



Male Hormone Deficiency: To Treat or Not to Treat?

It's a recurring scenario in any medical practice that cares for a significant number of older male patients. An older gentleman who is feeling less peppy with the passage of time will ask if his male hormone levels should be checked. You, as the caring and compassionate provider, immediately agree that it would be reasonable to see if a low level of testosterone could be contributing to his fatigue, his erectile dysfunction, his general lack of motivation and interest in life, etc.

That's how it begins. For many clinicians it can turn into a confusing conundrum over whether or not it's appropriate to treat a given patient with a testosterone preparation.

The first issue to resolve is whether or not the level of testosterone truly is low. Most providers start out simply by measuring a total testosterone level, which is fine if it returns well within the normal range. But if it comes back right at the lower limit of normal, or below that cutoff, which typically is 300 mg/dL, then further assessment is necessary. That's because there could be a problem with the amount of binding protein, known either as sex hormone binding globulin or as sex steroid binding globulin. If someone has a below-average amount of binding protein, which can happen for a variety of reasons, the total testosterone may appear to be low, even though the free, or active, hormone level is normal. The way around this problem is to order a free, or alternatively, a bioavailable testosterone level, either of which will correlate better with the true hormone status than will the total level.

So let's now assume that we have determined that a given patient does

indeed have a suboptimal level of testosterone. The question now becomes whether we will do him more good or more harm if we propose to treat his apparent deficiency of testosterone.

It might seem, at first blush, that this should be a real no-brainer. Don't we always replace hormones when we find them to be deficient? Don't we treat thyroid hormone deficiency (hypothyroidism) with sufficient thyroid hormone to return the blood levels to normal? Don't we treat diabetic patients with insulin deficiency, most classically the type 1 patients, with insulin injections to compensate for the pancreatic failure to produce enough insulin? Of course we do; and

the fact there is a natural age-related decline in testosterone levels. So the question of what's normal and what's pathologic becomes a lot murkier than we would like it to be. It's true that illness can accelerate the decline in testosterone levels, but it's also true that there is a natural decline in levels on a population basis as men age. So, are we merely remedying a hormonal deficiency when we give replacement hormone to the older patient, or are we actually giving that man a non-physiologic boost in his testosterone levels that might not ultimately be in his best interest?

The real problem here is that we are operating in a huge vacuum, with-

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so it might seem an inviolable maxim of endocrinology that you replace hormonal deficiencies with the appropriate missing hormones wherever you can.

THE DILEMMA

It's unfortunately not so simple when it comes to the question of whether or not to replace testosterone in older men with testosterone deficiency. (I'm assuming for our purposes here that a central problem of hypopituitarism has been ruled out, and that the testosterone deficiency is an isolated problem.) The dilemma relates to

out the appropriate prospective studies that one would want to assess whether we are doing more good or harm. To take the side of hormonal replacement for a moment, we know that certain age-related deteriorations in muscle (too little) and fat (too much) do correlate reasonably well with testosterone levels. So, when we give replacement therapy, we reduce the patient's fat and he increases his muscle bulk. And we also know that some older men will see an improvement in their deteriorating sexual performance when we treat them with male hormone. There may be some

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element of the placebo phenomenon at work here, but what's not to like about a therapy that gives you more muscle, less fat, and more oomph in the sack?

Well, possibly quite a bit. A recent National Institutes of Health-funded study of testosterone replacement was terminated prematurely when it appeared that the men on testosterone replacement were experiencing many more cardiac complications than those on placebo. However, there were major methodologic problems with the study; such that many of us felt that this particular study was ultimately meaningless and perhaps quite misleading. The definition of cardiac episodes was laughably imprecise and subjective, and it's probably best to put this study aside. But the larger concern over possible cardiac toxicity

from testosterone replacement therapy lingers, because it is well-established that testosterone lowers high density lipoprotein levels, providing a very plausible potential mechanism for a negative cardiac effect of replacement therapy. Another concern that also could be more than theoretical, relates to a possible role in stimulating occult prostate malignancies to become more clinically apparent. We already know we shouldn't give testosterone to patients with known prostate cancer because it can accelerate the growth of the malignancy.

In the final analysis, we do not have the data to tell us whether or not we are doing the right thing when we prescribe testosterone replacement therapy. It is very reasonable to give it a try in patients who request it, but it also is quite reasonable to make a

joint decision with a patient to forgo a therapy that we really know so little about. ●

Author disclosures

The author reports no actual or potential conflicts of interest with regard to this editorial.

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