

Mainstream Doctors' Ineptitude Put on Display in *The New England Journal of Medicine*

A study published in the **June 30, 2010** edition of *The New England Journal of Medicine* confirms how little conventional doctors know about prescribing **testosterone** to aging men.

The **Life Extension Foundation®** (and its medical advisors) long ago recognized that maturing men have a propensity to convert (aromatize) **testosterone** into **estrogen**. When you see an overweight man growing breasts, it is not directly because he eats too much. This phenomenon is instead caused by the testosterone he *converts* to breast-enlarging estrogen.

When men are prescribed testosterone gels or creams, they sometimes have to take an aromatase-inhibiting drug (like Arimidex®) to prevent their estrogen (measured as estradiol in the blood) from climbing to dangerous levels.

Optimal **estradiol blood levels** in men are between **20-30** pg/mL. Elderly males can have much higher estradiol levels that place them at substantial risk for developing **coronary atherosclerosis** and **thrombotic stroke**.

If elderly men are prescribed **large doses of topical testosterone** gel or cream, their **estradiol** blood levels have to be tested and properly controlled. Failure to manage estradiol in men receiving high-dose testosterone gel or cream can result in a catastrophic **estrogen surge** that increases vascular disease risk and premature death.

Enormous tax dollars squandered on flawed testosterone study

The Federal government provided a financial grant to an armada of doctors to evaluate the effects of high-dose testosterone on men that were so severely debilitated that they struggled to climb more than 10 stairs or walk the equivalent of two city blocks.

These men suffered numerous risk factors such as obesity, diabetes, hypertension, and elevated blood lipids that placed them at higher risk for cardiovascular events. Obese men tend to produce loads of estrogen in their abdominal fat — and typically have higher estradiol levels than thinner men.

The men with the worst vascular risk factors (such as highest triglyceride levels) were placed on a dose of topical testosterone that is **TWICE** the standard starting dose. These debilitated men were given testosterone in a way that is more likely to aromatize through the skin into estrogen.

Men with fewer vascular risk factors were given a placebo gel.

It should be no surprise to learn that this study was halted prematurely because the debilitated men given the high-dose testosterone (with no aromatase inhibitor) suffered more “atherosclerosis-related events” such as heart attack, stroke, and sudden death.

The official title of this study is “Adverse Events with Testosterone Administration.” A more accurate title may have been: ***“Elevated Estrogen Leads to Cardiovascular Events in Older Men.”***

Click here to read Life Extension®'s recent review about the dangers of estrogen imbalance in aging men, [click here](#)

Life Extension writes a letter to these doctors

The day this study was published, **Life Extension** wrote the doctors who conducted the study asking if there was any data regarding baseline and post-baseline blood **estradiol** levels. We have waited over four weeks, and the authors of *The New England Journal of Medicine* study have not responded to our repeated requests as to whether **estradiol** levels were ever measured.

From what was written in the paper, it does not appear that any attention was paid to the estrogen levels in these debilitated men. The authors wrote in the discussion section of the paper, ***“Testosterone and associated increases in estradiol may promote inflammation, coagulation and platelet aggregation.”*** Yet these doctors don't appear to have done anything to evaluate estradiol levels in the unfortunate study subjects given double-dose testosterone with no aromatase inhibitor to suppress the expected **estrogen surge**.

This study had numerous other flaws

Leaving aside the failure to manage **estradiol** levels in men given high-dose testosterone gel, there were numerous design flaws that call into question any conclusion that can be drawn from this study.

As mentioned earlier, the testosterone group at baseline was at greater risk for cardiovascular events as manifested by a greater proportion of men in the testosterone group with dyslipidemia who were undergoing statin and antihypertensive drug treatment.

In addition, triglyceride levels (higher) and HDL levels (lower) were trending against the testosterone group. Clearly, the baseline cardiovascular risk for the testosterone group was higher than the placebo group. The authors claim that a sensitivity analysis, as well as controlling for cardiovascular risk factors, did not change the results, but the small sample size and relatively short trial duration serve to magnify, not minimize, differences due to chance.

The study was not designed to systematically assess for cardiovascular events, and given the small sample size, lack of consistent pattern of events, diversity of serious events, and small number of serious adverse cardiac events (10 vs. 1) in the two treatment groups before study stoppage in this short duration trial strongly suggest that the results are due to chance. Another explanation of course is that the adverse vascular events were caused by the uncontrolled conversion of the topically-applied testosterone to estradiol in men who were already likely to have dangerously high estradiol blood levels to begin with.

Fodder for the media

The published scientific data documents low testosterone as being an independent risk factor for heart attack and a host of other age-related ailments.

The authors of this study acknowledge the benefits the testosterone group obtained from the drug and openly admitted the limitations of this study in providing guidance about the effects of testosterone on different population groups.

The media, however, has a propensity to publicize one negative study while ignoring hundreds of positive ones. We will not be surprised to see this horrifically flawed study used for decades to discredit the safety and efficacy of properly prescribed testosterone cream and aromatase-inhibition therapy.

Importance of blood testing in men supplementing with testosterone

In response to overwhelmingly favorable studies, record numbers of aging men are rubbing testosterone creams or gels on to their skin each day to restore this vital hormone to youthful levels.

Within 45-60 days of initiating testosterone replacement therapy, the following blood tests should be done to ensure safety and efficacy:

- **PSA** (prostate specific antigen) – To rule out prostate cancer
- **Estradiol** – To make sure testosterone is not converting to estrogen
- **Free & Total Testosterone** – To make sure enough testosterone is being absorbed
- **CBC/Chemistry** – To make sure liver enzymes are normal and red blood production has not increased too much

These tests can be done at your doctor's office, or you can order them all directly from Life Extension by calling **1-877-354-6513** (24 hours a day) and asking for the **Male Testosterone Panel**. These tests can retail for over \$500.00 at commercial labs, but Life Extension members pay only **\$125.00**. Order your blood tests now!

To review *Life Extension* articles describing benefits of testosterone replacement in aging men, click here: [Optimizing Testosterone Levels in Aging Men, Vindication](#).

Summary of 5 recent peer-reviewed studies noting adverse cardiovascular effects associated with elevated estrogen in aging men:

1) After adjustment for age, hypertension, diabetes, adiposity, cholesterol, atrial fibrillation, and other characteristics were made in a group of 2,197 men aged 71 to 93 years of age, men with the highest blood levels of estradiol had a 2.2-fold greater risk of stroke compared with those whose estradiol levels were lower. {Reference: **Abbott RD, Launer LJ, Rodriguez BL, et al. Serum estradiol and risk of stroke in elderly men. *Neurology*. 2007 Feb 20;68(8):563-8.**}

2) In a study of 313 men whose average age was 58, carotid artery intima-media thickness was measured at baseline and then three years later. After adjusting for other confounding risk factors, higher levels of estradiol were associated with thickening of the carotid artery wall. Researchers concluded, "Circulating estradiol is a predictor of progression of carotid artery intima-media thickness in middle-aged men." **{Reference: Tivesten A, Hulthe J, Wallenfeldt K, et al. Circulating estradiol is an independent predictor of progression of carotid artery intima-media thickness in middle-aged men. *J Clin Endocrinol Metab.* 2006 Nov;91(11):4433-7.}**

3) In an angiographic trial of coronary atherosclerosis in a group of men with stable coronary artery disease, significant positive correlations between estradiol levels and other known atherosclerotic risk factors was observed. Researchers concluded, "Our results indicate a possible role of estradiol in promoting the development of atherogenic lipid milieu in men with coronary artery disease." **{Reference: Wranicz JK, Cygankiewicz I, Rosiak M, et al. The relationship between sex hormones and lipid profile in men with coronary artery disease. *Int J Cardiol.* 2005 May 11;101(1):105-10.}**

4) In another angiographic trial of coronary atherosclerosis in men aged 40-60 years, compared with healthy age-matched controls, men with coronary atherosclerosis had higher levels of estrone and a low level of testosterone in the presence of a high level of estradiol. Researchers concluded, "Low levels of total testosterone, testosterone/estradiol ratio and free androgen index and higher levels of estrone in men with coronary artery disease appear together with many features of metabolic syndrome and may be involved in the pathogenesis of coronary atherosclerosis." **{Reference: Dunajska K, Milewicz A, Szymczak J, et al. Evaluation of sex hormone levels and some metabolic factors in men with coronary atherosclerosis. *Ageing Male.* 2004 Sep;7(3):197-204.}**

5) In a study of men having suffered an acute myocardial infarction (heart attack), a prior heart attack, and patients with normal coronary arteries, the results showed significantly higher levels of estradiol in both groups of heart attack patients compared with those without coronary disease. **{Reference: Mohamad MJ, Mohammad MA, Karayyem M, Hairi A, Hader AA. Serum levels of sex hormones in men with acute myocardial infarction. *Neuro Endocrinol Lett.* 2007 Apr;28(2):182-6.}**

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