Hormonal Aspects of Sexual Dysfunction: The Therapeutic Use of Exogenous Androgens in Men and Women

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Hormones exert a pervasive influence on sexual activity. Androgens are involved in the initiation and maintenance of libido and spontaneous arousal. In recent years, the clinical use of exogenous androgens for treatment of sexual dysfunction has received a great deal of attention. Good evidence exists that such treatment is effective for arousal difficulties in men and women in the setting of a hypo-androgenic state. This article reviews the relationship between androgens and sexual function.

Introduction

It has long been recognized that androgens exert potent prosexual effects, particularly in men. In the now classic studies performed by Berthold in the mid-19th century, he demonstrated that implantation of testes into the abdominal cavity of castrated roosters restored the sexual behaviors that had disappeared following castration. He postulated that a blood-borne substance, acting on the brain, must be responsible [1]. Modern endocrinologic investigations have confirmed the role of gonadal steroids, particularly androgens, in the coordination of sexual behavior with physiologic events in the body related to fertility [1]. Over the past century, androgens have been frequently used empirically to enhance sexual functioning in men, and in more recent years, in women [2,3]. This review, focuses on the clinical use of exogenous androgens for treatment of sexual dysfunction in men and women.

Androgen Physiology

The gonads (*ie,* testes in males, ovaries in females) and adrenals secrete several "male" sex hormones, called androgens. All are steroid hormones, that is, derived from cholesterol and containing a basic skeleton of four fused carbon rings. Testosterone is the most potent and abundant androgen. Gonadotropin-releasing hormone from the hypothalamus promotes anterior pituitary release of luteinizing hormone (LH) and follicle stimulating hormone (FSH). In males, LH stimulates the interstitial cells of Leydig in the testes to synthesize and secrete testosterone; approximately 7 mg of testosterone is secreted daily. Secretion occurs in pulsatile bursts, about six per day, with a morning peak and an early evening trough, and is regulated through a negative feedback on the hypothalamus and pituitary [4,5]. Premenopausal women produce approximately 0.3 mg of testosterone per day, and have a testosterone surge in the middle third of the cycle, which is concomitant with the midfollicular estrogen surge. The ovaries and adrenals contribute equally to testosterone production: 25% is produced in the ovaries (converted from androstenedione), 25% is produced directly by the adrenal cortex, and the remaining 50% is produced in peripheral tissues (primarily liver, skin, and brain) from adrenal and ovarian precursors.

In the circulation, approximately 98% of testosterone molecules are protein bound. Of this, about one-third are weakly bound to albumin, and the remainder are tightly bound to sex hormone-binding globulin (SHBG) [4,5]. SHBG, a β-globulin produced primarily in the liver, consists of different protein subunits, and one androgen-binding site. Fluctuations in SHBG levels affect the bioavailability of testosterone. For example, exogenous estrogen therapy leads to an increase in SHBG and a consequent reduction in free testosterone.

In target cells, testosterone is converted to two active metabolites: dihydrotestosterone (DHT) and estradiol. There is tissue variability in the concentration of the cytoplasmic enzymes required for this conversion, 5-α-reductase and aromatase, respectively, and differential tissue sensitivity to each of these metabolites. Both testosterone and DHT bind to the androgen receptor (AR); estradiol binds to the estrogen receptor [4–6]. The steroid-receptor complex binds to specific sequences of genomic DNA, which thereby influ-

ences messenger RNA production and modulates synthesis of a wide array of enzymatic, structural, and receptor proteins [4,5]. The AR gene has a polymorphic CAG microsatellite, which encodes variable-length glutamine repeats in the N-terminal of the AR protein. The length of the polymorphic CAG repeat is inversely correlated with the transactivation function of the AR. Recent studies have indicated that short CAG repeats are related to a higher risk of prostate cancer, younger age at diagnosis, and worse response to endocrine therapy, as well as to increased growth of benign prostatic hypertrophy [7]. Preliminary evidence from a large epidemiologic study suggests that this AR trait, coupled with low testosterone level, may be associated with significant depressive symptoms in middle-aged men (Seidman SN, Araujo AB, Feldman HA, McKinlay JB: Relationship between low testosterone level, CAG codon repeats, and depression: result from the MMAS, 2000; Unpublished data). Finally, testosterone influences cellular activity in a nongenomic manner through activation of membrane receptors, second messengers, and the membrane itself [2,6]. Such nongenomic actions appear to be especially important in the central nervous system [2,8,9].

Dehydroepiandrosterone

Dehydroepiandrosterone (DHEA) and its metabolite, DHEA sulfate (DHEA[S]), and androstenedione are the major androgenic steroids secreted by the adrenal cortex. Although not potent androgens themselves, they are converted in target organs to testosterone and DHT. This is likely of significant androgenic consequence in females [10]. DHEA(S) is also produced in situ in brain tissue and hence is termed a neurosteroid [11].

Plasma and cerebrospinal fluid DHEA(S) levels decline with age: at age 70, DHEA(S) levels are about 20% of those at age 20 [10]. Many, but not all, studies have reported lowered levels of DHEA(S) or lowered ratios of DHEA(S) to cortisol in patients with depression, chronic fatigue syndrome, postpartum depression and anxiety, poor life satisfaction, psychosocial stress, and functional limitations [10]. Similarly, in most, but not all [12], population-based studies of the elderly, DHEA(S) level has been positively correlated with cognitive and general functional abilities, leading some investigators to propose that DHEA(S) is a marker of "successful aging" [10,13]. There is speculation that DHEA(S) "buffers" the deleterious effects of excessive glucocorticoid exposure. Overall, accumulating descriptive and epidemiologic data suggest a relationship between DHEA(S) levels and functional abilities, memory, mood, and sense of well-being, though there are many inconsistencies in the literature.

Androgen Actions

During the male embryonal stage, testosterone is responsible for the growth of the penis and scrotum, development of the prostate and seminal vesicles, descent of the testes, and suppression of the development of female genitalia [4–6]. The testosterone surge of puberty causes the genitalia to enlarge about eightfold, promotes the development and maintenance of secondary sexual characteristics, and supports anabolic activity.

Androgen-sensitive physiologic effects occur at multiple levels, including metabolic processes [14], peripheral tissues (*eg*, the penis and clitoris [15]), the spinal cord [16], and the brain [1,17]. Testosterone affects hair distribution (including baldness), stimulates prostatic secretion and growth, masculinizes the larynx and the skin, promotes protein anabolism, leading to muscular development, bone growth, calcium retention, and an increase in basal metabolic rate, and increases red blood cell production and hemoglobin synthesis [4–6].

The relationship between androgens and behavior is complex and appears to be modulated by experience. Nonspecific metabolic effects (*eg*, increased hematocrit, anabolism) and stimulatory effects on genital tissue could indirectly influence sexual functioning (*eg*, via increased general arousal). Specific central nervous system activation occurs through binding of androgen receptors by testosterone or DHT, estrogen receptors by estradial, and through membrane-associated actions [1,17].

The sexual effects of testosterone include perinatal organizing effects and post-pubertal activating effects. It has been established in many mammalian species that testosterone, acting during a brief, critical developmental period, permanently alters brain structure and function [1,4,5,18]. Such organizing effects lead to behavioral predispositions in the setting of later re-exposure to testosterone; that is, testosterone-sensitive neural networks are wired. This has been demonstrated most clearly in rodents. For example, perinatal androgen exposure of female rats leads to masculinized sexual, aggressive, and exploratory behavior post-pubertally (particularly when activated by testosterone), and loss of the female pattern of gonadotropin secretion [1,4,5]. In humans, prenatal exposure of female fetuses to excessive androgens (as a consequence of congenital adrenal hyperplasia) is associated with the development of male-like play behavior during childhood, male-like sexual imagery and preferences in adulthood, and more aggressive behavior compared with that of female relatives [19,20].

Sexual Function, Androgens, and Age

Age

In men and women, androgen secretion declines and sexual dysfunction increases with age [21,22]. The relationship between these para-aging phenomena is unknown. In a comprehensive meta-analysis, Gray *et al*. [23] used 44 studies that met stringent criteria for reporting the relationship between mean testosterone level and age in men. They demonstrated that the age-related decline in testosterone level was particularly pronounced among healthier men

compared with men who had any illness. In a multiple regression model, the best predictors of both testosterone level and the slope of the age-related decline were good general health status and morning serum sampling (both of which predicted higher levels and steeper slopes). This was probably due largely to the blunting of the circadian early morning peak that occurs with age and illness [24]. Overall, the decline in free testosterone, about 1% per year after age 40, was about twice that of total testosterone.

In women, the relationship between age, menopause, sexual function, sex steroids, and social and relationship factors is complicated. Testosterone level declines linearly with age, and the mid-cycle testosterone surge is blunted [25]. In cross-sectional cohorts, testosterone levels among premenopausal women in their mid-40s are about half those of women in their 20s [26]. This apparent decline in testosterone secretion continues into the postmenopausal period and appears to be related more to age than to menopause [27]. Yet menopause, independent of age, is associated with a decline in sexual function: postmenopausal women, compared with women in their reproductive years, report fewer sexual fantasies, reduced vaginal lubrication during sex, and less sexual satisfaction [21,28,29••,30]. Hormone replacement therapy (HRT) with estrogen improves vaginal dryness and vasomotor symptoms but does not appear to affect libido [31–33]. Finally, lack of a partner and poor health of a partner are particularly important negative influences on the sexual activity of a large proportion of older women [34].

Male sexual function

In all male mammals studied, there is a dramatic reduction in sexual activity following the removal of testosterone by either surgical ablation of the testes or through seasonal regression [35]. In most male mammals, castration is followed first by loss of ejaculation, then intromission, and finally mounting; androgen replacement restores these sexual behaviors in reverse order [35]. Although among humans the role of testosterone in the maintenance of male sexual function is more complex, a large body of evidence supports a strong influence. For example, increasing plasma androgens at puberty is correlated with the onset of nocturnal emission, masturbation, dating, and infatuation [18]. Males with an early onset of androgen secretion, (precocious puberty), often develop in parallel an early interest in sexuality and erotic fantasies [16]. Postpubertal onset of hypogonadism is characterized by loss of libido and lack of vigor and a loss in sleep-associated and spontaneous erections [36]. Testosterone replacement of hypogonadal men leads to a dramatic increase in sexual desire, sexual activity, and frequency of erections [37]. Finally, suppression of testosterone secretion in eugonadal men leads to reduced sexual desire and activity, and a decrease in spontaneous and fantasy-driven erections, but no decrease in erectile response to erotic film (*ie,* externally driven erections) [35,38,39]. Notably, testosterone levels in eugonadal men do not generally correlate with sexual desire or performance, although studies have been inconsistent [35]. The clinical consensus has been that among men there is a "low testosterone threshold" (which may vary from person to person) below which some aspects of sexual function are impaired, particularly internally driven erections and arousal. However, such a threshold is not well established, and some data (presented subsequently) suggest that testosterone administration to eugonadal men can stimulate arousability and sexual interest [37,40].

Exogenous androgen administration

Sexual effects

A few well-controlled studies have been made of testosterone administration to eugonadal men with sexual dysfunction [40–42]. In general, they have demonstrated that administration of physiologic doses of testosterone 1) is no more effective than placebo for erectile dysfunction, 2) leads to a modest increase in sexual interest, and 3) does not lead to a change on self-report measures of mood. For example, Schiavi *et al.* [40] enrolled 18 eugonadal men (age range 46–67 years) who presented with the chief complaint of erectile dysfunction in a double-blind, placebo-controlled, cross-over study of testosterone 200 mg or placebo every 2 weeks for 6 weeks. They found that during the testosterone as compared with the placebo phase, ejaculatory frequency doubled; other measures of sexual arousal increased, but this was not statistically significant; erectile function and sexual satisfaction were unaffected; and mood, assessed by self-report instruments, was unaffected [40]. Most subjects could not correctly identify the phase in which they received testosterone and felt it was not helpful. Notably, the authors were unable to demonstrate that this schedule of testosterone administration led to an increase in circulating levels 2 weeks after each intramuscular injection, suggesting that this dose may have been too low to over-ride the compensatory feedback mechanisms operating in eugonadal men.

O'Carroll and Bancroft [42] administered testosterone to men with erectile dysfunction (n = 10) and hypoactive sexual desire (n = 10). There was no demonstrable effect of testosterone on erectile function and a clinically significant effect on desire in only three patients in the low-desire group. Carani *et al.* [43] administered testosterone to 14 men with sexual dysfunction and demonstrated it to be helpful only for those who were mildly hypogonadal.

Anderson *et al.* [37] randomized 31 eugonadal men, in single-blind fashion, to receive testosterone 200 intramuscularly (IM) for 8 weeks or placebo weekly for 4 weeks followed by testosterone 200 IM weekly for 4 weeks. A significant effect of testosterone was demonstrated on the psychosexual stimulation test, which measures the extent to which an individual seeks sexual stimuli. There was no effect on measures of sexual behavior, including intercourse frequency, erectile function, or masturbation, and no apparent effect on mood.

Rabkin *et al.* [44] openly administered physiologic doses of exogenous testosterone for 8 to 12 weeks to 112

HIV-positive men who had testosterone levels below 500 ng/dL and clinical symptoms of hypogonadism (low libido, low mood, and low energy). Of the 102 (91%) whose sexual function improved after testosterone treatment, 77 completed a 6-week, randomized, double-blind, placebo-controlled discontinuation trial. Seventy-eight percent of those randomized to testosterone maintained their improved sexual function, compared with 13% randomized to placebo.

Mood effects

Because low testosterone and excess testosterone states have powerful effects on libido, it has long been hypothesized that hypogonadism leads to depression, and that exogenous testosterone can help major depressive disorder (MDD) and depressive symptoms that evolve with age (*ie,* male "climacteric") [2,22]. Recent confirmation that testosterone level declines significantly with age [23] has given further momentum to the clinical practice of testosterone replacement as an antidepressant strategy. Yet few studies have systematically assessed the efficacy of exogenous testosterone using modern psychiatric diagnostic criteria or accepted clinical trials methodology.

In most clinical trials in which exogenous testosterone has been administered to nondepressed eugonadal men, the behavioral effects of testosterone were difficult to detect. For example, Tricker *et al.* [45] randomized 43 eugonadal men ages 19 to 40 to double-blind treatment with either testosterone 600 mg or placebo injections weekly for 10 weeks. They found no change in self-reported or observer-reported scales of hostility, anger, and mood during testosterone treatment. Matsumoto [46] administered testosterone 100 mg and testosterone 300 mg weekly for 6 months to 20 eugonadal men (n = 10 in each group). They demonstrated that compared with a 4- to 6-month pretreatment placebo phase, supraphysiologic testosterone was associated with an increased hematocrit, weight gain, mild truncal acne, and reduced LH and FSH levels, and reduced sperm count. No significant effects were detected using self-report mood inventories. Janowsky *et al.* [47] randomized 56 older men (mean age, 67 years) to receive testosterone or placebo patches for 3 months; there were no group mean differences in Profile of Mood States scores.

Reports from the older psychiatric literature on the "antidepressant" effects of testosterone, conducted mostly between 1935 and 1960, without standardized, syndromal psychiatric diagnoses or baseline testosterone levels, suggested that a substantial proportion of depressed men responded immediately and dramatically, and relapsed when treatment was discontinued [48–50]. Lack of any control group limits interpretation of these data. In the past 2 decades, there have been 10 published androgen treatment trials for male depression in which investigators used the Diagnostic and Statistical Manual of Mental Disorders diagnoses of MDD and systematically followed depressive symptoms. Most trials used the oral androgen mesterolone, which is a derivative of DHT, and therefore lacks the non-DHT actions of testosterone (*ie,* testosterone-specific and estrogenic activity) [5], and three trials used DHEA [10].

Itil *et al*. [52] performed three mesterolone trials [51,52]. First, they administered variable doses of mesterolone to 17 depressed men openly for 3 weeks and found that 8 (47%) improved, particularly in mood and anxiety level. Then, in a randomized, double-blind 4-week trial, low-dose mesterolone (*ie,* 75 mg/d) or placebo was administered to 38 dysthymic men. They reported that treatment led to improvement in symptoms such as anxiety, lack of drive, lack of desire, and impaired satisfaction [52]. Finally, they administered high-dose mesterolone (*ie,* 450 mg/d) or placebo in a 6-week randomized trial to 52 men (mean age, 40 years) with dysthymia, unipolar depression, and bipolar depression [51]. Both the mesterolone and placebo groups improved significantly, and there was no statistically significant difference demonstrable between the two. Mesterolone treatment led to a significant decrease in LH and testosterone levels, likely due to feedback inhibition at the hypothalamus and pituitary. Notably, of those patients who improved on mesterolone (initial drug responders and placebo nonresponders who were crossed over and responded), improvement in psychopathology was positively correlated with the decrease in testosterone levels during weeks 3 through 6 of treatment.

Vogel *et al.* [53] administered mesterolone openly for 7 weeks to 13 eugonadal men (mean age, 39 years) with refractory, chronic unipolar depression. Eleven responded, most by the second week, with a mean decrease the Hamilton Rating Scale for Depression (HAM-D) score (in these 11) from 21.1 to 5.6 ($P < 0.001$). The same investigators, in a 12-week randomized, double-blind trial, gave mesterolone or amitriptyline to 34 chronically depressed, eugonadal men aged 27 to 62 years [54]. Mesterolone was as effective as amitriptyline in reducing depressive symptoms: mean HAM-D score decreased by 8 in both groups.

My colleagues and I recently completed a clinical trial in which we enrolled 30 hypogonadal men (defined as testosterone level below 350 ng/dL) and comorbid MDD in a randomized trial of physiologic T replacement (*ie,* 200 mg/week) versus placebo [55]. Using a 50% decrease in HAM-D [56] to define response, 38% responded to testosterone and 41% responded to placebo [55]. In the clinical trial with HIV-infected men describe earlier [44], a retrospective analysis was done of the 34 patients with MDD or dysthymia who completed 8 weeks of open testosterone treatment. Mean HAM-D score decreased from 18.5 to 3.0 at week 8, as did symptom inventories for depressive, anxious, and somatic symptoms ($P < 0.001$). Among men who had low mood at study entry but did not meet MDD or dysthymia criteria, mean HAM-D score decreased from 11.9 to 2.7 by week 8 ($P < 0.001$). Such data suggest that exogenous testosterone may have a positive effect in some men with mild depression.

Finally, there appears to be a subpopulation of men who develop very profound psychiatric effects from exogenous or supraphysiologic testosterone [57–60]. Three clinical trials suggest that supraphysiologic doses of testosterone may produce mania in a subgroup of individuals. Su *et al*. [61] administered a high dose of testosterone (methyltestosterone 240 mg per day) for a short time (3 days at the maximum dose) to 20 eugonadal men. One man became manic and one hypomanic. Yates *et al*. [60] administered testosterone 500 mg per week for 14 weeks to 18 men; one (6%) became manic. In the most systematic psychiatric investigation of the effects of moderately supraphysiologic testosterone in eugonadal men, Pope *et al*. [59] randomized 66 men (age range, 20–50) who did not have psychiatric histories to receive testosterone in doses rising to 600 mg per week, or placebo, for 6 weeks, followed by a 6-week no treatment period, and then cross-over to the alternate treatment. They found that testosterone administration significantly increased the mean manic score on the Young Manic Rating Scale ($P = 0.003$) and on daily diaries ($P = 0.004$), the "like the way I feel" score on daily diaries ($P = 0.01$), and aggressive responses on the Point Subtraction Aggression Paradigm ($P = 0.04$). The effect of testosterone on sexual function was not reported.

Overall, the data suggest that in eugonadal men, exogenous androgen treatment has no effect on erectile dysfunction but may help hypoactive desire. In hypogonadal men, androgen replacement clearly improves desire and some aspects of erectile functioning. Finally, exogenous testosterone affects mood in susceptible subpopulations, but data do not support its efficacy as an antidepressant.

Female sexual function

Fewer data are available regarding the relationship between testosterone and sexual function among human females. Following the observation made in 1959 that among women who had undergone adrenalectomy or ovariectomy (to slow the progression of breast cancer), androgens and not estrogens appeared to be responsible for libido, a large body of supporting evidence has been accumulated [62]. Evidence from correlational studies has consistently supported an association between androgen level and female sexual function. In premenopausal women, multiple studies have demonstrated a positive correlation between androgen level (particularly midcycle [63]) and intercourse frequency [64], masturbation frequency [65] and vaginal response to erotic stimuli in the laboratory [66]. The reduction in testosterone following oophorectomy and adrenalectomy is associated with a dramatic reduction in sexual desire; testosterone replacement reverses this [3,67,68]. In postmenopausal women not receiving HRT, androgen level is correlated with sexual activity [69,70]. Finally, in a group of 59 healthy, postmenopausal women in their 60s, free testosterone was the only hormone correlated with increased sexual desire [71].

Exogenous androgen administration

Sexual effects

Multiple testosterone replacement trials in oophorectomized women have demonstrated improved sexual function, with an increase in sexual fantasy, satisfaction, arousal, libido, and energy [68,72]. Improvements in coital frequency and orgasm have not been consistently demonstrated. Testosterone replacement in premenopausal women with hypothalamic amenorrhea is associated with enhanced vaginal responsiveness [73]. In postmenopausal women who have a loss of libido, testosterone replacement in addition to estrogen HRT is associated with improved sexual function [29,74,75], pleasure from masturbation [76], and mood [77]. In many of these studies, supraphysiologic doses of testosterone were necessary to achieve prosexual effects [3,72]. Moreover, in postmenopausal women who do not complain of low libido, testosterone replacement in addition to estrogen HRT has not been shown to be different from estrogen HRT alone [76,78].

Recently, Braunstein reported results of a multicenter randomized testosterone replacement trial with 75 surgically menopausal women (presented at the Endocrine Society annual meeting, San Diego, June, 1999). Patients received testosterone patches that delivered the equivalent of either 150 or 300 μg per day twice weekly. Women enrolled in the 9-month trial ranged in age from 20 to 55, had mild to moderate menopausal symptoms (*eg,* fewer than 20 severe hot flashes per week), and were taking a mean dose of 0.88 mg day of conjugated estrogen. At baseline, testosterone levels were low, SHBG levels were high, and mean scores on two self-report questionnaires, the Basic Inventory of Sexual Function for Women (BISF-W) and the Psychological General Well-Being Index were lower than the norms for age-matched women. Women who received testosterone 300 μg had normalization of free testosterone, LH, and FSH levels and moderately supraphysiologic total testosterone levels. There was a statistically significant improvement in their BISF-W score and a significant improvement in the depression component of the psychological general well-being questionnaire. In addition, they reported more interest in sexual activity, greater frequency of intercourse, and greater frequency and quality of orgasms when they were using the patch versus the placebo. The women did not report any incidence of acne or hirsutism. Notably, women under 47 years of age experienced a high placebo response.

Tuiten *et al*. [73] administered sublingual testosterone or placebo in a double-blind, crossover design to eight healthy premenopausal women (mean age 28 years). The intervention was followed by erotic visual stimuli every 1.5 hours, during which vaginal photoplethysmography (a reliable measure of genital vasocongestion), plasma hormone levels, and self-report questionnaires were collected. Crossover to the alternative intervention (test-

osterone or placebo) occurred 5 days later. Testosterone was associated with a significant increase in vaginal pulse amplitude, which peaked 3 hours following administration, and subjective experiences of genital sensations and sexual lust, which peaked 4.5 hours following testosterone administration. Notably, testosterone level peaked in the 15 minutes following sublingual testosterone administration and returned to baseline after 1.5 hours. Thus, the prosexual effects of testosterone occurred 2 to 4 hours after testosterone level returned to baseline.

Finally, a 12-month trial of 10% DHEA vaginal cream in 14 postmenopausal women suggests that DHEA may have beneficial effects on the vagina, without significant adverse effects, through the transformation of DHEA into androgens or estrogens or both in peripheral tissues [79,80]. Notably, the endometrium remained atrophic while vaginal epithelium maturation was stimulated. In a placebo-controlled trial, Arlt *et al*. [81] demonstrated that DHEA replacement enhances libido in women with adrenal insufficiency.

Mood effects

Some data suggest that testosterone acts synergistically with estrogen in the treatment of hormone-responsive depression. Two well-controlled clinical trials with menopausal women suggest that the combination of testosterone with estrogen is superior to estrogen alone for symptoms such as energy, well-being, and appetite [72,77]. Androgen (compared with placebo) administration to surgically menopausal women improves well-being and energy. DHEA replacement enhances mood in women with adrenal insufficiency [81].

Androgen therapy should be individualized and considered for those menopausal women who have sexual or mood symptoms that are not adequately relieved with traditional HRT. At lower doses, androgenizing side effects are infrequent but should be discussed.

Conclusions

In summary, good evidence exists to support the following: 1) androgen levels decline with age; 2) low androgen level is associated with reduced sexual interest; and 3) androgen replacement is associated with improved sexual function. Androgens have libido-enhancing properties in men and women who have low endogenous androgen levels. There is limited, though suggestive, evidence that exogenous androgen treatment has arousal-enhancing effects in individuals who have normal testosterone levels. There are no data that support the efficacy of testosterone for male erectile dysfunction in eugonadal men.

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