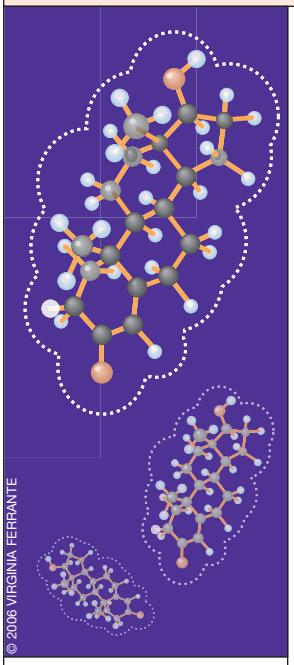

Androgen therapy for low female libido

Libido—or sexual desire—can be affected by several factors. Sexual motivation, emotional intimacy and sexual skills of the couple, psychological and biological factors and sex hormones—including estrogens and androgens—all play roles. Decreased levels of androgens in late reproductive years contribute to the decline in sexual interest/desire in older women. Several investigators agree that androgens influence libido and behavior but not activity or response—such as lubrication and orgasm.

Mohamad S. Mahmoud, MD
Resident, Department of Obstetrics and Gynecology
Oakwood Hospital and Medical Center
Dearborn, MI

Michael P. Diamond, MD
Professor, Department of Obstetrics and Gynecology
Wayne State University
Kamran S. Moghissi Professor
Associate Chair, Department of Obstetrics and Gynecology
Wayne State University
Detroit, MI

Richard Balon, MD
Professor, Dept Psychiatry
Wayne State University
Associate Director, Residency Training
Detroit, MI

KEY POINTS

- Human sexual response doesn't follow a linear model as once thought, rather the phases overlap and are complex.
- Motivation to have sex (including increasing emotional intimacy, self-image and well-being) leads to subjective arousal, which triggers desire, leading to a responsive sexual arousal and orgasm and/or satisfaction.
- Low libido is associated with the conditions that decrease the physiologic levels of androgens, such as oophorectomy, adrenal gland dysfunction or hypopituitarism.
- Decreased testosterone levels are associated with loss of libido, fatigue and decreased feelings of well-being.
- Androgen formulations are available—alone or in combination with estrogen—for treatment of low libido in women.
- It is important to take a thorough sexual and general psychiatric history to exclude mental illness associated with sexual dysfunction, preoccupation with a life crisis, and/or core relationship problems and to find out whether the patient's psychological profile is fairly intact.

The World Health Organization defineas sexual dysfunction as "the various ways in which an individual is unable to participate in a sexual relationship as he or she would wish." In 1988, the Sexual Function Health Council of the American Foundation for Urologic Disease (AFUD) provided the first consensus–based definition of female sexual dysfunction (FSD). This classification divides FSD into 5 categories: hypoactive sexual desire disorder (HSDD), sexual aversion disorder, sexual arousal disorder (FSAD), female orgasmic disorder (FOD) and sexual pain disorder.[1] This classification is based on the linear model of sexual response described by the work of Masters and Johnson and revised by Kaplan.[2] In this model, Masters and Johnson assumed a linear progression from desire to arousal, meaning genital swelling and lubrication, to orgasm and resolution. Current data has in fact proven that human sexual response doesn't follow such a linear model; the phases described rather overlap and are more complex.[3]

In the new model of the sex response cycle, motivation to have sex (including increasing emotional intimacy, self image and well being) leads to subjective arousal, which triggers desire, leading to a responsive sexual arousal and orgasm and/or satisfaction. There are two types of desire: innate desire, or desire preceded by some form of motivation.[2]

Based on this new model, the new classification encompasses a wide spectrum of pathologies related to sexual function (see Table 1).[3]

The largest study done on FSD showed it affects 43% of women in the United States. This study based on the U.S. National Health and Social Life Survey of 1992 also found that among women with FSD, 51% had low libido. This makes it the most prevalent female disorder (22% of all women), followed by arousal problem (33%) and pain disorders (16%).[4] Unfortunately, prevalence of the recently defined categories is largely unknown. The 51% of women with low libido in this survey are those with lack of initial spontaneous desire, which doesn't constitute a sexual disorder by itself in the new definition.

The role of estrogen deficiency in FSD has always been controversial: in fact some studies have found that estrogen deficiency was responsible for delayed or absent vaginal lubrication, decreased congestion of the vagina and reduced contractions with orgasm.[2] Estrogen improved libido and orgasm in postmenopausal women,[5] and systemic estrogen replacement improved vaginal lubrication, blood flow and vaginal compliance in menopausal women.[6,7] However, others found that systemic estrogen alone was insufficient to cure symptoms of sexual dysfunction.[8,9] Since oral estrogen can increase the level of sex hormone-binding globulins, the use of oral contraceptives containing estrogen, or oral estrogen alone, for menopausal symptoms can result in decreasing free testosterone levels.[10]

Androgen physiology, pharmacology and role in sexuality

Androgens in women are made by the ovaries and the adrenal glands, and are partially regulated by the pituitary gland. The major androgens in women include: dehydroepiandrosterone–sulfate (DHEAS), androstenedione (A), testosterone (T), and dihydrotestosterone (DHT). Some would also include dehydroepiandrosterone (DHEA) as an androgen precursor. An anatomical presentation of the pathways of these androgens is given in Figure 1.

Dehydroepiandrosterone–sulfate, DHEA and A are considered pro-androgens, because they need to be converted to T, the most potent androgen, to express their effect. The adrenal *zona fasciculata* produces 25% of circulating T and is regulated by adrenocorticotropic hormone (ACTH). The ovarian stroma, under the effect of leuteinizing hormone (LH), produces 25% of circulating T. The rest is produced by peripheral tissue conversion of circulating A.[11]

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Testosterone in the plasma exists in three forms: free testosterone (FT), testosterone nonspecifically bound to albumin (AT), and testosterone specifically bound to sex hormone binding globulin (SHBG). The sum of FT and AT is referred to bioavailable testosterone. It is estimated that 66% of T is bound to SHBG and 1%–2% is estimated to be free or biologically available.[12] There is enough evidence that the bioavailable fraction rather than total testosterone reflects the clinical mi-

TABLE 1

Categories of female sexual dysfunction (FSD)*

Type	Common symptoms
Sexual desire/ interest disorder	Feeling of sexual interest or desire, sexual thoughts or fantasies, and responsive desire are absent or diminished. Motivating reasons or incentives for attempting to become sexually aroused are scarce or absent. The lack of interest is beyond the normative lessening that may occur with life cycle and relationship duration.
Combined sexual arousal disorder	Absent or markedly reduced subjective sexual arousal (feelings of excitement, pleasure) from any type of stimulation, and absent or impaired genital sexual arousal (vulvar swelling, lubrication).
Subjective sexual arousal disorder	Absent or markedly reduced subjective sexual arousal (feelings of excitement, pleasure) from any type of stimulation. Vaginal lubrication and other signs of physical response still occur.
Genital arousal disorder	Absent or impaired genital sexual arousal: minimal vulvar swelling or vaginal lubrication from any type of sexual stimulation, and reduced sexual sensation from caresses of the genitalia. Subjective sexual excitement still occurs from non-genital sexual stimuli.
Persistent sexual arousal disorder	Spontaneous, intrusive and unwanted genital arousal (tingling, throbbing) when sexual interest or desire is absent. Any awareness of subjective arousal is typically but not invariably unpleasant. The arousal is unrelieved by orgasm, and the feelings persist for hours or days.
Orgasmic disorder	Despite self-report of high sexual arousal, orgasm from any kind of stimulation is lacking, markedly diminished in intensity or considerably delayed.
Vaginismus	Persistent or recurrent difficulties in allowing vaginal entry of a penis, finger or any object, despite the woman's expressed wish to do so. There is often (phobic) avoidance; anticipation, fear of experience of pain; and variable involuntary contraction of pelvic muscles. Structural or other physical abnormalities must be ruled out.
Dyspareunia	Persistent or recurrent pain with attempted or complete vaginal entry or penile-vaginal intercourse.

*Adapted from reference 2.