

## MINDFUL PRACTICE

## Testosterone for Low Libido After Menopause

BY JON O. EBBERT, M.D., AND ERIC G. TANGALOS, M.D.

## The Problem

A 51-year-old female physician presents to you for follow-up of impaired fasting glucose, hypertension, migraine, and allergies. Her body mass index is 32 kg/m<sup>2</sup>, and her blood glucose level is 112 mg/dL. Her blood pressure is well controlled on hydrochlorothiazide, and she also takes fexofenadine and rizatriptan. She tells you that she has experienced gradually decreasing libido over the past 1-2 years. Her last menstrual period was 22 months ago, and she is not depressed. She reports that her relationship with her husband is excellent, and she wonders if she can take a hormone for her low libido.

## The Question

In menopausal women with impaired sexual functioning, does testosterone increase libido and increase clinically important side effects, compared with placebo?

## The Search

You log on to PubMed ([www.pubmed.gov](http://www.pubmed.gov)) and use "testosterone" and "sexual dysfunction" as your search terms. You limit the results to randomized, controlled trials. You find a relevant study. (See box at right.)

## Our Critique

The study was well conducted, and the blinding seemed appropriate. The selection of the primary end point was clinically relevant and patient-centered. Baseline sexual function seems reasonable, with subjects rating 50% of sexual encounters as satisfying. Some concern is raised regarding the observed breast cancers in the testosterone group. Although the androgenic events did not increase the likelihood of subjects discontinuing the trial, patients would need to be fully informed of the possibility of these events. The reversibility of these events after discontinuation of therapy is unknown.

## Clinical Decision

After reviewing and discussing the study results, you and the patient decide not to pursue this course of action. She further discloses that she had refilled testosterone prescriptions for some of her older female patients when she first entered practice, but she has since stopped doing so.



DR. EBBERT and DR. TANGALOS are with the Mayo Clinic in Rochester, Minn. They have no conflict of interest to report. To respond to this column or suggest topics for consideration, write to Dr. Ebbert and Dr. Tangalos at our editorial offices or e-mail them at [imnews@elsevier.com](mailto:imnews@elsevier.com). DR. THOMAS JAEGER of the Mayo Clinic contributed to this column.

## S.R. Davis, et al.

*Testosterone for low libido in postmenopausal women not taking estrogen. N. Engl. J. Med. 2008;359:2005-17.*

► **Design and Setting:** This randomized, double-blind, placebo-controlled trial was conducted at 65 clinical centers in five countries.

► **Subjects:** Potential subjects had to meet criteria for hypoactive sexual desire based upon a questionnaire consistent with established definitions. Subjects had to be women who either had surgically induced menopause at age 20-70 years and were postmenopausal for at least 1 year, or had undergone natural menopause at age 40-70 years and were postmenopausal for at least 2 years. Subjects over 40 years of age had to have normal breast and cervical cancer screening and a level of sex hormone-binding globulin above 12 nmol/L. All subjects had to be in a stable, monogamous relationship with partners available at least 50% of the time during the study period. Potential subjects were excluded if they had used estrogen and/or progestin during the prior 3 months, had used any androgen therapy during the prior 3 months, had a serious medical condition or breast/gynecologic cancer, or used a medication that could affect sexual function.

► **Intervention:** Subjects were randomized to receive either placebo, testosterone 150 mcg/day, or testosterone 300 mcg/day. Testosterone was delivered for 52 weeks via a patch that was changed twice weekly.

► **Outcomes:** The primary outcome was the change from baseline in the frequency of satisfying sexual events during weeks 21-24. Adverse events were assessed at each visit (weeks 6, 12, 24, 36, and 52). Specifically, facial and scalp hair changes, acne, and voice changes were assessed, and breast and cervical exams were conducted. Serum levels of free/total testosterone and sex hormone-binding globulin were assessed.

► **Results:** A total of 814 women were randomized (277 to placebo, 267 to 150 mcg/day, and 270 to 300 mcg/day). Subjects were comparable at baseline, reporting that 50% of sexual encounters were satisfying. Compared with the placebo group, the 300-mcg/day group had significant increases in the frequency of satisfying sexual episodes during weeks 21-24 (2.1 episodes vs. 0.7;  $P < .001$ ), but the 150-mcg/day group did not (1.2 episodes vs. 0.7;  $P = .11$ ). By week 24, 78% of sexual episodes were satisfying in the 300-mcg/day group, compared with 65% in the placebo group. Both testosterone groups had significant increases in scores for sexual desire and decreases in scores for personal distress from baseline to 24 weeks. Treatment effects did not differ in women undergoing surgical menopause, compared with those undergoing natural menopause. The overall incidence of androgenic events was highest in the 300-mcg/day group, and the most common event was hair growth (19.9% with testosterone vs. 10.5% with placebo).

## Menopause Differs Among Ethnic Groups

BY DAMIAN McNAMARA

LAKE BUENA VISTA, FLA. — Menopause symptoms vary significantly by ethnic group, based on data emerging from a longitudinal study.

Acculturation of women immigrants to the United States and socioeconomic status are two of the factors that might account for these differences, said Dr. Nanette F. Santoro, an endocrinologist who has coauthored multiple studies based on the Study of Women's Health Across the Nation (SWAN) data.

The study included women from seven sites: Boston; Newark, N.J.; Pittsburgh; Detroit; Chicago; Oakland, Calif.; and Los Angeles. Each site recruited white women and women from one ethnic minority group: black, Hispanic, Chinese, or Japanese. More than 10 years later, about 85% of the participants remain in the study. "We found differences by ethnicity—very intriguing differences," Dr. Santoro said.

For example, in one study of 11,652 women from SWAN, Dr. Santoro and her colleagues found that 126 participants (1.1%) reported onset of menopause before age 40 years, also known as premature ovarian failure (Human Reprod. 2003;18:199-206). This occurred in 1.0% of white women, 1.4% each of black and Hispanic women, 0.5% of Chinese women, and 0.1% of Japanese women. (See box.) These differences were statistically significant.

Acculturation of immigrants is "a double-edged sword," Dr. Santoro said at the annual meeting of the North American Menopause Society. It can improve socioeconomic status, access to health care, and attainment of higher education, but also worsen health through a less-nutritious diet.

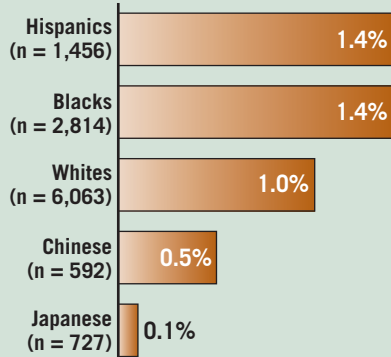
In contrast to other minorities, Hispanic women in SWAN and similar studies tend to improve little or even worsen in terms of health once they are assimilated, she said. Watch for the "Hispanic paradox": Health outcomes are worse among this population with increased acculturation, despite better socioeconomic status, because of factors such as higher rates of teen pregnancy and cigarette smoking, said Dr. Santoro, director of the division of reproductive endocrinology and infertility, Albert Einstein

College of Medicine, New York.

She cautioned that the Hispanic population is heterogeneous and cannot be addressed as a single entity. The Hispanic SWAN participants came from many different countries and cultures and displayed some internal differences. For example, women from Puerto Rico were more vulnerable to acculturation and reported more menopause-related sleep problems and depressive symptoms than did other Hispanics.

Meanwhile, acculturation of Japanese women was associated with fewer menopausal symptoms than were seen in Hispanics. Similarly, Chinese participants reported fewer symptoms compared with white, black, and Hispanic women in SWAN.

## Prevalence of Premature Ovarian Failure



Note: Based on data from the Study of Women's Health Across the Nation.  
Source: Dr. Santoro

"There are clear-cut differences in symptom reporting by ethnicity," Dr. Santoro said.

Hispanic and black women were more likely to report depressive symptoms, and Chinese and Japanese women were less likely to do so. "This is confounded, possibly, by lower socioeconomic status in the African American and Hispanic groups and a higher socioeconomic status in Chinese and especially Japanese women," she said.

Black women in SWAN reported the most hot flashes. Dr. Santoro proposed that increased adiposity among these women might provide more insulation and make them less heat tolerant. Black women, however, were less bothered by hot flashes, compared with Hispanic women, who reported more embarrassment with vasomotor symptoms.

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