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## Female Sexual Dysfunction Clinical Approach

*Guest Editor*

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# Sexual desire disorders: Clinical approach

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*ABSTRACT. Hypoactive sexual desire disorder may affect 32% of women between 18 and 59 years of age. The percentage of affected women increases with age. However, the distress associated with loss of sexual desire is inversely associated with age. Biological, psychosexual and context dependent factors may modulate its neurobiological basis and clinical correlates. The neurobiology of sexual desire and of leading causes contributing to women's sexual desire disorders will be reviewed. A first line informative history taking to qualify the diagnosis will be presented. The basic diagnostic work-up and treatment guidelines will be finally considered.*

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## INTRODUCTION

Hypoactive sexual desire disorder (HSDD) is the leading female sexual complaint (1, 2). It is often associated with other sexual complaints: sexual arousal disorders, orgasmic disorders and/or sexual pain disorders. Co-morbidity is indeed frequently reported in women. Attention to what came first is key, as the current complaint may be different from the triggering disorder. HSDD may have a multifactorial etiology: psychosexual (3-5), context-dependent (1, 5) and biologic (6-8). After decades of almost exclusive focus on the psychodynamic etiology, new attention is currently dedicated to investigate its potential biological etiologies. The importance of sexual desire in both its biological component and motivational side as a marker of quality of life is increasingly recognized. The clinician is increasingly asked to address the HSDD complaint in an effective way.

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## DEFINITION AND PREVALENCE

Women's sexual interest/desire disorder indicates that "there are absent or diminished feelings of sexual interest or desire, absent sexual thoughts or fantasies and a lack of responsive desire. Motivations (here defined as reasons/incentives) for attempting to become sexually aroused are scarce or absent. The lack of interest is considered to be beyond a normative lessening with life cycle and relationship duration" (9).

Sexual Aversion Disorder indicates the "extreme anxiety and/or disgust at the anticipation of/or attempt to have any sexual activity" (9).

HSDD is the sexual dysfunction most frequently reported by women. Population data indicate a prevalence of 32% in women between 18 and 59 years of age (1). A recent European survey on 2467 women, in France, UK, Germany and Italy, indicates that the percentage of women with low sexual desire is 19% in the age cohort from 20 to 49; is 32% in the same age cohort, in women who underwent surgical menopause; is 46% in postmenopausal women aged 50 to 70 with natural menopause and 48% in the same age cohort, after surgical menopause (2). The percentage of women distressed by their HSDD was respectively 27% in fertile women and 28% after surgical menopause, in the age cohort 20 to 49; 11% in women with natural menopause and 14% in those with surgical menopause aged 50 to 70 (2). The likelihood of HSDD increases with age, whilst the distress associated with the loss of desire is inversely correlated with age.

## PATHOPHYSIOLOGIC SCENARIO

The complex nature of human sexual desire will be briefly reviewed, to ease the understanding of the clinical approach when HSDD is complained of. Human sexual desire can be defined as the expression of a complex associative function, activated by endoge-

nous and/or exogenous stimuli, that induce the need or desire to behave sexually (4, 8). Endogenous stimuli include the erotic imagery, voluntary and spontaneous sexual fantasies, erotic dreams as well as pulsional drives, emotions and/or feelings. They concur to activate the cerebral centers and pathways which coordinate the seeking behaviour, the associated emotions and motor correlates (7, 8, 10, 11). Exogenous stimuli include all the signals, conscious and unconscious, which are conveyed to the limbic lobe and new sensorial cortex (occipital, parietal and temporal) through the sensory organs and related pathways (7, 8, 10, 11). Biological, motivational and cognitive factors contribute to sexual desire; when disrupted they may cause HSDD (3, 4, 8).

Biological factors design the basic scenario of sexual drive in women as well as in men. Age is the first negative factor affecting sexual desire in women (2). Menopause is the second (see Dennerstein, this issue). Centers and pathways related to sexual behaviour are primed and modulated by sexual hormones (6, 8, 10-13). The dramatic changes in sexual hormone's levels associated with the menopause are summarized in Table 1. The loss of androgens after surgical menopause is higher than 50%. Androgens have a central initiating and a peripheral modulating role:

Table 1 - Mean steroid levels in women (converted to pg/mL).

	Reproductive age	Natural menopause	Iatrogenic menopause
Estradiol	100-150	10-15	10
Testosterone	400	290	110
Androstenedione	1900	1000	700
DHEA	5000	2000	1800
DHEAS	3,000,000	1,000,000	1,000,000

From Lobo R., 1999.

their loss, associated with age and/or surgical menopause, is the leading biological cause of Androgen Insufficiency Syndrome (AIS) (12, 13) and HSDD. Key symptoms of AIS, a still difficult to operationalize clinical entity, include low libido, persistent and inexplicable fatigue, blunted motivation and a general reduced sense of well-being. Other signs of androgen insufficiency include reduced pubic hair, bone mass, muscle mass, poor quality of life, and more frequent vasomotor symptoms, insomnia, depression and headache (12, 13) (see Nappi et al., this issue). AIS should be investigated when clinical history suggests it. Estrogens modulate the hypothalamic function, the perception of femininity and somatic correlates and concur to sexual desire through the modulation of central, peripheral and genital arousal. Prolactin has an increasing inhibiting role with increasing plasmatic levels: likelihood of HSDD parallels its increase. Progestins have a different role, according to their biochemical structure and receptor modulation: neutral or mildly inhibiting sexual desire for natural progesterone and progestins derived from 19-norprogesterone, like norgestrel acetate; inhibiting, for progestins with antiandrogenic properties, such as cyproterone acetate; enhancing, for progestins structurally related to testosterone, such as noretisterone acetate, or for different molecules like tibolone. The choice of a well tailored progestin is key in women treated with Hormonal Replacement Therapy, more so if they complain of HSDD. Thyroid hormones, oxytocin and vasopressin further contribute to the central scenario (6). Quality of general health and well being do contribute to sexual desire's modulation. Cardiovascular disease and diabetes may affect sexual desire, in comorbidity with arousal disorders (see Salonia et al., this issue). Sexual pain disorders may as well secondarily inhibit sexual desire (see Graziottin, this issue).

From the neurobiological point of view, the basic "seeking", appetitive feeling is a positive

emotion, mediated by dopamine in both sexes (6, 10, 11). It promotes curiosity, interest, expectancy, and has long been known as a "reward" system. Its emotional, perceptive side is to generate the feeling that something good (food, water, sex, protection, shelter etc.) will happen or be obtained if the subject explores the environment or interacts with others (10, 11). Its motor side is to promote exploratory behaviour (6, 10, 11). The system is heavily activated during sexual arousal and other appetitive states. In both sexes it is inhibited, among others, by antidopaminergic drugs or drugs that, as a side effect, increase prolactin (6, 14). It is activated when dopaminergic drugs are used (e.g. in parkinsonian patients) (14). In the sexual domain, testosterone plays an important role in priming and maintaining the intensity of the desire and arousal in the hypothalamic/limbic seeking system in both sexes although on average more powerfully in men than in women. Its loss is a leading biological factor in the etiology of sexual desire: the first etiology is surgical menopause, which on average causes the loss of 50% of total androgens (8, 12, 13). The impact of surgical menopause on both loss of sexual desire and distress associated with it is well indicated in a recent european survey (2). The gratification or "lust" subsystem is an important part of the seeking, appetitive pathway and is associated with gratification, when consummation of appetite is realized (11). The command neuropeptide of this system is endorphin, which can be considered the chemical correlate of feelings of satisfaction and emotional well being in both sexes. Drugs such as cocaine and amphetamines stimulate the seeking system by artificially generating positive expectancies, and enhance the perception of sexual drive by generating pseudoappetitive behaviours (6, 10, 11, 14) in both sexes. On the other hand opiates, which stimulate the pleasure centres of the lust subsystem directly, mimicking an already obtained gratification (pseudoconsummatory), blunt sexual drive,

again in the same way in men and women. Sustained underarousal of the seeking system, typical of depressed subjects, is also associated with low or loss of sexual drive (7, 8, 10, 11, 14). Antidepressant may further modulate the seeking system and correlated behaviours (Leventhal and Kotz, this issue). Women who on average have lower basic sexual drives than men are more vulnerable to depression from puberty onwards and more susceptible to the further inhibiting effect of depression on sexual drive. Depression and loss of sexual desire can both be triggered by frustration of basic emotional needs, e.g. intimacy and attachment for women, thus explaining the frequent comorbidity of depression and sexual desire from the psychodynamic point of view (3, 8).

Motivational factors do further modulate the expression of sexual desire (3, 4, 15). Emotional and affective meanings and intimacy needs, that seem to be particularly relevant to women, may contribute to and modulate the basic sex drive, or blunt it. Previous sexual abuse may have long lasting inhibiting effect on sexual desire (Rellini and Meston, this issue). In our species, motivation for sex may shift from the primary biological goal, reproduction, to recreational sex, where the pursuit of pleasure is key, and/or to instrumental sex, where sex is performed as a means to obtain advantages and express motivations different from procreation and/or pleasure (4, 8). Psychosexual factors contributing to the motivational sides of sexual desire, couple dynamics and partner related issues further contribute to the final perception and expression of it. Over time women are more vulnerable than men to a loss of interest and frequency of sexual relations but their pleasure from the relations seems to remain relatively stable over the years, well addressing the prevalent "responsive" nature of women's sexual disposition in stable couples (4, 8).

Cognitive factors, namely wishes and risks to behave sexually are set against the former

two contributing factors in ultimately determining sexual behavior.

Listening to and recording of biological, motivational and cognitive factors is key to understand predisposing, precipitating and maintenance factors that may contribute to cause and maintain HSDD in women.

## CLINICAL APPROACH

With an appropriate clinical history, the physician should be able to: i) define if HSDD is in play, recording potential accompanying disorder(s) – arousal disorders, orgasmic difficulties, sexual pain disorders – with a balanced attention to both biological and psychodynamic and/or interpersonal factors (3, 4, 8); ii) put the problem in a life-span perspective, with adequate subtyping: lifelong vs acquired, generalized vs situational, and slow or rapid onset; iii) focus on a preliminary definition of potential etiology (organic, psychogenic, mixed, or unknown) and intensity of associated distress (2, 9). The most important issues to be investigated are concisely summarized in Table 2: however, the clinician will select the questions and their sequence more adequate to the individual case.

During the diagnostic work-up, the physician should: 1) assess the potential role of hormonal factors, loss of androgens first, with appropriate plasmatic sample (total and free testosterone, DHEA, SHBG, estrogens, prolactin); 2) recognise psychobiological factors that may interfere with the motivational-affective bases of sexual response, namely binge eating disorders and amenorrhea in adolescents; depression, anxiety, chronic stress and insomnia, all of which may be present in comorbidity with HSDD at any age and may worsen after menopause; 3) investigate lifestyle related factors, such as alcohol abuse, use of drugs such as opiates, work-aholism, or context-related factors that may impair sexual desire; 4) diagnose pelvic floor dysfunctions and genital anatomic factors, including poor

Table 2 - Sexual history in hypoactive sexual desire disorders and associated sexual comorbidity.

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**General well being**

- How do you feel (physically and mentally)?
- Are you currently sexually active?
- If not, is that a concern for you? If yes, how's your sex life?

**Sexual function**

- Did you always suffer from low sexual desire ("lifelong") or did it fade recently ("acquired")?
- Do you suffer from other sexual symptoms?
- For example, do you experience vaginal dryness?
- Do you have difficulty in getting aroused or lubricated?
- Do you have difficulty reaching orgasm?
- Do you feel pain during or after intercourse?
- Do you suffer from cystitis 24-72 hours after intercourse and/or of other urinary symptoms?
- Is there any life-style related factor that may affect your sexual desire (body weight, alcohol or drug abuse, little sleep, fatigue, professional distress...)?
- What, in your opinion, is causing or worsening your sexual disorder? Is it a psychological problem, a past or current negative event (like sexual harassment or abuse), something related to your physical health, to your relationship, or something else?

**Sexual relationship**

- Do you have a stable relationship?
  - How's your relationship? Are you satisfied with it?
  - How is your partner's health (general and sexual)?
  - Do you feel that your current sexual problem is more dependent on a physical or couple (loving/intimacy) problem?
  - Is your sexual problem present in every context and/or with different partners ("generalized"), or do you complain of it in specific situations or with a specific partner ("situational")?
  - What made you aware of it and willing to look for help (e.g., intolerable personal frustration, fear of losing the partner, partner's complaints, new hope for effective treatment, more self-confidence in reporting)?
  - Are you personally interested in improving your sex life?
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Modified from Graziottin, 2004, with permission.

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outcome of surgery, that may lead to problematic physical responses such as pain during intercourse, with a secondary loss of sexual desire; 5) diagnose concurrent diseases, cardiovascular and diabetes first, as well as urogenital and iatrogenic factors (drugs!) that may increasingly interfere with the biology of sexual response, particularly in elderly patients; 6) inquire about psychosexual and relationship factors as well as partner-specific problems, such as erectile disorder. A few appropriate questions (Table 2) may help the clinician to better define the etiology of the complaint and to determine the need for further information. He/she should try to become comfortable with these quite intimate questions, choosing ways of asking them that he/she feels at ease with. With time, proper training and familiari-

ty with this issue will be increasingly rewarding in terms of diagnostic accuracy, patient satisfaction, and improvement of doctor-patient relationship.

With an appropriate clinical approach, three basic situations may be defined: 1) the woman reports low physical drive but high/normal motivation, because she loves her partner: sexual asthenia is likely. A biological etiology, androgen loss first, is to be investigated, more so if surgical menopause is reported; 2) she reports average sexual drive but no motivation to have sex with the current partner: sexual disaffection is likely and relational issues should be investigated and treated; 3) she reports no physical drive nor motivation to sex: sexual anergia is likely and depression is the first cause to be investigated.

## TREATMENT

Sexual desire disorders have the lowest success treatment rate among sexual dysfunctions, ranging between 25-35% overall. Etiologic complexity, the importance of relationship issues, intimacy frustration, delay between onset of HSDD and request of clinical help, and/or low motivation to improve sexual relations with the current partner may explain why the response to treatment is generally so disappointing, particularly in unmotivated patients. Better results may be possible in highly motivated patients, when hormonal loss (with or without Androgen Insufficiency Syndrome) is the leading etiology (as in surgical menopause) and appropriate hormonal replacement therapy (HRT) may restore libido and a satisfactory sexual response. Based on the etiologic diagnosis, biological, psychogenic/relational, or combined treatment by the family physician may be required, with referral to or collaboration with specialists. Therapy may include: a) hormonal replacement therapy, systemic or topical, with estrogens, when co-morbidity with genital arousal disorder is key and vaginal dryness is a leading complaint; androgen replacement should be considered, if androgen insufficiency syndrome is diagnosed: indeed, data on testosterone patches are extremely promising; b) hypoprolactinemic drug, if high prolactin is diagnosed; c) thyroxine, if hypothyroidism is present; d) low dose antidepressant, better with bupropione, if a mood disorder is a co-factor; e) better glycemic control, in diabetic women; f) check and modification of drugs potentially causing iatrogenic loss of libido, such as levosulpiride, because of its hyperprolactinemic effect; g) life-style improvement: smoking and alcohol reduction, weight control and regular physical exercise to improve body image and mood, better diet, sleep improvement to restore vital energy. Appropriate counseling and medical support is key in all patients suffering from a persistent low

sexual desire after a serious or chronic illness (5, 15). Partner referral to the uro-andrologist is key if he is the symptom "inducer" and the woman, complaining of loss of sexual desire consequent to his sexual problems, is the "carrier" of the disorder to the clinical attention. Couple therapy is indicated if relationship issues and couple dynamics appear to be the leading etiological factor in the HSDD.

## CONCLUSIONS

HSDD is a leading complaint in women. Its likelihood increases with age, whilst distress associated with it is inversely correlated with aging. Surgical menopause is the leading biological etiology of low sexual desire in women aged 20 to 49. Physicians are increasingly required to effectively address the HSDD, with a comprehensive diagnosis inclusive of potential biological, psychodynamic and context-dependent factors. A multidisciplinary approach and appropriate referral, when indicated, are as well important to improve the clinical outcome. Further research is ongoing to investigate the promising role of androgens as leading biological factors to promote and maintain a satisfying sexual desire in women.

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