

Treating androgen deficiency in the aging male: a Urologist perspective

by Matthew Thom

Introduction

Normal aging in men is accompanied by a decline in testosterone (T) production and function that may contribute to detrimental changes to overall male health. Hypogonadism displays numerous clinical manifestations and the degree and timing of onset is variable and not universal for all men. This can lead to difficulty in diagnosis and treatment. A typical man with low T may be between the age of 40 to 69 and present with signs and symptoms of fatigue, low energy, depressed mood and low sexual drive.

What is Low T and what causes it?

Low T or symptomatic late-onset hypogonadism is a clinical and biochemical syndrome characterized by deficiency in androgen activity which may affect the function of multiple organ systems and result in significant detriment in quality of life. More than 500,000 new cases may be diagnosed each year but remains under diagnosed and treated. Numerous theories to its cause are present with a combination of factors contributing to the problem. These include aging hypothalamus with decrease production of gonadotropins, primary testicular failure, changes in androgen receptor activity/function, and effects on T metabolism that lead to decrease function regardless of T levels.

What are the effects of androgen deficiency?

Presentation of the hypogonadal patient is variable which can make diagnosis difficult. Common signs and symptoms include low energy, depressed mood, sleep disturbances, depressed cognition, impotence, and low libido. But low T may also unknowingly contribute to systemic disease including metabolic syndrome, increased cardiovascular risk, and osteoporosis.

How is low T diagnosed?

Clinical diagnosis is problematic because neither low T nor symptoms are truly diagnostic. The most common symptoms – tiredness, depressed sexual drive, and dysphoria – should tip the physician to further evaluate for hypogonadism. Several screening questionnaires are available to aid in the diagnosis, but unfortunately are not specific. Initial testing should include T levels obtained between 8am and 11am, with total T being sufficient. Any low level should be confirmed and may include LH, prolactin if clinically warranted. Unfortunately, there is much variability in T level reporting and the parameters for hypogonadism. This is currently under scrutiny by medical groups and societies with hope to standardized reporting to ensure better research, trials and patient care.

How is T replaced?

Intramuscular injections reliably increase T levels for hypogonadal men but T levels may reach supraphysiologic levels and the normal circadian rhythm is absent. This will make patients complain of a “roller coaster effect”. Also, current preparations available require repeat injections typically every 2-3 weeks. Oral preparations are rarely used in US due to erratic effects on T levels and problems with liver toxicity and hyperlipidemia. Transdermal patches and gels are popular yet require daily administration with definite risk for transference to others. One of the newer formulations available is T pellets implanted subcutaneously every 3-6 months. It has benefits with fewer administrations and no risk of transference. But T pellet implantation requires a procedure and there is risk of extrusion of pellets, poor absorption and other procedure site side-effects.

What are the adverse effects of T replacement?

A prior history of prostate or breast cancer is considered an absolute contraindication for hormone replacement. This “truth” has been questioned particularly in light of current treatment of low risk prostate cancer. Hormone replacement in hypogonadal men with clinically cured or untreated low risk disease has been studied showing no significant increase risk of recurrence or progression. However, most practicing urologists

discourage T replacement for these men. The belief of increase prostate size or PSA thus worsening lower urinary tract symptoms or risk of prostate cancer has not been demonstrated in several short-term studies. Long term effects of T replacement are not well known at this time. T replacement may also lead to increase red blood cell mass and hemoglobin. Side effects from excessive supplementation of T and other rare problems include infertility, testicular atrophy, priapism, fluid retention, liver toxicity (uncommon with current preparations), hepatitis and hepatic tumors, sleep apnea and gynecomastia. Infertility caused by T supplementation may require treatment with gonadotropins to increase testosterone and attempt to restore normal spermatogenesis. Side-effects from the route of administration may also occur.

Conclusion

Hypogonadism is a common yet under recognized problem in aging men. Not only will low T level lead to sexual side effects it may also effect psychological, physical and overall wellbeing of older men. Replacement is indicated for men who have signs and symptoms of hypogonadism accompanied by subnormal serum T levels. T supplementation can provide important health benefits to these hypogonadal men. T supplementation requires medical surveillance in order to identify early signs of possible adverse effects. Although the benefits and risks of long-term T supplementation have not been definitely established, the weight of current evidence does not suggest an increased risk of heart disease or prostate cancer with long-term use of T.

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