Editorial

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Low Testosterone in Elderly Patients: To Treat or Not To Treat?

Here's a common scenario that can lead to a treatment dilemma: During a routine primary care visit, a male patient in his sixties or seventies mentions that he is experiencing erectile dysfunction (ED). A review of his history may reveal manifestations of vascular insufficiency (stroke, myocardial infarction, angina, or peripheral arterial disease) that suggest a generalized atherosclerotic process is contributing to the problem. You also may learn of such contributing factors as use of medications associated with ED (including various antihypertensives) or excessive alcohol use.

Eventually, though, laboratory testing—including measurement of the hormones testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin—will be performed. Very often the serum testosterone results will come back on the low side, accompanied by FSH and LH values that are either low or normal and a normal prolactin level.

What to do now? Well, it depends on just how low the testosterone is. If it's below 100 mg/dL or above 300 mg/dL, there's no need to press on with a free testosterone level, a bioavailable testosterone level, or a free androgen index. Levels below 100 mg/dL are unequivocally low and those above 300 mg/dL are unequivocally normal. When the patient's level falls between 100 and 300 mg/dL, however, it is necessary to get one of these additional studies in order to rule out the possibility of a relative deficiency of the binding protein for testosterone known as sex steroid binding globulin (SSBG).

Let's assume that this patient does, indeed, have a low testosterone level. So our next step should be to replace the missing hormone, right? After all, that's what we do when we identify clinical syndromes involving low levels of thyroid hormones, adrenal hormones, or insulin.

Actually, it's not quite that simple. The unfortunate fact is that we don't really know whether testosterone replacement therapy does more good than harm to an aging man.

True, the therapy may have some positive effects for the patient in our scenario. It might make him feel a little stronger, younger, and healthier while increasing his muscle strength—although these results are unlikely to be dramatic. And we can be certain that it will strengthen his bones, especially if dual energy x-ray absorptiometry studies have shown some degree of osteopenia or osteoporosis.[1]

But testosterone replacement therapy is unlikely to improve the patient's ED. One of the phosphodiesterase type 5 inhibitors—sildenafil, vardenafil, or tadalafil—probably would be much more helpful in this regard.

And testosterone replacement therapy could have some disadvantages, especially with regard to its stimulation of prostate tissue. There is clear evidence that the therapy can worsen urinary symptoms of benign prostatic hyperplasia (BPH), such as hesitancy, frequency, and urgency.[2] Another possibility—which is potentially more serious but not yet verified by data—is that it may fuel the growth of undetected prostate cancer. We know that the growth of prostate cancer is partially due to testosterone. And a major modality of prostate cancer treatment is androgen deprivation therapy.

Another concern is that the therapy might increase overall cardiovascular risk, which certainly would be a significant drawback for aging men. We don't have any evidence on how the therapy affects cardiovascular risk over the long term, but some data indicate that it may carry "guilt by association." For example, we know that testosterone reduces high-density lipoprotein levels modestly. And we know that it can unmask or exacerbate sleep apnea,[3] which is one of the many clinical conditions known to accompany the features of metabolic syndrome.

With all these factors in mind, let's return to the question of whether the patient described here should be treated with testosterone replacement therapy. According to clinical practice guidelines published recently by The Endocrine Society, the answer is this: If he wants to try it and he has no significant symptoms of BPH, a trial of the therapy is reasonable.[4] If the patient is less than enthusiastic about testosterone replacement, however, it seems equally appropriate to forgo this therapy.

Incidentally, the testosterone replacement dilemma is not unlike the debate over estrogen replacement in aging women. For many years, we were pretty confident that we were doing the right thing by passing out estrogens fairly routinely to postmenopausal women—until the findings of the Women's Health Initiative (WHI) suggested an increased risk of heart disease and other cardiovascular events.[5] Since then, more penetrating analysis of WHI data has confused the picture further, suggesting that women actually may receive some cardioprotective benefit from estrogen replacement in the immediate postmenopausal period.[6] Even so, our old, simplistic faith in the

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automatic benefits of replacing hormones that decline normally with age has been shaken.

The field clearly is crying out for a long-term, randomized, controlled trial of testosterone replacement therapy similar to the WHI—but with a better experimental design. Unfortunately, no such trials are on the horizon. It seems likely that, for the foreseeable future, we'll have to continue making tough, case-by-case decisions regarding testosterone replacement without the help of strong data. ●

Author disclosures

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REFERENCES

1. Behre HM, Kliesch S, Leifke E, Link TM, Nieschlag E. Long-term effect of testosterone therapy on bone mineral density in hypogonadal men. *J Clin Endocrinol Metab*. 1997;82(8):2386–2390.
2. Behre HM, Bohmeyer J, Nieschlag E. Prostate volume in testosterone-treated and untreated hypogonadal men in comparison to age-matched normal controls. *Clin Endocrinol (Oxf)*. 1994;40(3): 341–349.
3. Matsumoto AM, Sandblom RE, Schoene RB, et al. Testosterone replacement in hypogonadal men: Effects on obstructive sleep apnoea, respiratory drives, and sleep. *Clin Endocrinol (Oxf)*. 1985;22(6):713–721.
4. Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in adult men with androgen deficiency syndromes: An Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2006;91(6):1995–2010.
5. Manson JE, Hsia J, Johnson KC, et al; for Women's Health Initiative Investigators. Estrogen plus progestin and the risk of coronary heart disease. 2003;349(6):523–534. http://content.nejm.org/cgi/reprint/349/6/523.pdf. Accessed November 19, 2007.
6. Manson JE, Allison MA, Rossouw JE, et al; for WHI and WHI-CACS Investigators. Estrogen therapy and coronary-artery calcification. *N Engl J Med*. 2007;356(25):2591–2602.