

## Medical/Non Medical Therapies for Female Sexual Dysfunction Treatment

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Aside from relieving hot flashes and preventing osteoporosis, estrogen can improve genital Sensation and decrease pain and burning during intercourse. It is recommended that the lowest dosage of estrogen necessary for control of symptoms should be used.

With oral estradiol, the usual initial dosage is 0.05-2.0 mg/d, which is then adjusted as needed. Transdermal estrogen is available in patches (0.025 mg-0.1 mg), and the usual initial dosage is 0.0375 mg twice a week, also adjusted as needed.

While the Women's Health Initiative clinical trial stated that the overall health risks exceeded the benefits from use of combined estrogen plus progestin in healthy postmenopausal women, each woman must be assessed for risks versus benefits of HRT and the appropriate regimen prescribed for her needs.

In response to the Women's Health Initiative study, the American College of Obstetricians and Gynecologists (ACOG) commented on several points of concern regarding the study, including these: First, while the risk of breast cancer and cardiovascular disease increased, the magnitude of actual risk was small, less than one-tenth of a percent per year. Second, no increased risk of breast cancer was reported with estrogen-only use. Finally, the study tested only one drug regimen (conjugated equine estrogen 0.625 mg/d and medroxyprogesterone acetate (Prempro) 2.5 mg/d).

ACOG further stated that HRT for the treatment of acute menopausal symptoms, when indicated, continues to be appropriate for short-term use (up to 4 years) without an apparent increase in risk of breast cancer. In menopausal women and in those who have had an oophorectomy, complaints of vaginal irritation, pain, or dryness can be relieved with a vaginally delivered estrogen (Estrace, Ogen, Premarin, etc.). There is also a vaginal estradiol ring (Estring) that delivers continuous low-dose estrogen locally and may be occasionally prescribed for breast cancer patients and others who are unable to use oral or transdermal estrogen. Topical estrogen is also available as a tablet (Vagifem), which delivers low-dose estrogen locally for relief of vaginal symptoms.

Androgen replacement therapy: Androgens are known to have a variety of physiologic and behavioral functions with beneficial effects on sexual desire. Some researchers of sexual dysfunction have shown that androgen deficiency syndrome can be alleviated with androgen replacement therapy. Randomized controlled trials studying the efficacy of combined estrogen-androgen preparations on sexual function in postmenopausal women have concluded that these agents induced a greater sense of energy and well-being with fewer adverse effects compared with estrogen alone.

A potential indication for combined estrogen-androgen treatment would be decreased libido occurring during perimenopause or postmenopause, specifically in woman who reports being previously satisfied with her level of libido.

Transdermal testosterone (Testoderm, Androderm) has also been tested in women with impaired sexual functioning. In a recent trial, 75 women who had undergone oophorectomy were randomized to receive oral estrogen therapy plus placebo or low- (150 microgram/d) or high-dose (300 microgram/d) transdermal testosterone. Sexual function and psychological well-being were significantly improved in the higher-dose group compared with the placebo group. A critical question that should be explored involved the appropriate levels of serum androgens required for adequate symptomatic improvement.

Topical testosterone propionate cream 2% can be used in women who have complaints of vaginal dryness and diminished genital sensation. A testosterone gel (AndroGel 1%) is also available. These topical formulations can be applied up to three times a week. Heightened clitoral sensitivity, decreased vaginal dryness, and increased libido have been reported with the 2% testosterone cream.

Oral methyltestosterone is available alone (Android, Oreton Methyl, Testred) or in combination with estrogen (Estratest). Experts have noted a lack of analytical sensitivity and reliability with current, commercially available androgen assays for women, however. Thus, without an adequate diagnostic test to assess androgen deficiency, it is difficult for clinicians to treat the disease in women. Assays are now being developed to detect lower levels of free testosterone in women.

Recent work has focused on over-the-counter dehydroepiandrosterone (DHEA), one of the major currently available androgen supplements, as a form of testosterone replacement. Preliminary results in women with androgen insufficiency suggest that DHEA improves desire, arousal, lubrication, satisfaction, and ability to achieve orgasm. Bear in mind that such androgenic dietary supplements do not require regulatory review, nor have they undergone formal trials of efficacy and safety, and for these reasons should be used with caution.

Before beginning any form of testosterone therapy, levels of free and total testosterone, lipids, and liver enzymes should be measured. The dose of testosterone should be adjusted according to baseline levels and titrated at follow-up visits

(every 6-8 weeks) according to the patient's side effects and symptoms. Given the paucity of long-term, controlled clinical trials, patients should be fully informed of the potential side effects of androgen therapy, which include acne, weight gain, excess facial and body hair, permanent lowering of the voice, emotional changes, and adverse lipid changes.

### Medical Devices

**The Eros-Clitoral Therapy Device:** This is the first treatment approved by the FDA for arousal and orgasmic disorders in women. This small handheld device applies a gentle vacuum to the clitoris, increasing blood flow to the clitoris and surrounding tissue. Clinical trials involving 52 patients showed improvement in postmenopausal and premenopausal women with sexual arousal disorder or orgasmic disorder.

**Interstim:** The InterStim (Medtronic) sacral nerve stimulating system is an implantable device designed to treat urge urinary incontinence. It uses mild electrical stimulation of the sacral nerves to modulate bladder contractility. Anecdotal reports suggest it may benefit sexual arousal and the ability to achieve orgasm in women. Multicenter studies are underway.

### Pharmacotherapies

**Sildenafil citrate (Viagra),** a selective type 5 (cGMP specific) phosphodiesterase inhibitor, decreases the catabolism of cGMP, the second messenger in nitric oxide-mediated relaxation of clitoral and vaginal smooth muscle. In animal studies, sildenafil produced dose-dependent relaxation of clitoral and vaginal smooth muscle strips.

In a recent pilot study, sildenafil significantly increased physiologic and subjective parameters of sexual response in 48 women with arousal disorder. Some studies have failed to demonstrate any significant benefit of sildenafil on subjective sexual arousal, even when enhanced vaginal engorgement was verified.

Others, however, have shown improved sexual functioning in premenopausal women with sexual arousal disorder, postmenopausal women with various disorders, and women with spinal cord injury. Several others have found that sildenafil benefits antidepressant-induced sexual dysfunction in women. The most recent study found that sildenafil was effective and well tolerated in 202 postmenopausal women with FSAD without concomitant HSDD or contributory emotional, relationship or historical abuse issues. However, it is important to note that all positive changes in arousal disorders in women took place under regulated androgen and estrogen levels.

Until androgen is approved for general usage in women, the true efficacy of sildenafil cannot be demonstrated and prescribed for women. The usual dose of sildenafil in these trials was 50-100 mg before sexual activity.

**L-Arginine and yohimbine Hcl:** L-Arginine is an amino acid that functions as a precursor to the formation of nitric oxide, which mediates relaxation of vascular and nonvascular smooth muscle. Yohimbine (Aphrodyne, Dayto Himbin, Yocon, etc.) is an alkaloid agent that blocks presynaptic alpha-2 adrenoreceptors.

Effects on the peripheral autonomic nervous system include a relative decrease in adrenergic activity and enhanced parasympathetic tone. Reports on the ability of yohimbine to induce penile erections have shown mixed results, and a recent study of 24 postmenopausal women with sexual arousal disorder found little difference in subjective reports of sexual arousal among those treated with yohimbine (5 mg), yohimbine (6 mg) plus L-arginine glutamate (6 g), or placebo.

**Alprostadil (prostaglandin E1):** In the form of an intraurethral pellet, it has been used to treat ED. In two small studies, topical alprostadil formulations were shown to enhance subjective and physiologic arousal in women. Phase II clinical studies are under way in postmenopausal women with sexual arousal disorder to assess the safety and efficacy of an alprostadil based formulation using a permeation enhancer to deliver the drug vaginally.

**Phentolamine (Regitine):** Phentolamine is a nonspecific alpha-adrenergic blocker that relaxes vascular smooth muscle. An experimental oral formulation (Vasomax) has been studied in the treatment of ED and a pilot study in menopausal women with sexual dysfunction showed mildly improved vaginal blood flow and subjective arousal at a dose of 40 mg qd.

**Bupropion HCl (Wellbutrin):** This antidepressant is a weak blocker of the neuronal uptake of serotonin and norepinephrine; it also inhibits the neuronal reuptake of dopamine to some extent, although the exact mechanism of action is not clear. Unlike SSRIs, which may cause decreased libido and exacerbate sexual dysfunction symptoms, bupropion is not only effective in treating SSRI-induced sexual dysfunction, but has also been shown to improve sexual function in women who are not depressed.

**Apomorphine Hcl** is a short-acting dopamine agonist that facilitates erectile responses. In addition to developing a nasally administered apomorphine for treatment of ED in men, a phase 2 clinical trial is being conducted in women with sexual dysfunction to assess the safety and efficacy of nasally administered apomorphine in increasing their sexual satisfaction.

**Alpha-Melanocyte-stimulating hormone:** This is an endogenous regulatory hormone with diverse physiologic functions,

including the regulation of body weight, pigmentation, adrenal function, energy homeostasis, and immune and sexual function. Studies of a nasally administered synthetic peptide analogue of alpha-melanocyte-stimulating hormone (PT-141) for the treatment of female sexual dysfunction are underway.

Herbals: Several herbal remedies (such as Zestra, Avlimil and ArginMax) are currently available and recommended by some sexual health professionals for enhancement of sexual function . Like androgenic dietary supplements, they require no regulatory review.

Additional resources on female sexuality are available from MayoClinic.com:

<http://www.mayoclinic.com/health/kegel-exercises/WO00119>

<http://www.mayoclinic.com/health/sexual-health/HA00035>

<http://www.mayoclinic.com/health/womens-health/WO00110>

<http://www.mayoclinic.com/health/sexual-health/HQ01363>