# Improving Sexual Function with Androgen Therapy

Androgen therapy for men and women with sexual dysfunction has been successfully used to restore sexual function for over 80 years in an off-label setting. The FDA has not approved androgen therapy for treatment of male or female sexual dysfunction. The only FDA approved pills for male erectile dysfunction are Viagra and Levitra. The FDA has approved testosterone use only for men with “male hypogonadism” including low interest, osteoporosis, depressed mood, low energy, etc. There are no FDA approved pharmaceutical treatments for women with sexual dysfunction. There are limited long term safety data for use of androgens in women, and there is much to learn. Androgen therapy for men and women for sexual dysfunction is a new field.

## Biochemical Facts about Androgens

Androgens are sex steroids which structurally have 19 carbons. All steroids are derived from enzyme breakdown of cholesterol. There are three groups of steroids: mineralocorticoids – synthesized, in part, in the zona glomerulosa of the adrenal gland, corticosteroids – synthesized, in part, in the zona fascicularis of the adrenal gland and sex steroids – synthesized, in part, in the zona reticularis. There are 7 total androgens: dehydroepiandrosterone, delta 5 androstenediol, androsterone, delta 5 androstanediol, delta 4 androstendione, testosterone and dihydrotestosterone. The other sex steroids are estrogens (18 carbons): estradiol, estrone, estriol. Androgens are synthesized in the: gonad (ovary or testicle) from cholesterol; adrenal gland (zona reticularis) from cholesterol and periphery from DHEA. Androgens are sex steroids as natural to women as are estrogens.

## Physiologic Facts About Androgens

Androgens have actions on multiple areas of the body including bone, muscle, skin, liver, kidney, brain, immune system, bone marrow and genital organs. Contemporary evidence is accumulating from animal/human studies that androgens are critical for male and female sexual function – desire, arousal, orgasm function. The exact mechanism of action of androgens on the body may involve synthesis of critical sex steroid dependent proteins or growth factors which act on the nerves, arteries, smooth muscles and connective tissue of the genitals maintaining structure and function.

## Epidemiologic Facts About Androgens

Androgen values consistently decrease with age in both genders. By age 40 – 50, men and women have less than half of the DHEA and testosterone they had at age 20 years.

## Pathophysiologic Facts About Androgen Insufficiency

There are five major categories or types of etiology of androgen insufficiency: Gonadal (chemo- or radiation-therapy, oophorectomy), Adrenal (adrenal failure or insufficiency), Hypothalamic-

Pituitary (hypopituitarism), Drug-Related (corticosteroids, anti-androgenic agents, oral contraceptive pill, oral estrogen therapies) and Idiopathic (age-related).

Androgen insufficiency may be indicative of, or causally related to other medical, psychiatric or psychosocial factors such as (i) a major life stress or relationship conflicts (ii) thyroid disease (i.e. hypo- or hyper-thyroidism), (iii) major metabolic/nutritional disorders like iron or vitamin D deficiency or other causes of chronic fatigue like Lyme disease orchronic fatigue syndrome; psychiatric disorders such as major depressive disorder; or other potential etiological conditions or pre-disposing factors which have been implicated including: anorexia nervosa, various immunologic disorders, such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and HIV-AIDS. SHBG (sex hormone binding globulin), a carrier protein produced in liver, is elevated in many of these syndromes. There is a dilemma with elevated SHBG. The bioavailable form of testosterone is free or unbound testosterone. Free testosterone is equal to the total testosterone divided by the free testosterone. In patients with elevated SHBG values, total testosterone values have to be elevated to even higher values, so that free testosterone values are adequate. In particular, production of SHBG is highly estrogen sensitive – oral intake of estrogen results in a profound dose-dependent INCREASE in SHBG.

Conditions in women where androgen values are associated with decreased activity of critical enzymes include sexual dysfunction after childbirth and sexual dysfunction associated with the transition and the menopause. In women, oral contraceptive medications are associated with decreased ovarian synthesis of testosterone and increased synthesis of SHBG. In women, estrogen medications are associated with increased synthesis of SHBG. In women, lupron, zoladex medications are associated with decreased ovarian synthesis of testosterone.

## Therapy Guidelines and Adverse Effects

Androgen therapy demands a clear indication. No patient is too old if indicated. For men, digital rectal examination and PSA blood tests are mandatory if the patient is older than 40. In women, estrogen levels are indicated. Androgen therapy is contraindicated in men and women with breast and prostate cancer. In men androgen therapy is contraindicated in severe LUTS (lower urinary tract symptoms). In women, androgen therapy is contraindicated in pregnancy. All patients on androgen therapy should have quarterly follow-up in the first year. Clinical and biochemical changes (androgens, estrogens, SHBG, LH, FSH, prolactin, CBC, LFT’s, lipid profile) are useful in establishing best dosing regimen. Given the paucity of long-term, controlled trials, patients should be fully informed of potential risks and carefully monitored for potential adverse reactions. Potential side effects of androgen therapy for women include acne, weight gain, excess facial and body hair, permanent lowering of the voice and adverse lipid changes. Based upon available clinical trial data and the 4 year experience at the Center for Sexual Medicine, these side effects are infrequent if androgen levels are maintained within normal physiological ranges and the delivery system of androgen administration is via topical testosterone therapy. Lowered HDL cholesterol, increased hematocrit levels and abnormal liver function tests have been reported with certain oral or intramuscular testosterone preparations. Potential virilization of a female fetus is a serious risk in reproductive-aged women.

More research in the field of male and female sexual dysfunction is needed.