

Testosterone substitution in women

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Neurobiology of sexual desire and central (mental) arousal, and the peripheral neurovascular response are substantially modulated by sexual hormones. Androgens have a leading role in the initiation and modulation of sexual function, in women as in men. Multiple neurotransmitter systems in the brain, especially the areas known to regulate mood and desire (including the amygdala, hippocampus and hypothalamus) are heavily influenced by sex hormones; new evidence supports their role in cognition (Davis et Al, 2006) The serum levels of testosterone and of proandrogens exceed that of estradiol, even during peak reproductive years. In women, about half of circulating testosterone is secreted directly by the ovarian stroma and adrenal zona fasciculata in roughly equal quantities; the other half is derived from conversion of the proandrogen androstenedione, which is secreted by the same tissues. The proandrogen dehydroepiandrosterone sulfate (DHEAS) is produced entirely in the adrenal zona reticularis; conversion of DHEAS accounts for about 30% of circulating dehydroepiandrosterone (DHEA), with the remaining DHEA secreted by the adrenal zona reticularis and the ovarian theca. Recent data indicates that the most important source of testosterone is within the target cells. Intracellular conversion from pro-androgens to testosterone is indicated as intracrinology: its increasingly recognized importance questions the predictive value of plasmatic levels of free testosterone as a marker of sexual disorder (Davis et Al, 2005). The role of androgens in maintaining urogenital health and sexual function (in addition to their importance in overall health, mood and sexual desire) is the subject of much current research. In contrast to the relatively sharp decline in circulating estrogens during natural menopause, androgen levels tend to peak when women are in their 20s and drop gradually with age; at 40 they are on average half those at age 20; typical serum levels of testosterone and androstenedione at age 60 are about half those at age 40. At age 60 the biological fuel of sexual drive is therefore reduced to one fourth of its level at 20.

Much of the current understanding of androgen effects in women has been derived from the symptomatology of women with androgen insufficiency. The pattern of symptoms, and symptom frequency, following bilateral oophorectomy (surgical menopause) has validated their tie to androgen deficiency. The proportion of testosterone contributed by the ovaries rises dramatically after menopause, from under 30% to about 50%; thus, oophorectomy removes a substantial source of circulating testosterone. In contrast to the 50% of women who report severe symptoms following natural menopause, about 90% experience severe symptoms following surgical menopause, in which a primary source of androgens has been removed. In addition, women who have undergone chemotherapy or pelvic/whole body radiation therapy for cancer treatment may also experience iatrogenic androgen loss. Despite having ovaries in place, such therapies may irreversibly destroy not only follicles but the Leydig cells that are responsible for ovarian androgen production, leading to characteristic symptoms of androgen deficiency. These women constitute an often-unrecognized subgroup of iatrogenic premature menopause patients (Graziottin, 2006).

The prevalence of sexual desire disorders is also higher among women following surgical menopause. A recent European survey of 2467 women (in France, UK, Germany and Italy) showed that in the age cohort from 20 to 49 the percentage of women with low sexual desire is 19%, but is 32% in women who have undergone surgical menopause. This difference disappears when comparing naturally post-menopausal women (ages 50 to 70) and age-matched surgically menopausal women (46% and 48%, respectively). The percentage of women *distressed* by their HSDD was 27% in fertile women and 28% after surgical menopause in the age cohort 20 to 49, compared to 11% in women with natural menopause and 14% in those with surgical menopause in the age cohort 50 to 70. Thus although the probability of HSDD increases with age, the *distress* associated with the loss of desire is inversely correlated with age (Dennerstein et Al, 2006). Physiology of androgens, their actions on the brain and genital function, consequences of the Androgen Insufficiency Syndrome (AIS) and treatment outcomes of testosterone substitution in women will be presented with a clinical perspective (Alexander et Al, 2006, Davis et Al, 2006, Shifren et Al, 2006). Current evidence indicate its direct, positive role in significantly improving sexual desire, arousal, orgasm, satisfaction and self-image, while reducing concerns and sexual distress. Other positive effects involve improved mood, well being and vital energy and reduced anxiety: sexual hormones modulate as well the neurobiological substrate of psychological feelings, which indirectly may impact women's sexuality.

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