

## Urologist Mark Sigman, MD, addresses FDA panel on testosterone replacement therapy

*Advisory panel voted nearly unanimously to tighten regulation of multibillion-dollar testosterone industry; recommended studies to demonstrate benefit, safety of testosterone-replacement products*

PROVIDENCE – **MARK SIGMAN, MD**, chief of urology at The Miriam and Rhode Island hospitals, co-director of the Men's Health Clinic at The Miriam Hospital, and chief of urology at The Warren Alpert Medical School of Brown University, spoke about hypogonadism last month at a joint meeting of the Bone, Reproductive and Urologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee.

The combined United States Food and Drug Administration (FDA) advisory panel, whose advice the FDA often follows, gathered to discuss who should receive testosterone replacement therapy, as well as the potential for cardiovascular risk related to the therapy. The FDA has been exploring the risk of stroke, heart attack and death among men taking FDA-approved testosterone products in response to conflicting studies examining the cardiovascular risks in men undergoing testosterone therapy.

"The first testosterone product, which appeared in the 1950s, was prescribed for patients with 'Classic' Low T (testosterone) – hypogonadism due to known underlying medical conditions," Dr. Sigman says. "At that time, drug companies had only to show that testosterone products raised testosterone – not that they improved symptoms. Since then, in spite of the surge in testosterone replacement therapy for Low T, there haven't been any major changes to the indications for the use of testosterone products – so this is a significant industry development."

Among the advisory panel's recommendations in the almost unanimous committee vote were making changes to what has been called vague testosterone-replacement product labels to address the increasingly prevalent use of testosterone for hypogonadism related to aging – or Andropause – Low T due to decreased T production that accompanies aging. The number of testosterone prescriptions has increased approximately eight-fold since 2000. The panel also voted at the meeting to require drug makers to conduct tests or studies to assess the cardiovascular risk related to use of testosterone drugs.

Testosterone deficiency (TD) indicates a low testosterone level in the blood. Hypogonadism indicates a low testosterone level in the presence of symptoms of low testosterone. Testosterone deficiency afflicts approximately 20 to 30 percent of men ages 40-79 years old, with an increase in prevalence strongly associated with aging and common medical conditions including obesity, diabetes and hypertension.

Dr. Sigman's presentation about hypogonadism to the FDA panel focused on what male age-related hypogonadism is and how to diagnose it; the difference between age-related and classical hypogonadism; the reasons behind diagnosing and treating hypogonadism, and the risks of testosterone treatment for hypogonadism. Dr. Sigman spoke about symptoms, indications for treatment, and how all guidelines require symptoms of hypogonadism. He also discussed how Low T alone is insufficient without symptoms – and how the prevalence of Low T (by blood test alone) is greater than the prevalence of hypogonadism (Low T plus symptoms of Low T). While there are a variety of types of testosterone measurements (total testosterone, free testosterone, and bioavailable testosterone), Dr. Sigman says most studies and guidelines are based on Total T.

Dr. Sigman received his medical degree from University of Connecticut School of Medicine. He is a nationally recognized expert on male infertility and sexual dysfunction with over 25 years of experience in the diagnosis and treatment of urologic and reproductive problems. ❖



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### Dr. Sigman's conclusions presented to the panel

- Clinical hypogonadism is common.
- Many symptoms and co-morbidities are associated with low testosterone.
- Criteria for who to treat is controversial, as it's difficult to clearly separate those who benefit from those who don't.
- Reasonable evidence exists that treatment is beneficial for some with either classical or age-associated hypogonadism.
- Long-term safety will not be determined without large clinical trials.