

## **MEditorial June 2011**

### **“Testosterone”**

**Analogous to the prostate cancer versus breast cancer paradigm, (i.e., prostate cancer is an “in vogue” malignancy and its treatment options are now as controversial as breast cancer treatments have been for 20 years) is the issue of male hormonal replacement therapy (testosterone, sometimes referred to as “T”) versus female hormones (estrogen).**

**Whether or not there is a true [male] “andropause”, as there certainly is female menopause, is debatable. Testosterone production, 95% by the testicles and 5% by the adrenal glands (located near the kidneys), seems to surge when men are developing in utero, as a means of “masculinizing” the male brain as well as the developing genitals. Lack of this production--or tissue insensitivity to testosterone--can lead to errors in male genital development (like the urethra not making it to the tip of the penis or the two side of the scrotum having a cleft in between, appearing more like the female labia) and may even play a role in boys having more interest in “girl things”, i.e., playing with dolls.**

**After birth and until puberty, testosterone production remains dormant, only to surge during adolescence. After age 40, there is a gradual unpredictable decline by decade of life, but not the dramatic cessation as is seen in estrogens at menopause. Men in their 80’s can have normal testosterone levels (as well as good sexual functioning!).**

**It is even controversial as to what constitutes a “low” testosterone level. Most labs have their default normal levels (usually between about 250 and 800 nanograms per deciliter) set not based on what clinically is an adequate male hormone level--but rather “statistically”—based on what levels are observed in 95% of the population (so-called “confidence interval”). Thus it is possible a man may have signs of inadequate “T” (medically called hypogonadism) and yet fall within the normal blood test range. Since once produced, testosterone appears in the bloodstream in many forms, often attached to “carrier” protein molecules produced by the liver, like albumin and sex hormone binding globulin, it may be**

more relevant to discuss the concept of “free T”, that is the fraction NOT attached to a carrier molecule, since this form seems to be more available to stimulate cells influenced by male hormones.

In clinical practice, there has been an evolution of thought as to what male symptoms are caused by too low a testosterone (or “free T”). It is not too common that poor erections, per se, are explainable by low T although this blood test should be measured in men with impotence, more so those with low sex drive (libido). It is now felt that there are non-sexual symptoms attributable to male hormone imbalance--but *since these complaints can be caused by many other problems, and there are risks to being on testosterone replacement therapy (TRT)*, the correct remedy is not always clear. For example, bone weakening (osteopenia/osteoporosis), lack of physical stamina well as mental concentration, and even depression, could be partly due to hypogonadism and therefore respond nicely to TRT; but other causes of often “vague” symptoms need to be assessed usually by the patient’s Internal Medicine doctor. Note depression itself can cause poor sexual function, and as a corollary, some antidepressants including SSRI drugs related to Prozac can suppress sex drive and responsivity.

I see a lot of men already on TRT, sometimes for years, who have no idea of what abnormal level(s) led to treatment--or even what exactly was the goal of this drug intervention. If I am going to treat a man for hypogonadism, I want to see from the start more than one lab test showing either low total or free testosterone. I want to correlate the low level with the symptoms. I suggest avoiding TRT only to “treat a low lab test”. Pituitary hormones that stimulate testosterone production may need checking, since rarely, the “master” hormonal organ (pituitary, located at the base of the brain) can be deficient, e.g., due to a benign tumor producing prolactin which crowds out the production of LH (luteinizing hormone), a messenger hormone telling the testes to “function better”. It is also important to have a goal in mind, not to simply tell a man he will be on TRT for life--but rather as long as it takes to see if the a patient’s manifestation of hormonal insufficiency is responding appropriately. A six month trial of replacement therapy will help differentiate those whose will

benefit from those who won't. Non-responders should have blood free/total testosterone levels checked on therapy, just to be sure they are being adequately dosed.

Traditionally TRT was done with oral pills or injections. The former had a higher incidence of liver problems and the latter the issue of uneven blood level, high after a shot and low a few weeks later. Some doctors feel the "excess highs" could cause problems, e.g., overstimulation of red blood cell production by bone marrow. More often nowadays, I prescribe a daily transcutaneous form of testosterone applied by the man after drying off from a shower. This provides a steady level of TRT with low side effects. Some men are opting for long-acting testosterone pellets, done in an office injection procedure; such pellets can give off a steady level of testosterone for up to 6 months. The latter get around the issue of "forgetting" to apply the testosterone gel or patches; and avoid the messiness or rash issues.

I feel testosterone replacement should be stopped if it does not help; or if it causes major side effects; or if prostate cancer is suspected/untreated/persistent after initial cancer treatment. Testosterone is not felt to "cause" prostate cancer even though growth of prostate cancer cells seems often dependent on testosterone; in fact, there is some evidence that [paradoxically] men with chronically low "T" levels may be MORE subject to getting prostate cancer. I would worry about a man with low "T" and a high prostate cancer blood test (PSA). *In a man successfully treated for prostate cancer who needs extra testosterone to treat symptoms, TRT is currently felt to be a safe intervention.*

Men interested in having children should be aware the TRT can inhibit sperm production, probably by suppressing a pituitary signaling mechanism that allows utilization of intratesticular testosterone by the developing sperm cells. Regular testosterone preparations, well as the far more potent (often illegal) "anabolic steroids" can lead to infertility issues.

In terms of related hormones marketed to men both over the counter and as prescriptions to either help potency, or bathe men in the "fountain of youth", I

neither condone these nor do I prescribe them. I do not have much respect for “hormone mills”, where doctors give men concoctions of hormones to feel better. Some of these drugs include HGH (human growth hormone) and DHEA (a weak cousin of testosterone).

If you or a loved one has concerns about “low T”, ask your doctor--but also do a reality check so as not to *overestimate* the benefit of TRT, or to look at it as a panacea or the main/ only solution to less-than-optimal health.

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