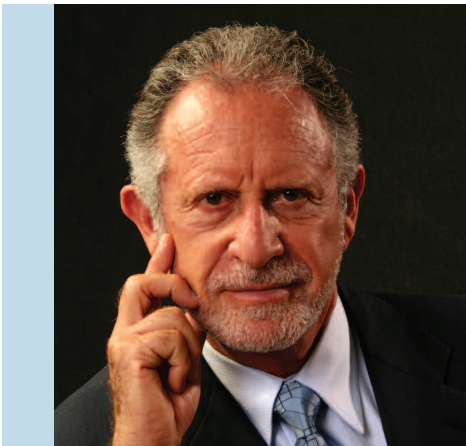


From the EDITOR



Dr. Wulf H. Utian, consultant in women's health and reproductive endocrinology, has served as Editor-in-Chief of *Menopause Management* since its inception in 1988. The Arthur H. Bill Professor Emeritus of Reproductive Biology and Obstetrics and Gynecology, Case Western Reserve University School of Medicine, he is also Consultant, Obstetrics, Gynecology and Women's Health Institute at the Cleveland Clinic, and Executive Director of The North American Menopause Society (NAMS). He is Chairman of the Advisory Board of Rapid Medical Research, Cleveland. He received his medical degree from the University of Witwatersrand, Johannesburg, South Africa, and his PhD from the University of Cape Town, South Africa, and is a Fellow of the Royal and American Colleges of Obstetricians and Gynecologists, as well as the International College of Surgeons. In 2007 he earned the DSc(Med) degree from the University of Cape Town, its highest degree and only awarded 11 times in over 100 years.

A pioneer in Women's Health issues and menopause research, in 1967 he established the Groote Schuur Menopause Research Clinic in Cape Town, the world's first such clinic. He was one of the three original founders of the International Menopause Society in 1976, of which he is Honorary Past President, and founded the North American Menopause Society in 1989.

He is the recipient of numerous national and international awards and research grants, and is still an active investigator with multiple grants. Dr. Utian has written over 200 papers related to the reproductive system in women and has authored five books on menopause and its effects on women. He is editor of *Menopause: The Journal of The North American Menopause Society*.

HSDD and the Testosterone Dilemma

When it comes to helping women with hypoactive sexual desire disorder (HSDD), we face an extraordinary clinical dilemma. In a 2005 article in this publication, I wrote: "In addition to the well-characterized somatic symptoms of menopause, sexual dysfunction such as low sexual desire may occur in oophorectomized women. Loss of sexual desire in surgically menopausal women can cause considerable concern and a diminished quality of life. Physicians are encouraged to take a proactive approach to the identification and management of sexual problems such as HSDD through discussion with their patients. A thorough sexual, medical, psychological and psychosocial history is warranted when sexual dysfunction is suspected based on initial questioning."¹

This seems a perfectly sound, evidence-based and logical statement, and would certainly apply to the non-oophorectomized population as well. I then went on to state: "The etiology of HSDD is often multifactorial, but depletion of testosterone levels may be a common contributor to loss of desire postoperatively. Testosterone patch therapy has been shown to significantly increase sexual desire and activity scores in controlled clinical trials in surgically menopausal women with HSDD receiving concomitant estrogen. Additional studies are needed to define the long-term safety and efficacy profiles of individual testosterone formulations in this population. With the impending availability of new therapies for HSDD in surgically menopausal women, physicians are encouraged to carefully review existing and emerging clinical trial data to help ensure the appropriate use of these therapies in the office practice setting."¹

But that "impending availability" did not come to be. As the medical world anticipated the imminent approval of the testosterone patch, the FDA dashed the high hopes, stating that long-term effects of testosterone on post-

menopausal women, especially in relation to risk for cardiovascular disease (CVD), were unknown and required further clarification. Nor has there been uniform consensus on whether there is such a problem as an “androgen-deficiency syndrome” in women.²

The Dilemma

So here is the dilemma. Irrespective of whether there is an androgen-deficiency syndrome, there is evidence for the efficacy of low-dose testosterone patch therapy in alleviating HSDD. But in the absence of any FDA-approved treatment, is it worth the time and effort to make the diagnosis?

In comparison to men, relationships and mental health in women are proving to be more important predictors of sexual well-being than the physiologic factors of sexual arousal and response.³ Moreover, some women are motivated more by a desire for intimacy, while the need for sexual pleasure and orgasm may be more important for others. For the former, wise counseling is all that may be necessary. For the latter, there remains the dilemma of the role of testosterone. For both, recent evidence suggests that sexual problems are infrequently discussed with physicians.⁴

Developing Research

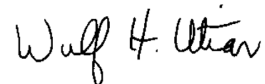
Meanwhile, where is the research going in relation to testosterone therapy and CVD risk? Actually, it is moving in a somewhat different direction than originally anticipated. In contrast to the FDA's concern that testosterone might increase cardiovascular risk, the question is now: “Might testosterone actually reduce mortality?”⁵ There is some evidence that low testosterone levels are associated with an increased mortality rate in men. The mechanisms are not clear but speculation includes reduced fracture-related mortality, or induced metabolic risk factors like central obesity, reduced muscle mass, metabolic syndrome and diabetes mellitus. Alternately, the data suggest that, at least in men, testosterone sufficiency might be beneficial to survival.

How does this information apply to postmenopausal women? Here, the data are quite

conflicting. On the one hand, there is evidence that the most beneficial hormone profile to delay progression of vascular disease may be increased free estradiol and sex-hormone-binding globulin with a concomitant decrease in free testosterone.⁶ On the other hand, contrasting findings have, interestingly, come from the long-term treatment of transsexuals with “cross-sex” hormones.⁷ Androgen deprivation plus an estrogen milieu in male-to-female transsexuals has a larger deleterious effect on cardiovascular risk factors than inducing an androgenic milieu in female-to-male transsexuals. To date, neither group has demonstrated elevated cardiovascular morbidity/mortality, but the data do provide potentially positive implications for the longer-term use of testosterone in lower doses in postmenopausal women.

Resolving the Dilemma?

Given this promising direction of evidence on testosterone and CVD, one can only hope that the necessary research is accelerated, and delivered to the FDA's satisfaction. Meanwhile, with regret, I can offer no solution to our dilemma. In the absence of the necessary data, our patients will remain as frustrated as we are!



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References

1. Utian WH. Problems with desire and arousal in surgically menopausal women: advances in assessment, diagnosis and treatment. *Menopause Management* 2005;14:11-22.
2. Wierma ME, Basson R, Davis SR, et al. Androgen therapy in women: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2006;91:3697-3710.
3. Bancroft J, Loftus J, Long JS. Distress about sex: a national survey of women in heterosexual relationships. *Arch Sex Behav* 2003;32:193-208.
4. Lindau ST, Schumm LP, Laumann EL, et al. A study of sexuality and health among older adults in the United States. *N Engl J Med* 2007; 357:762-74.
5. Snyder PJ. Might testosterone actually reduce mortality? *J Clin Endocrinol Metab* 2007;93:32-3.
6. Karim R, Hodis HN, Stanczyk FZ, et al. Relationship between serum levels of sex hormones in progression of subclinical atherosclerosis in postmenopausal women. *J Clin Endocrinol Metab* 2008;93:131-8.
7. Gooren LJ, Giltay EJ, Bunck MC. Long term treatment of transsexuals with cross-sex hormones: extensive personal experience. *J Clin Endocrinol Metab* 2008;93:19-25.