Testosterone Therapy and Prostate Health
examining barriers to treatment
of Hypogonadism

Saturday, May 19, 2012
Georgia World Congress Center
Atlanta, Georgia

Testosterone Update offers free downloadable CME, tools, and resources on hypogonadism for clinicians and their patients.

TU is a unique CME-certified initiative committed to alleviating the symptoms of patients suffering from hypogonadism, through accurate diagnosis and reestablishment of constant physiologic testosterone levels, for improved overall health and well-being.

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Testosterone Therapy and Prostate Health
examining barriers to treatment of Hypogonadism

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Chairperson

Culley C. Carson III, MD
Rhodes Distinguished Professor and Chief of Urology
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina

Faculty

Mohit Khera, MD, MBA, MPH
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Chief of Urology
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Intended Audience

Urologists and other healthcare professionals interested in the management of hypogonadism attending the AUA Annual Meeting

Statement of Need

Despite evidence to the contrary, persistent concerns about the relationship between testosterone and the prostate continue to impede the treatment of hypogonadism. Mounting evidence demonstrates that there is a lack of association between testosterone therapy and prostate cancer progression, and preliminary studies have investigated the role of testosterone therapy in patient populations for whom it was once not considered. At present, there are strong indications that eugonadal testosterone levels play a protective role in the natural history of prostate cancer. Furthermore, preliminary studies suggest that testosterone therapy may improve lower urinary tract symptoms (LUTS). Because hypogonadism and LUTS are associated, it is critical to optimize the management of these comorbid conditions. Various studies support the proven benefits of testosterone therapy, which include increased lean body mass, decreased fat mass, and improved bone mineral density, sexual desire and function. To overcome barriers to successful treatment of hypogonadism, physicians need targeted education focused on properly diagnosing hypogonadism, safely initiating testosterone therapy, and monitoring patients receiving testosterone therapy.

Educational Objectives

At the conclusion of this activity, participants should be better able to:

1. Explain the noncausal relationship between testosterone therapy and increased prostate cancer risk or benign prostatic hyperplasia (BPH) development
2. Recognize the beneficial effects testosterone therapy may have on lower urinary tract symptoms in hypogonadal men with BPH
3. Manage hypogonadism properly to improve treatment outcomes

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Abraham Morgentaler, MD, receives research support from Auxilium Pharmaceuticals, Inc.; Endo Pharmaceuticals; GlaxoSmithKline; and Slate Pharmaceuticals, Inc. He is a consultant for and/or serves on the advisory boards of Abbott Laboratories, Endo Pharmaceuticals, Pfizer Inc., and Slate Pharmaceuticals, Inc.

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www.TestosteroneUpdate.org
Culley C. Carson III, MD, is Rhodes Distinguished Professor and Chief of Urology, University of North Carolina at Chapel Hill, and Associate Chairman of the Department of Surgery, University of North Carolina School of Medicine, Chapel Hill.

Dr Carson received a medical degree from George Washington University School of Medicine, in Washington, DC. He completed a surgical internship and residency at Dartmouth-Hitchcock Medical Center, in Hanover, New Hampshire, and a urology fellowship at the Mayo Clinic, in Rochester, Minnesota.

Dr Carson’s research is focused on the prevention of infections in penile prostheses and histologic studies of Peyronie’s disease. He is principal investigator of a long-term follow-up study of inflatable penile prostheses. He also has studied the effects of apomorphine, sildenafil, tadalafil, vardenafil, and other drugs on erectile dysfunction. In addition, Dr Carson has developed several instruments and devices, including the Carson zero tip ureteral dilation balloon and the Goldwasser Carson renal tourniquet.

A frequent contributor to the medical literature, Dr Carson has written extensively on male sexual dysfunction, specifically, penile prosthesis infection, Peyronie’s disease, and complications of the vacuum erection device. He is Editor in Chief of Contemporary Urology, Associate Editor of American Journal of Urology Review, and Website Editor for the Society for the Study of Impotence and serves on the editorial board of Urology Research and Treatment and as a reviewer for Journal of Urology, Urology, and International Journal of Impotence Research.

Dr Carson is President of the National Foundation for Sexual Health Medicine, President of the Southeast Section of the American Urological Association, and Past President of the Sexual Medicine Society of North America. He is a fellow of the American College of Surgeons and a member of the American Association of Clinical Urologists and the American Association of Genitourinary Surgeons, among others.

Mohit Khera, MD, MBA, MPH, is Assistant Professor of Urology in the Scott Department of Urology of Baylor College of Medicine, in Houston, Texas. He is also Medical Director of the Houston Hospital for Specialized Surgery and Director of the Laboratory for Andrology Research of McNair Medical Institute, Baylor College of Medicine.

Dr Khera earned a Doctor of Medicine degree at the School of Medicine of the University of Texas Health Science Center at San Antonio; a Master of Business Administration degree at Boston University Graduate School of Management, in Massachusetts; and a Master of Public Health degree at Boston University School of Public Health. He completed an internship in the Department of Surgery of Baylor College of Medicine and a residency in the Scott Department of Urology, where he also held a fellowship in the Division of Male Reproductive Medicine and Surgery.

Dr Khera’s research has concentrated on Peyronie’s disease treatment, testosterone therapy after radical prostatectomy, and the correlation between erectile dysfunction and benign prostatic hyperplasia. He has spoken widely on these and other topics and published his work on testosterone therapy, fertility, prostate health, hypogonadism, and restoring erectile function in peer-reviewed journals, including Journal of Urology, Journal of Andrology, Journal of Sexual Medicine, and International Journal of Impotence Research. He edited Urology and the Primary Care Practitioner and has contributed chapters to several other books, including most recently, Fertility Preservation in Men With Cancer.

He serves on the International Society for Sexual Medicine Strategy and Development Committee and holds memberships in the American Medical Association and the American Urological Association. Dr Khera was awarded the Sexual Medicine Society of North America Basic Science Award in 2009.
Abraham Morgentaler, MD, is Associate Clinical Professor of Surgery (Urology) at Harvard Medical School, in Boston, Massachusetts. He is Founder and Director of Men’s Health Boston and is affiliated with Beth Israel Deaconess Medical Center, in Boston.

Dr Morgentaler received a medical degree from Harvard Medical School and completed a residency with the Harvard Program in Urology.

Among his primary research interests are male hypogonadism and erectile dysfunction (ED). He teaches the pathophysiology of male reproductive and sexual disorders at Harvard Medical School and lectures frequently on an international basis on the topics of sexuality, ED, and issues related to low testosterone.

Dr Morgentaler has contributed numerous journal articles, book chapters, and letters to the medical press. His work has been published in New England Journal of Medicine, Lancet, and Journal of the American Medical Association, among others. In addition, Dr Morgentaler has published 2 books, including most recently, The Viagra Myth: The Surprising Impact on Love and Relationships.

Dr Morgentaler is a Fellow of the American College of Surgeons and a member of the American Society of Reproductive Medicine, the International Society for Impotence Research, the Sexual Medicine Society, the Society for the Study of Male Reproduction, and the American Society of Andrology. In addition, he is co-chair of the Endocrine Forum at the annual meeting of the American Urological Association and has been a State-of-the-Art Lecturer at the annual meeting of the American Society for Reproductive Medicine. He has been awarded the prestigious New Investigator Award from the American Foundation for Urological Disease.

Jacob Rajfer, MD, is Professor in the Department of Urology of the University of California, Los Angeles (UCLA) and Chief of Urology at the Harbor-UCLA Medical Center, in Torrance.

Dr Rajfer received a medical degree from Northwestern University Medical School, in Chicago, Illinois. He completed an internship in medicine at Los Angeles County–University of Southern California Medical Center and residencies in surgery, at St. Joseph’s Hospital, in Denver, Colorado, and urology, at Johns Hopkins Hospital, in Baltimore, Maryland.

Dr Rajfer has focused his research on erectile dysfunction (ED). He is investigating the role of nitric oxide in aging-related ED and how oral phosphodiesterase type 5 inhibitors modulate the changes within the corpora after radical prostatectomy.

A frequent contributor to the medical literature, Dr Rajfer has published more than 200 journal articles and book chapters. His work has appeared in Urology, Neuroendocrinology, JAMA, New England Journal of Medicine, and other journals.

Dr Rajfer is a member of numerous medical organizations, including the American Urological Association, the American Society of Andrology, and the Sexual Medicine Society of North America. In 2010, he was inducted into the Society of Scholars of Johns Hopkins University.
For 7 decades, the assertion that high serum testosterone is risky for prostate cancer and low testosterone is protective has been axiomatic. 1 Over the past decade, conventional wisdom has been turned upside down, and there has been a radical shift in our understanding of the relationship between androgens and prostate cancer. A growing body of evidence highlights the importance of consistently assessing testosterone levels and that the presence of low serum testosterone is associated with an increased risk of prostate cancer, particularly high-grade prostate cancer. 1-6

Nevertheless, despite increased awareness of the consequences of low testosterone as well as the beneficial effects and the safety of testosterone therapy, treatment of low testosterone has been hindered by lingering concerns about prostate cancer. In 2006, Gooren et al’s multinational physician survey, published in Aging Male, demonstrated that a large number of men remain untreated because of physicians’ concerns that testosterone therapy may increase the risk of prostate cancer. 7

In Gooren and Behre’s recently published report comparing results from the 2006 study and their 2010 follow-up data, it was noted that, although more men were treated with testosterone in 2010, 11% of eligible candidates did not receive therapy. 8 Though physicians are becoming more sensitive to diagnostic symptomatology—as shown by a marked increase in
considering ED, low libido, obesity, and even depression as signals for hypogonadism—strong concerns about general prostate pathology and prostate cancer actually increased. Furthermore, in spite of increased information and educational efforts, significantly more physicians expressed concerns about the adverse effects of testosterone treatment in 2010 than in 2006 (78% versus 54%). It is pressing to place these clinical concerns in the context of the latest evidence.

Urologists are now faced with a new level of seemingly sophisticated and complex clinical conundrums. With the advent of increased prostate cancer screening, should patients with biochemical or symptomatic hypogonadism be treated if they have been diagnosed with localized prostate cancer? This is particularly important to address because treating patients who have been diagnosed with any stage of prostate cancer with exogenous testosterone has been prohibited.9,10

In this highly interactive discussion session, we will evaluate the historical underpinnings of prostate-cancer concerns. We will assess whether there is any evidence supporting an etiologic relationship between exogenous

Testosterone Therapy After Radical Prostatectomy

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PSA, prostate-specific antigen.
testosterone and prostate cancer and the lack of reports of cancer flare occurring in patients with localized prostate cancer who were treated with exogenous testosterone. We will examine the effect of testosterone therapy on prostate-specific antigen levels in hypogonadal patients, showing how this further supports the Saturation Model. We will review recent studies evaluating the effect and safety of testosterone therapy in select patient populations who previously remained untreated with testosterone therapy, namely patients post-prostate cancer treatment, and testosterone-deficient men with untreated prostate cancer who have received testosterone therapy. We will conclude by discussing current treatment and monitoring paradigms and which patient populations should be considered candidates for testosterone treatment in light of the current evidence, the Saturation Model, and the shifting intellectual zeitgeist.
Testosterone Therapy and Prostate Health: Examining Barriers to Treatment of Hypogonadism

References


NOTES
Testosterone plays an important role in physiologic, biochemical, and structural aspects of erectile function.1 Numerous studies have reported a strong association between lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) that is independent of age and other comorbidities.2,3 Also well-recognized is the relationship between ED and hypogonadism, and evidence suggests that testosterone levels inversely correlate with ED severity.1,4

Benign prostatic hyperplasia (BPH) is one of the most common diseases in older men. It has been suggested that testosterone therapy may exacerbate symptoms of BPH/LUTS.5 The labeling information for every testosterone therapy reinforces that clinicians should monitor patients with BPH for worsening of signs and symptoms. Therefore, it seems imperative that we consider whether compelling data suggest that testosterone therapy contributes to worsening of LUTS or promotion of urinary retention.

The precise impact of testosterone on androgen-dependent tissue remains to be elucidated.6 Microanatomical changes causing fibrosis and loss of tissue elasticity, which in turn may correspond with the effect of testosterone on penile tissue in men with hypogonadism, may

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**Testosterone Therapy Dual Function: Relief of Hypogonadism Symptoms and LUTS**

Culley C. Carson III, MD
Jacob Rajfer, MD

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**Relationship Between Aging, Comorbidities, Hypogonadism, and ED**

Aging

- Metabolic syndrome
- RhoA/Rho-kinase
- Pathway inhibitors?
- NO
- PDE5 inhibitors
- Testosterone

AH, autonomic hyperactivity; ED, erectile dysfunction; NO, nitric oxide; PDE5, phosphodiesterase type 5.
help explain the apparent relationship between LUTS and metabolic syndrome. A recent preclinical model showed that testosterone protects the prostate from metabolic syndrome-induced prostatic hypoxia, fibrosis, and inflammation that can play a role in the development and progression of BPH/LUTS. Considering the body of evidence reinforcing the benefits of testosterone therapy on parameters of metabolic syndrome, it is important to explore the potential benefits of testosterone therapy on and its relationship with BPH/LUTS.

Clinicians should carefully explain the sexual effects of BPH treatment (eg, phosphodiesterase type 5 [PDE5] inhibitor, α-blocker, 5α-reductase inhibitor [5-ARI]) when evaluating therapy choices with patients. It has been suggested that, particularly in patients with BPH, testosterone therapy should be monitored closely, both because the prostate is androgen-dependent and because LUTS may be exacerbated by testosterone therapy. Studies investigating the effects of normalizing testosterone levels in older men suggest that reestablishing eugonadal testosterone...
levels may positively affect International Prostate Symptom Score (IPSS).\textsuperscript{5,6,8,10} This warrants further investigation in sufficiently powered, randomized, placebo-controlled trials.

We will examine how all patients presenting with BPH/LUTS or ED should be assessed for hypogonadism. We will carefully weigh the evidence suggesting that testosterone therapy exacerbates symptoms related to BPH against the latest studies suggesting positive effects of testosterone on symptoms of BPH/LUTS. Finally, we will assess which patient populations with comorbid conditions associated with hypogonadism may benefit from testosterone therapy and evaluate the risks and benefits.


Testosterone Therapy and Prostate Health: Examining Barriers to Treatment of Hypogonadism

References


NOTES
Suggested Reading


Testosterone Therapy and Prostate Health: Examining Barriers to Treatment of Hypogonadism


Kupelian V, Page ST, Araujo AB, Travison TG, Bremner WJ, McKinlay JB. Low sex hormone-binding globulin, total testosterone, and symptomatic androgen deficiency are associated with development of the metabolic syndrome in nonobese men. J Clin Endocrinol Metab. 2006;91(3):843-850.


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