A longitudinal study of the effects of free testosterone and other psychosocial variables on sexual function during the natural traverse of menopause

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Objective: This study examines the effect of free T levels on sexual function during the natural traverse of menopause. Other psychosocial variables, which may also contribute to change in sexual function, are studied—including participant's job satisfaction, satisfaction with financial resources, confidence in ability to manage symptoms, stressful life events, exercise, body image, and quality of personal relationships.
Design: Prospective clinical study.
Setting: Clinical research center, university hospital.
Patient(s): Fifty-seven women between the ages of 45 and 55 years were enrolled at the beginning of the study. Thirty-seven women completed all but the final measurement of free T and 23 completed all aspects of the study at year 1 and year 5.
Intervention(s): Questionnaires were administered and blood samples obtained in year 1 and year 5.
Main Outcome Measure(s): Free T, sexual satisfaction, and other psychosocial variables.
Result(s): Exercise is the only variable significantly associated with sexual satisfaction. There was a lack of association between free T and sexual satisfaction both at year 1 and year 5.
Conclusion(s): Focus on the hormonal aspects of menopause has promoted a disregard of other important psychosocial factors affecting sexual function. This study shows no correlation between T levels and sexual function, whereas exercise is clearly associated with sexual satisfaction. A key area for future research is the effect of lifestyle changes on sexual function in menopausal women. (Fertil Steril® 2005;83:643–8. ©2005 by American Society for Reproductive Medicine.)

Key Words: Natural menopause, sexual function, free T, exercise

Data collected by the National Health and Social Life Survey suggests that 43% of American women experience sexual dysfunction (1). Laumann et al. (2) assessed sexual dysfunction across sex, age, and demographic groups, noting a need for expanded study of etiology and concomitant medical and mental health disorders. The average life expectancy for American women currently approaching menopause is now estimated to be 85 years of age, with the timing of menopause remaining close to 50 years. Women in this study's population can expect to live more than half of their adult lives after menopause.

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Buoyed by studies that demonstrate restored receptivity in female Rhesus monkeys treated with high levels of testosterone (T), researchers have attributed menopausal libidinal changes to declining steroids, while others have suggested multiple etiologies (3–9). Because androgens as a group have been considered essential to energy, well-being, and sexual desire, sexual dysfunction has become synonymous with androgen deficiency in the lay press (10). However, female sexual dysfunction is a highly complex, multifactorial syndrome, and the role of specific androgens, as well as the biomechanisms by which they operate, is poorly understood (11).

Androgen replacement therapy remains highly controversial. Some researchers who have devoted careers to the study of sexuality question the effectiveness of T replacement in restoring libido in the presence of other confounding physiologic, psychosocial, environmental, and behavioral factors (6, 12–15).

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This particular study was designed to learn more about changes in free T during the menopause transition and its effect on sexual satisfaction, as well as to identify other factors correlated with changes in sexual satisfaction.

Early research attributed a decline in sexual response to a decline in total T. More recently, sex hormone-binding globulin (SHBG) has also become a critical player in understanding T. The SHBG is suppressed by exogenous glucocorticoids, androgens, and progestins, but elevated by estrogens (E) (found in oral contraceptives [OC] and hormone replacement therapy [HT]). As SHBG increases, total T increases, but the free or active T decreases, possibly giving false information about the actual level of T, which is biologically active, and possibly supporting sexual desire (16).

Landmark research on the subject is severely limited. The Cutler and Garcia (6) results have not been reproduced in the two decades since their original study. Sherwin (7) based early conclusions on populations of college-aged or surgically menopausal women. Rosen (11) cited three randomized controlled studies to date suggest the importance of T in postmenopausal women. Schrifren et al. (8) linked T replacement to improved sexual function by treating oophorectomized women with superphysiologic doses of T. Lobo (17) found increased sexual desire in postmenopausal women treated with estrogen and T over estrogen alone. Davis (18) found in women, with total T levels of less than 2 ng/dL, a positive effect on sexual function when treated with transdermal T cream.

A 2001 Princeton conference provided the forum for international researchers to reach consensus about current scientifically based knowledge regarding female androgens (19). Although it was agreed that androgens, including T, gradually decline with age, it was noted that the vast majority of androgen insufficiency in women is iatrogenic. Hormone replacement therapy, OCs, oophorectomy, and adrenal suppression are common causes of androgen insufficiency in premenopausal as well as postmenopausal women. An algorithm for the diagnosis and treatment of androgen insufficiency was established at Princeton with the measurement of free T the final step before a trial of T replacement is recommended (16). Lower limits of androgen established for menopausal women are arbitrary, with total T less than 15 ng/dL and free T less than 1% (2 pg/mL).

The Melbourne Women's Midlife Health Project revealed that T levels in women naturally traversing menopause are more related to age than to final menstrual period. Burger et al. (20) also reported that the free androgen index (FAI) was not related to age or E_2, but rather to body mass index (BMI).

The significance of this study lies in the ability to compare changes of free T in perimenopausal women during a 5-year period with the changes in sexual satisfaction, while eliminating such iatrogenic influences as HT, OCs, oophorectomy, and obesity.

MATERIALS AND METHODS

Data for year 1 of this study were collected during the second screening visit of the 57 premenopausal women between the ages of 45 and 55 years, volunteering to participate in a 5-year study of energy metabolism and body composition, initiated in 1995 by Eric T. Poehlman at the University of Vermont College of Medicine. Premenopausal status was defined as having an FSH level of no higher than 30 mIU-ml, three consecutive menstrual cycles in 3 months preceding baseline visit, absence of surgically induced menopause, no hormone therapy, and a BMI between 22 and 27. Exclusion criteria eliminated women who were pregnant, had serious medical problems that could affect menopausal transition time or outcome variables, or had a history of drug or alcohol abuse. In addition, subjects were queried about the use of medications known to influence factors under study (e.g., insulin, thyroid hormones, estrogens, antihypertensive drugs, or psychotropic medications). Women on these medications were excluded from the study. Each participant gave informed consent to be included in the study, which was approved by the University of Vermont Committees on Human Research.

The study participants completed a three-part psychosocial questionnaire designed by the primary investigator. The first part included psychosocial information such as level of education, number and ages of children, marital status, financial, and career satisfaction. This was used to tabulate current number of psychosocial stressors. The second part consisted of 18 questions about sexual satisfaction (current level of desire, change in desire during the past 5 years, body image, communication, extent of experience, sexual initiative, and sexual satisfaction in the various contexts of a committed relationship, fling, or masturbation). The third part focused on menopause symptoms and ability to control disturbing symptoms. The scores on the sexual satisfaction scale ranged from a low of 8 (indicating little/no sexual satisfaction) to a high of 40 (indicating high sexual satisfaction). Chronbach's alpha for this scale was 0.70 for data collected in year 1 and 0.68 for data collected in year 5, indicating acceptable reliability (21).

Thirty-five study participants completed this psychosocial questionnaire at year 1 and year 5 of the study. Free T levels were obtained on 23 women at year 1 and year 5. The free T measurements (DSL, free T EIA kit) were performed in a single assay at the University of Vermont Obstetrics and Gynecology Research Laboratory. This assay evaluates serum free T levels using a competitive binding biotin immunoassay format with standards, controls, and patient samples incubated with biotin-labeled T and rabbit anti-T antiserum in microtitration wells coated with goat antirabbit gamma globulin where the unlabeled and biotin-labeled antigens compete for a limited number of anti-T-binding sites. After incubation for 60 minutes at room temperature, the wells are washed five times and streptavidin-HRPO is added to bind to biotinylated testosterone for 30 minutes. Unbound streptavidin-HRPO is