelerate the growth of an existing prostate cancer. Cancer-screening tests such as a PSA test are necessary before replacement therapy. Testosterone-replacement therapy is contraindicated in men with known prostate cancer.

## THE IMPORTANCE OF BLOOD TESTING

The most efficient way for me (or other doctors) to prescribe the proper dose of low-cost individually compounded testosterone cream is for patients to bring their recent blood test results to my office during the initial visit. Life Extension's comprehensive Male Blood Test Panel provides the biochemical data I need to help safely restore testosterone to youthful ranges, while suppressing excess estradiol if necessary. The Male Blood Test Panel can be ordered by calling 1-800-208-3444. I encourage men over age 35 to have this comprehensive blood test and evaluation performed annually.

Life Extension members who reside in the Southern Utah area are welcome to call my office at 435-688-8582 to schedule an appointment for a medical consultation.

## TESTOSTERONE AND DEPRESSION

Depression is a leading cause of disability worldwide. In a recent study of 3,987 older men in Australia, researchers found that those with depression had significantly lower testosterone concentrations than men without depression.<sup>25</sup> The authors suggested that older men with depression may benefit from systematic screening of testosterone levels and testosterone supplementation where appropriate. In my own practice, I have seen both younger and older men with low testosterone levels and depression improve remarkably after testosterone supplementation. Other studies have shown an improvement in depression scores with testosterone therapy in patients with depression who are unresponsive to conventional treatments.<sup>26,27</sup> Further research in this area is ongoing.

## TESTOSTERONE IMPROVES COGNITIVE ABILITIES

Testosterone supplementation clearly seems to be beneficial for proper male mental and verbal function. Several studies have shown that decreased serum testosterone levels appear to adversely affect verbal memory in healthy young men. Short-term testosterone administration exerts a beneficial effect on spatial and verbal memory and enhances cognitive function in healthy men.<sup>28-31</sup>

## MANAGEMENT OF LOW TESTOSTERONE LEVELS

Optimizing testosterone levels in men requires a multi-faceted approach that includes proper lifestyle, nutrition, nutritional supplements (such as lignan and plant extracts),<sup>32,33</sup> dietary modifications, and exercise, as well as testosterone supplementation and other prescriptive approaches when indicated.



Initially, a medical history and physical examination should be performed, along with a blood-testing panel that includes not only testosterone levels, but also other important parameters such as fasting glucose, PSA, estradiol, and complete blood counts (CBC). It is important to work closely with a knowledgeable physician who is readily accessible and who can adjust treatment as needed. Careful, thoughtful optimization of testosterone levels with a comprehensive evaluation and treatment plan can result in dramatic improvements in one's overall health and well-being.

For men who no longer produce enough testosterone, an experienced doctor can prescribe a topically applied cream to restore testosterone to youthful ranges. These testosterone creams usually come in delivery systems that enable the precise amount of this hormone to be applied to the skin each day for absorption into the bloodstream.

The reason testosterone cream is used as opposed to tablets is that the oral ingestion of testosterone can result in rapid

degradation in the liver and wildly inconsistent blood levels. A testosterone cream, on the other hand, gradually releases into the bloodstream, which is more analogous to the way testosterone is naturally secreted each day by the testicles of younger men.

Compared with brand name testosterone topical drugs, consumers can save more than 85% by using natural testosterone cream made by a compounding pharmacy. For example, the name brand Androgel® cream costs around \$225 for a month's supply. The identical amount of natural testosterone can be obtained from a compounding pharmacy for less than \$25 a month. For those patients in whom a cream is not the best choice, testosterone injections can be prescribed.

Follow-up blood testing 30-60 days later is important to ensure that PSA, estradiol, and other blood markers stay in normal ranges. Some men will aromatize (or convert) testosterone into estrogen, which necessitates the use of a drug like Arimidex® or nutrient-lifestyle changes to inhibit excess aromatase activity.

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

### **ABOUT PAUL NAVAR, MD**

Dr. Paul Navar specializes in integrating bioidentical hormone-replacement therapy, lifestyle/nutritional programs, and the best of conventional medical treatments to achieve optimal health for his patients.

His integrative medical practice uses the most effective treatments from conventional medicine and natural medicine to restore health and vitality to patients with hormone- and age-related health decline.

Paul D. Navar, MD can be reached at: 166 N. 300 W., Suite 3, St. George, Utah 84770

Email: [info@drnavar.com](mailto:info@drnavar.com)

Website: [www.drnavar.com](http://www.drnavar.com)

Phone: (435) 688-8582

Fax: (435) 688-1995

Editor's note: Whether supplementing with natural testosterone or not, aging men may consider using the prescription drug Avodart® to reduce levels of dihydrotestosterone, a potentially dangerous metabolite of testosterone. Studies show that men using agents that lower dihydrotestosterone have reduced rates of both benign and malignant prostate disorders.<sup>34</sup>

---

### **References**

---

1. Available at: <http://www.census.gov/ipc/www/usinterimproj/natprojtab02a.pdf>. Accessed April 24, 2008.
2. Khaw KT, Dowsett M, Folkard E, et al. Endogenous testosterone and mortality due to all causes, cardiovascular disease, and cancer in men: European prospective investigation into cancer in Norfolk (EPIC-Norfolk) Prospective Population Study. *Circulation*. 2007 Dec 4;116(23):2694-701.
3. Tan RS, Salazar JA. Risks of testosterone replacement therapy in ageing men. *Expert Opin Drug Saf*. 2004 Nov;3(6):599-606.
4. Available at: <http://www.drugs.com/ppa/methyltestosterone.html>. Accessed April 28, 2008.
5. Farrell GC, Joshua DE, Uren RF, Baird PJ, Perkins KW, Kronenberg H. Androgen-induced hepatoma. *Lancet*. 1975 Feb 22;1(7904):430-2.
6. The extent and nature of testosterone use [news release]. Fairfield, Conn: IMS Health, Inc; September 2006.
7. Miner MM, Seftel AD. Testosterone and ageing: what have we learned since the Institute of Medicine report and what lies ahead? *Int J Clin Pract*. 2007 Apr;61(4):622-32.
8. Jones RD, Nettleship JE, Kapoor D, Jones HT, Channer KS. Testosterone and atherosclerosis in aging men: purported association and clinical implications. *Am J Cardiovasc Drugs*. 2005;5(3):141-54.

9. Dobrzycki S, Serwatka W, Nadlewski S, et al. An assessment of correlations between endogenous sex hormone levels and the extensiveness of coronary heart disease and the ejection fraction of the left ventricle in males. *J Med Invest*. 2003 Aug;50(3-4):162-9.
10. Hak AE, Witteman JC, de Jong FH, et al. Low levels of endogenous androgens increase the risk of atherosclerosis in elderly men: the Rotterdam study. *J Clin Endocrinol Metab*. 2002 Aug;87(8):3632-9.
11. Malkin CJ, Pugh PJ, Morris PD, et al. Testosterone replacement in hypogonadal men with angina improves ischaemic threshold and quality of life. *Heart*. 2004 Aug;90(8):871-6.
12. Kang SM, Jang Y, Kim JY, et al. Effect of oral administration of testosterone on brachial arterial vasoreactivity in men with coronary artery disease. *Am J Cardiol*. 2002 Apr 1;89(7):862-4.
13. Zou B, Sasaki H, Kumagai S. Association between Relative Hypogonadism and Metabolic Syndrome in Newly Diagnosed Adult Male Patients with Impaired Glucose Tolerance or Type 2 Diabetes Mellitus. *Metab Syndr Relat Disord*. 2004 Spring;2(1):39-48.
14. Spark RF. Testosterone, diabetes mellitus, and the metabolic syndrome. *Curr Urol Rep*. 2007 Nov;8(6):467-71.
15. Kalyani RR, Dobs AS. Androgen deficiency, diabetes, and the metabolic syndrome in men. *Curr Opin Endocrinol Diabetes Obes*. 2007 Jun;14(3):226-34.
16. Fukui M, Kitagawa Y, Ose H, Hasegawa G, Yoshikawa T, Nakamura N. Role of endogenous androgen against insulin resistance and atherosclerosis in men with type 2 diabetes. *Curr Diabetes Rev*. 2007 Feb;3(1):25-31.
17. De Pergola G. The adipose tissue metabolism: role of testosterone and dehydroepiandrosterone. *Int J Obes Relat Metab Disord*. 2000 Jun;24 Suppl 2S59-S63.
18. Naharci MI, Pinar M, Bolu E, Olgun A. Effect of testosterone on insulin sensitivity in men with idiopathic hypogonadotropic hypogonadism. *Endocr Pract*. 2007 Oct;13(6):629-35.
19. Saad F, Gooren LJ, Haider A, Yassin A. A dose-response study of testosterone on sexual dysfunction and features of the metabolic syndrome using testosterone gel and parenteral testosterone undecanoate. *J Androl*. 2008 Jan-Feb;29(1):102-5.
20. Rebuffe-Scrive M, Marin P, Bjorntorp P. Effect of testosterone on abdominal adipose tissue in men. *Int J Obes*. 1991 Nov;15(11):791-5.
21. Allan CA, Strauss BJ, McLachlan RI. Body composition, metabolic syndrome and testosterone in ageing men. *Int J Impot Res*. 2007 Sep;19(5):448-57.
22. Pechersky AV, Mazurov VI, Semiglazov VF, et al. Androgen administration in middle-aged and ageing men: effects of oral testosterone undecanoate on dihydrotestosterone, oestradiol and prostate volume. *Int J Androl*. 2002 Apr;25(2):119-25.
23. Marks LS, Mazer NA, Mostaghel E, et al. Effect of testosterone replacement therapy on prostate tissue in men with late-onset hypogonadism: a randomized controlled trial. *JAMA*. 2006 Nov 15;296(19):2351-61.
24. Rhoden EL, Morgentaler A. Risks of testosterone-replacement therapy and recommendations for monitoring. *N Engl J Med*. 2004 Jan 29;350(5):482-92.
25. Almeida OP, Yeap BB, Hankey GJ, Jamrozik K, Flicker L. Low free testosterone concentration as a potentially treatable cause of depressive symptoms in older men. *Arch Gen Psychiatry*. 2008 Mar;65(3):283-9.
26. Pope HG, Jr., Cohane GH, Kanayama G, Siegel AJ, Hudson JI. Testosterone gel supplementation for men with refractory depression: a randomized, placebo-controlled trial. *Am J Psychiatry*. 2003 Jan;160(1):105-11.
27. Seidman SN, Rabkin JG. Testosterone replacement therapy for hypogonadal men with SSRI-refractory depression. *J Affect Disord*. 1998 Mar;48(2-3):157-61.
28. Cherrier MM, Asthana S, Plymate S, et al. Testosterone supplementation improves spatial and verbal memory in healthy older men. *Neurology*. 2001 Jul 10;57(1):80-8.

29. Cherrier MM, Anawalt BD, Herbst KL, et al. Cognitive effects of short-term manipulation of serum sex steroids in healthy young men. *J Clin Endocrinol Metab.* 2002 Jul;87(7):3090-6.
30. Cherrier MM, Craft S, Matsumoto AH. Cognitive changes associated with supplementation of testosterone or dihydrotestosterone in mildly hypogonadal men: a preliminary report. *J Androl.* 2003 Jul;24(4):568-76.
31. Cherrier MM, Plymate S, Mohan S, et al. Relationship between testosterone supplementation and insulin-like growth factor-I levels and cognition in healthy older men. *Psychoneuroendocrinology.* 2004 Jan;29(1):65-82.
32. Tou JC, Chen J, Thompson LU. Dose, timing, and duration of flaxseed exposure affect reproductive indices and sex hormone levels in rats. *J Toxicol Environ Health A.* 1999 Apr 23;56(8):555-70.
33. Adimoelja A. Phytochemicals and the breakthrough of traditional herbs in the management of sexual dysfunctions. *Int J Androl.* 2000;23 Suppl 2:82-4.
34. Tindall DJ, Rittmaster RS. The rationale for inhibiting 5alpha-reductase isoenzymes in the prevention and treatment of prostate cancer. *J Urol.* 2008 Apr;179(4):1235-42.

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

**LifeExtension®**

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.