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Monothematic Issue

Female Sexual Dysfunction
Clinical Approach

Guest Editor
Alessandra Graziottin

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CONTENTS OF VOLUME 14, No. 2

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BUSINESS INFORMATION

EDITORIAL

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Women's right to a better sexual life

It is a great honour and pleasure to be the invited editor of this issue of *Urodinamica*, dedicated to Female Sexual Dysfunctions (FSD). The right of women to get a better sexual life is increasingly recognized. However, this goal cannot be achieved without a thorough understanding of their sexuality in physiologic and pathologic conditions (1-6), in different contexts and cultures (7, 8), with different religious and ethic backgrounds. Classification's changes reflect both the effort of perfectly describing women's experiences and complaints and yet the limits of the current understanding of FSD (9, 10). The latest classification of FSD is summarized in Table 1 (10).

Fortunately, after decades of marginal interest, the topic of female sexual function and dysfunction is currently receiving dedicated research and clinical attention. Health care providers are indeed increasingly required to address FSD in an effective way.

However, concise, updated, and authoritative books or journals dedicated to the clinical approach to FSD are rare (11). Many focus on a single aspect (12, 13). Excellent books are available but their volume often discourages the busy clinician (14). This volume of *Urodinamica* is therefore timely. I am honoured to present here the contributions of some of the most brilliant experts of the world in the area of FSD. They have kindly agreed to focus on the clinical approach of each aspect considered, to ease the reader in his/her perception of the clinical relevance of data and expertise they are reporting and discussing.

A few points, that the readers will find discussed in greater detail in the individual chapters, will be highlighted here. Women's sexuality is *multifactorial*, rooted in biological, psychosexual and context-related factors (1-8), either correlated to couple dynamics but also family and sociocultural issues. It is *multisystemic:* in men and women, a physiologic response requires the integrity of

Table 1 - Classification of female sexual disorders.

Women's sexual interest / desire disorder
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.

Sexual Aversion Disorder
Extreme anxiety and/or disgust at the anticipation of/or attempt to have any sexual activity.

Subjective Sexual Arousal Disorder
Absence of or markedly diminished cognitive sexual arousal and sexual pleasure from any type of sexual stimulation. Vaginal lubrication or other signs of physical response still occur.

Genital Sexual Arousal Disorder
Complaints of absent or impaired genital sexual arousal. Self-report may include minimal vulval swelling or vaginal lubrication from any type of sexual stimulation and reduced sexual sensations from caressing genitalia. Subjective sexual excitement still occurs from non genital sexual stimuli.

Combined Genital and Subjective Arousal Disorder
Absence of or markedly diminished subjective sexual excitement and awareness of sexual pleasure from any type of sexual stimulation as well as complaints of absent or impaired genital sexual arousal (vulval swelling, lubrication).

Persistent Sexual Arousal Disorder
Spontaneous, intrusive and unwanted genital arousal (e.g. tingling, throbbing, pulsating) in the absence of sexual interest and desire. Any awareness of subjective arousal is typically but not invariably unpleasant. The arousal is unrelieved by one or more orgasms and the feelings of arousal persist for hours or days.

Women's Orgasmic Disorder
Despite the self-report of high sexual arousal/excitement, there is either lack of orgasm, markedly diminished intensity of orgasmic sensations or marked delay of orgasm from any kind of stimulation.

Dyspareunia
Persistent or recurrent pain with attempted or complete vaginal entry and/or penile vaginal intercourse.

Vaginismus
The persistent or recurrent difficulties of the woman to allow vaginal entry of a penis, a finger, and/or any object, despite the woman's expressed wish to do so. There is often (phobic) avoidance and anticipation/fear of pain. Structural or other physical abnormalities must be ruled out/addressed.

Modified from (10).

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the hormonal, vascular, nervous, muscular, connective and immunitary system: a fact too often overlooked in women, until recently (1-5). Three major dimensions: *Female Sexual Identity*, *Sexual Function* and *Sexual Relationship* interact to give to women's sexual health its full meaning or its problematic profile (6, 11). Women's sexuality is *discontinuous* throughout the life cycle and is dependent on personal, current contextual and relationship variables as well as historical factors (9, 10).

FSD is *age related*, *progressive* and *highly prevalent*, affecting up to 20% to 43% of women in the fertile age (14), and 46% of the elderly ones, still sexually active in the late post-menopause (15). Prevalence figures vary greatly among studies, due to methodological biases. Unbiased prevalence estimates from population samples have been rare, and incidence estimates have been non-existent.

FSD may occur along a continuum from *dissatisfaction* (with potential integrity of the physiologic response but emotional/affective frustration) to *dysfunction* (with or without pathological modifications), to severe *pathology*, biologically rooted (9, 10). However, sexu-

al dissatisfaction, disinterest and even dysfunction may be appropriate for an "antisexual" context (for example, a partner affected by Male Sexual Disorders or abusive) and they should not be labeled per se as "diseases" or dysfunctions worth of medical treatment (16). FSD may occur with or without significant personal (and interpersonal) distress (15, 16). Sexual problems reported by women are not discrete and often co-occur: co-morbidity is one of the leading characteristics of female sexual dysfunctions (9, 10).

Co-morbidity between FSD and medical conditions – urological, gynecological proctological, dismetabolic, cardiovascular and nervous diseases, to mention a few – is as well beginning to be recognized. For example, latent classes of sexual dysfunctions by risk factors in women indicate that urinary tract symptoms have a RR= 4.02 (2.75-5.89) of being associated with arousal disorders and a RR=7.61 (4.06-14.26) of being associated with sexual pain disorders, according to the epidemiological survey of Laumann et al. (14), credited to be the best survey produced up to now. Endocrine, infectious, muscular, vascular, nervous (particularly pain associated) and psychosexual factors contributing to the shared pathophysiology between FSD and associated medical conditions deserve therefore to be thoroughly investigated. The attention dedicated to comorbidity – both between FSD and between FSD and medical conditions – in this issue reflects the clinical relevance of this association, especially in the uroginecological domain. The clinical approach to single dysfunctions has been enriched with other papers focusing on aspects of clinical relevance for the clinician. The increasing awareness of pelvic floor disorders as key factors both in sexual pain disorders and urinary tract symptoms, the life span perspective in urological symptoms and associated FSD, new histological evidence on the extension of corpora cavernosa around the urethra, the role of neuropathic pain and neurogenic inflammation, will be discussed in detail as well. Age and menopause will be considered as leading factors causing FSD. The role of endocrine factors, testosterone first, in modulating sexual drive, central and peripheral arousal will be addressed in a dedicated chapter. Depression and the role of psychoactive drugs on FSD is the subject of another paper. Controversial issues, such as "hypersexuality" in women, and "new" syndromes, like the Persistent Sexual Arousal Disorders (PSAS) will be briefly described as well. Psychosexual issues, like the outcome of sexual abuse, have been considered. Many other topics related to FSD, for sake of concision, have been only briefly mentioned. Considering the main interest of the readers of *Urodinamica*, the focus of the issue has a priviledged medical perspective. However, as repeatedly stressed in the last consensus conferences on FSD, for a more accurate definition of the sexual symptoms, the physician should as well briefly investigate the so called "descriptors" of the disorders. They include: A) *contextual factors*, which appear to be most salient to qualify the disorder: 1) negative upbringing/losses/trauma (physical, sexual, emotional), past interpersonal relationships, cultural/religious restrictions, 2) current interpersonal difficulties, 3) partner sexual dysfunction, inadequate stimulation and unsatisfactory sexual and emotional contexts, 4) medical conditions, inclusive of psychiatric, medications, substance abuse, 5) the disorder being generalised or situational; B) *time-related factors*, i.e. the disorder being lifelong or acquired; C) *the distress scale*, that can indicate a mild, moderate, or severe impact on the personal life. The use of validated measurement of the distress may be preferable. Sexual distress should be distinguished from non-sexual distress and from depression. The degree of reported distress may have implications for the woman's motivation for therapy and for prognosis.

Indeed *sociocultural factors* may further modulate the perception, expression and complaining modality – i.e. the "wording" – of a sexual disorder. The meaning of sexual intimacy is to be understood, as it is indeed a strong modulator of the sexual response and of the quality of satisfaction the woman experiences, besides the simple adequacy of the sexual response (4, 8-11, 17, 18). Quality of feelings for partner and partner's health and sexual problems may further contribute to FSD (4, 8, 9, 19).

To address the complexity of FSD requires a balanced clinical perspective between biological and psychosexual/relational factors. Apart from addressing the FSD complaint in a competent way when the issue is openly raised by the patient, a physician, who is prepared to listen, can contribute to improving the quality of (sexual) life of his/her patients, by routinely asking them, during the clinical history taking: "How's your sex life"? thus offering an overture to current or future disclosure.

The wish is that this issue will significantly contribute to increase both the physician's confidence in asking and listening to FSDs complaint and his/her "clinical impact factor", i.e. his/her ability to appropriately diagnose and effectively treat FSD in an increasing number of women – and couples – who seek for help in a difficult moment of their sexual life.

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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.

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 endogenous and/or exogenous stimuli, that induce the need or desire to behave sexually (4, 8). Endogenous stimuli include the erotic imaginery, 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 nomegestrol 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 prolactine (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% ot 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.

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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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.

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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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Mid-aged women's sexual functioning

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ABSTRACT. *The aim of this paper is to determine the effects of aging, hormonal and psychosocial factors on female sexual functioning during the menopausal transition. The paper reviews findings from observational studies. These show that both aging and length of relationship adversely affect sexual functioning of both men and women. However, women have an additional incremental adverse effect related to the menopausal transition. The Melbourne Women's Midlife Health Project found a dramatic decline in women's sexual functioning with both ageing and the menopausal transition and that this effect was mediated by declining estradiol.*
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INTRODUCTION

Sexual problems are amongst the three most frequently reported complaints by women attending menopause clinics (1). This would seem to suggest that menopausal status (and underlying hormonal change) may be linked to adverse effects on sexuality. Yet relatively few of the population studies on the menopausal transition in mid-aged women have inquired about sexual functioning. Even fewer have used a validated questionnaire to assess the different aspects of sexual functioning. The role of ageing *per se* has to be disentangled from that of menopause, with which it is often confounded. The menopausal transition is a time of psychosocial as well as biologic change. Longitudinal studies of samples derived from the general population are in the best position to sort out whether there is a change in sexual functioning, and if so whether this reflects ageing, health status, hormonal or psychosocial factors.

Teaching aim to determine:

- effects of aging on female sexual functioning,
- changes in female sexual functioning reflecting hormonal factors underlying the menopausal transition,
- which hormone is responsible for any menopause related change in sexual functioning,
- relative roles of hormonal and psychosocial factors,
- clinical implications.

EFFECTS OF AGEING

Ageing and length of the relationship are known to affect sexual functioning of both men and women. For example, James (2) used cross-sectional and longitudinal data to show that coital rate halved over the first year of marriage and then took another 20 years to halve again. A number of studies report an additional decrement in aspects of sexual functioning occurring in mid-age. The sharpest increase in decline in sexual interest for women occurred around the mean of age of menopause (3). The Swedish cross-sectional and longitudinal studies of Hallstrom (4) and Hallstrom and Samuelsson (5) found a dramatic decline in sexual interest, capacity for orgasm and coital frequency with increasing age. Not all women reported a decrease but the majority of the postmenopausal women did. The number reporting increase in interest or orgasmic capacity was small and less likely with rising age. The Oxford studies of women aged 35-59 again found that the older women had less frequent intercourse, orgasm and enjoyment of sexual activity (6) and increased sexual dysfunction (7).

AGEING VERSUS MENOPAUSAL STATUS

Most population surveys which addressed this issue found an additional adverse effect of menopausal status on sexual functioning over that of ageing per se (4, 8-10). These findings indicate a contribution from the climacteric independent of the age factor alone.

MENOPAUSE, HORMONAL CHANGE OR PSYCHOSOCIAL FACTORS?

Population based surveys have found many factors impact significantly on female sexual functioning in midlife (4, 6-8, 11-13). These include presence of a sexual partner, partner's age and health, length of the relationship, feelings towards the partner, level of past sexual functioning, social class, educational level, experience of physical or psychological ill-health, stressors, employment, personality factors, and negative attitudes towards the menopause.

The Melbourne Women's Midlife Health Project is one of the few longitudinal population-based studies to follow women through the menopausal transition with annual validated rating scales (the Personal Experiences Questionnaire), interviews and physical measures including hormone assessments.

Using data from the first eight years of the longitudinal study (14) we found a dramatic decline in women's sexual functioning. The number of women with scores indicating sexual dysfunction increased from 42% in the first year of study when women were in the early phase of the menopausal transition to 88% by the eighth year of study when women were postmenopausal.

We found that as women passed through the menopausal transition there was a significant decline in SPEQ total scores, and in Sexual Responsivity, Frequency of Sexual Activities, Libido and in Feelings towards the Partner (15). A significant increase occurred in Vaginal Dyspareunia and Partner's Problems (14).

Statistical analyses found that both age and declining estradiol had significant decremental effects on the total score of sexual functioning, libido and sexual responsiveness (arousal, sexual pleasure, orgasm) (14).

IMPLICATIONS FOR CLINICIANS

Population-based studies suggest a decrement in several aspects of female sexual functioning associated with the midlife years. There is growing evidence that this reflects hormonal changes of the menopausal transition. However, hormonal change is only one aspect of the many factors that impact on sexual functioning. These include the woman's own premorbid level of sexual functioning, educational level, stress, physical and psychological health status, and the presence and quality of a sexual relationship.

When mid-aged women report sexual problems, the clinician must explore all these aspects in detailed history taking involving the woman and her partner. Given the range of factors affecting sexual functioning and the significantly more powerful effect of partner factors over that of hormonal factors, a broadly based biopsychosocial approach is needed. Estradiol replacement should be considered for acquired female sexual dysfunction associated with the menopausal transition.

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Androgens in the etiology and treatment of desire disorders in women

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ABSTRACT. Recent data support an emerging role of androgens in influencing women's health with particular regard to sexual function. Androgens secure libido by acting in the central nervous system throughout genomic and non-genomic mechanisms. In addition, androgens modulate vaginal and clitoral physiology by influencing the muscular tone of erectile tissue and vaginal walls. The production of androgens is dynamic over the menstrual cycle, is influenced by hormonal manipulations, and declines with age. Menopause, especially when induced surgically, may be accompanied by the so-called androgen-insufficiency syndrome, which has a great impact on mental and sexual sense of well-being. Several therapeutic strategies, including the addition of androgens to estrogen replacement preparations and the use of tibolone, have been considered to relieve desire disorders in order to improve postmenopausal women's sexual function and satisfaction.
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GENERAL VIEW ON WOMEN'S ANDROGENS

The major androgens in women include dehydroepiandrosterone sulphate (DHEAS), dehydroepiandrosterone (DHEA), androstenedione (A), testosterone (T) and dihydrotestosterone (DHT). However, DHEAS, DHEA and A are considered pro-androgens as they require to be converted to T to express their effects. Testosterone (T) is the most potent androgen; it is secreted by the adrenal zona fasciculata (25%) and the ovarian stroma (25%), while the remaining amount (50%) derives from peripheral conversion of circulating A.

Plasma T levels are in the range 0.2-0.7 ng/mL (0.6-2.5 nmol/L), with significant fluctuations related to the phase of the menstrual cycle, being highest at ovulation, lowest during the

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early follicular phase and higher during the luteal phase compared with early follicular phase. In addition, T shows circadian variations, with a peak in the early morning hours. T is converted to DHT, but it can also be aromatizable to E_2 (Estradiol), in target tissues; DHT is the principal ligand to androgen receptors. While estrogen decreases sharply at menopause, plasma T levels fall slowly with age. At physiological menopause, the cessation of follicular activity is characterized by a significant decline of ovarian production of A, more than T, and the progressive fall of plasma T concentrations is the consequence of the reduced peripheral conversion from its major precursor and from DHEA and DHEAS, which decline with age. Indeed, the adrenal production of androgenic precursors declines over time and the final result is that plasma T and A levels at 60's are about half those in women aged 40 years (1).

As far as surgical menopause is concerned, bilateral oophorectomy both premenopausally and postmenopausally leads to a sudden 50% fall in circulating T levels. Low androgens are associated with significant deterioration of sexual desire in premenopausal and postmenopausal women. However, no cut-off level for a normal range of T has been agreed on. The lack of consensus on the definition of low T levels depends on the difficulties with sensitive assays of total and free T in women and on the fluctuations during the menstrual cycle and in different life ages. Therefore, the so-called androgen insufficiency syndrome is a clinical entity comprising specific symptoms, such as 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 (2, 3). Apart from surgical menopause, other causes of androgen insufficiency include normal aging [physiological

menopause with not enough benefits from conventional hormonal replacement therapy (HRT) and premenopausal women reporting low libido and with circulating free T levels at lower limits of detection], ovarian insufficiency (unilateral oophorectomy, hysterectomy, spontaneous premature ovarian failure or after chemotherapy or radiotherapy, hypothalamic amenorrhea), adrenal insufficiency (adrenal failure or surgery), combined (hypopituitarism, autoimmune adrenal and ovarian failure), iatrogenic (treatment with exogenous oral estrogens, antiandrogen therapy, oral contraceptives, GnRH agonist therapy, chronic exogenous corticosteroid administration) (1).

According to the state of the art, plasma T values at, or below the lowest quartile of the normal range for women in their reproductive years allow the hypothesis of androgen insufficiency (2).

ANDROGENS IN THE ETIOLOGY OF DESIRE DISORDERS

During the entire reproductive life span, sex hormones exert both organization and activation effects, which are relevant to sexual behavior, and their actions are mediated by non-genomic as well as direct and indirect genomic pathways (4, 5). Androgens are essential for the development of reproductive function and the growth and maintenance of secondary sex characteristics directly or throughout their conversion to estrogens. However, they modulate the physiological function of many tissues and organs, including the central nervous system, the cardiovascular system, the muscle-skeletal apparatus, the immune system, etc., in both sexes (1).

The androgen influence over female sexual response has been hypothesized for a long time, but only in recent years basic research in laboratory animals and clinical trials with androgenic compounds are helping to understand the role of androgens on libido and sex-

ual arousal in women (6). Apart from modulating cortical coordinating and controlling centers, interpreting what sensations are to be perceived as sexual, and issuing appropriate commands to the rest of the nervous system, androgens, together with estrogens, affect the sensitivity of both genital organs and hypothalamic-limbic structures where they elicit conscious perception and pleasurable reactions by influencing the release of specific neurotransmitters and neuromodulators. Circulating T levels are aromatized to E_2 or bind to androgen-receptor (AR), following conversion to DHT, within several areas of the central nervous system. A further non-genomic action by T metabolites on sexual receptivity has been described at hypothalamic level (7). At the genital level, androgens modulate vaginal and clitoral physiology by influencing the muscular tone of erectile tissue and vaginal walls. The androgenic facilitation of vaginal smooth muscle relaxation occurs especially in the proximal vagina, producing distinct physiological responses in comparison with estradiol. Androgens down-regulate arginase activity by reducing L-arginine concentrations, a substrate for NOs, a crucial enzyme for vaginal lubrication and genital sensation. Indeed, NO has been identified in clitoral smooth muscle, and the enzyme responsible for cGMP degradation, phosphodiesterase type V, has been isolated in culture from smooth muscle cells of clitoral origin and is inhibited by sildenafil, which causes a dose-dependent relaxation of smooth muscle strips from rabbit clitoris and vagina. In addition, androgens interact with the synthesis and release of nitric oxide synthase (NOs) in the proximal vagina by facilitating vaginal and clitoral smooth muscle relaxation to electric field stimulation. Aging process and surgical castration induce a reduction of vaginal NO and cause the increase of vaginal fibrosis in female rats that are dependent both on estrogens and androgens (1, 8). The recent evidence of phosphodiesterase type V activity in the anterior wall of human vagina allows the hypothesis that NO system is highly operating even in women at the anatomical site corresponding to the so-called G spot (9).

In clinical practice, the inadequate hormonal-dependent vaginal receptivity is the precipitating factor of dyspareunia, which in turn may cause other sexual symptoms that contribute to amplify pain during coital activity. Indeed, it is extremely common to observe a decline of libido following a history of dyspareunia; the consequent reduction of orgasmic capacity may, then, reduce sexual satisfaction, which negatively influences sexual motivation in a kind of self-sustaining "loop". This model clearly explains the high degree of comorbidity displayed by sexual symptoms in women.

Studies conducted in the fertile age found an increase in establishing interpersonal relationship and in exchanging sexual pleasure during the periovulatory period, corresponding to the plasma androgenic peak, even though no clear correlation has been reported between plasma androgen levels and the entity of sexual response. We should keep in mind that the strong motivation to sexual activity at the time of ovulation may be due to E_2 peak.

Estrogen-progestin use, particularly in monophasic regimen, seems to interfere with the spontaneous expression of sexual desire, but even the effects of the pill on mental well-being may play a role on sexual motivation. There is no doubt that hormonal contraception increases plasma SHBG levels and reduces free and total T, together with the absence of marked endogenous E_2 fluctuations, but how these features relate to sexual function remains to be established (10). Some authors have reported that serum T levels related to genital response and to subjective physical sensation (lubrication and breast sensitivity) in response to visual erotic stimulation both in premenopause and postmenopause. Moreover, antiandrogen administration has

been associated with low libido in females. Further evidences suggest that circulating free T relates to sexual desire and masturbation in young women. Finally, 5α-reductase activity is significantly impaired in target tissues in those women reporting low libido following menopause, while a significant correlation has been found between high levels of circulating T and A and a lower index of vaginal atrophy.

ANDROGENS IN THE TREATMENT OF DESIRE DISORDERS

A recent systematic review including all randomized and placebo-controlled trials of treatment for women's sexual dysfunction in postmenopausal women concluded that many treatments that are used in practice are not supported by adequate evidence (11). The first-line treatment is always represented by estrogen replacement therapy to restore adequate plasma E_2 levels in order to secure the vaginal environment. As a second therapeutic step, after excluding other organic and psycho-relational issues, androgen supplementation may be proposed. Only one trial on estrogen replacement therapy (ERT) was randomized and placebo-controlled, and investigated the effects of estrogen and progestin on sexual desire, arousal and mood in healthy postmenopausal women, without assessing frequency of sexual activity and orgasm. Sherwin concluded that there was a significant improvement of sexual desire and arousal on a short-term basis (12). The most interesting findings on positive sexual effects of sex hormones at menopause come from studies with oral and transdermal combination of estrogens and exogenous T, even though only two trials were randomized and placebo-controlled. The first trial, conducted on a small sample of subjects (n=20), reported that sexual desire, satisfaction and frequency in postmenopausal women taking hormonal therapy were improved significantly by combined estrogen-androgen therapy but not by

estrogen or estrogen-progestin therapy. Sexual function improved with estrogen-androgen therapy, even though circulating estrogen levels were lower than those measured during previous estrogen therapy, leading to the conclusion that androgens play a pivotal role in sexual function, with estrogens not having a significant impact on levels of sexual drive and enjoyment. The second trial was conducted in surgical menopause, with two doses of transdermal T (150 and 300 mcg/d) versus placebo, and reported a significant improvement in sexual function with a further increase in scores for frequency of sexual activity and orgasm when women were taking the higher dose. However, there was an extremely strong response in sexual function in women on placebo, and 24% of study participants withdrew from the trial because of androgen-related adverse side-effects. A very recent study demonstrated that the addition of testosterone undecanoate improved specific aspects of sexual function more than treatment with estrogen alone, but supraphysiological levels were achieved in a significant proportion of the women (13). Therefore, the use of androgens in the clinical management of menopause needs a certain degree of caution, even because the long-term effects of such preparations on women's general health are still unknown. In addition, estro-androgenic treatments are still unavailable in several countries. In Europe, a long-term experience for the treatment of climacteric symptoms and low mood and libido is available with tibolone, a synthetic steroid with tissue-specific estrogenic, progestagenic and androgenic properties. Apart from direct effects of its metabolites in the vagina and in brain areas relevant to well-being, tibolone lowers SHBG, thus increasing free E_2, T and DHEA-S levels. In randomized studies versus placebo or E_2/NETA (norethisterone acetate), tibolone treatment (2.5 mg/d) alleviates vaginal dryness and dyspareunia, ameliorating to a greater extent libido, arousal and sexual satis-

faction in postmenopausal women. Moreover, tibolone shows a positive effect on sexuality which is superimposable to that observed with estro-androgenic preparations. This data, together with recent observation that tibolone significantly increases vaginal pulse amplitude at baseline and following erotic stimulation versus placebo, further supports the notion that such tissue-specific compound is a good therapeutic option to relieve low libido, arousability and lubrication at menopause, because of both its estrogenic and androgenic properties (14). DHEA, as a precursor of E_2 and T, has been proposed in the treatment of low libido both pre- and postmenopausally with encouraging results. Studies conducted in elderly women have shown a positive effect of DHEA on mental well-being and motivational aspects of sexuality, with a mild relief of climacteric symptoms (15).

Further studies are needed to clarify the relevance of androgens to women's sexuality and the impact of hormonal treatments on the clinical expression of sexual symptoms. The role of the clinician in identifying all the possible biological factors leading to low androgen levels is mandatory to design therapeutic strategies tailored on women's need.

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Depression, antidepressants and female sexual dysfunction in women: Clinical approach

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ABSTRACT. *Sexual dysfunction has been found in over 40% of the general population of women. Affective disorders, including anxiety and depression, are also highly prevalent, affecting roughly a third of all women. In many cases, sexual dysfunction accompanies affective disorders. While antidepressant therapy can relieve the sexual dysfunction caused by depression, this same therapy may cause Antidepressant Associated Sexual Dysfunction (AASD). The clinician should assess for baseline sexual function before providing antidepressant therapy, and address AASD when it occurs. When treating midlife women, an assessment of changes in sexual function related to gonadal hormones should be made, with treatment provided accordingly.*
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INTRODUCTION

Sexual dysfunction and affective disorders are both common problems among women. This brief review will discuss the prevalence of these conditions, the association between the two, and clinical approaches to treating affective disorders with attention to sexual function.

Prevalence of female sexual dysfunction across the population

Sexual dysfunction is more common among women than men. A study of the general population in England found that 41% of women and 34% of men could report a current sexual problem (1). A population study of 1749 men and women, ages 18-59, in the United States found the prevalence of sexual dysfunction to be 43% among women and 31% among men. The most common problems among women were problems of desire, lack of interest in sex (22% and 32%, respectively), and problems with or-

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gasm (26%) (2). Another study of the American population showed that 24.4% of women reported marked distress about their sexual functioning.

Prevalence of affective and anxiety disorders across the population

Affective disorders are also very common among women. The lifetime prevalence for major depressive disorder among women is 17% (3). The prevalence of anxiety disorders in women is 30.5%. This would include all anxiety disorders: specifically phobia, social anxiety disorder, agoraphobia with panic, generalized anxiety disorder, panic disorder, and post-traumatic stress disorder (4). Women have a greater burden of affective and anxiety disorders than men. While anxiety disorders affect 30.5% of women, only 19.2% of men are affected. The prevalence of depression among women is about 21%, compared to 13% among men (3). Dysthymia, a milder form of depression, also has a greater prevalence in women, 8% compared to 5% for men (4). Depression with anxiety symptoms is quite common and is seen more often than depression alone (5). Co-morbidity of these two disorders is equally common and often makes these patients somewhat more difficult to treat (6).

Gender-specific differences also include a greater seasonal effect on mood (7), with women having approximately 80% of the cases of seasonal affective disorder (4% prevalence among women compared to 1% among men) (8). Stressful life events are more associated with depression among women as well (9). Premenstrual dysphoric disorder (PMDD), affects approximately 3-8% of women with a definition of meeting five or more DSM IV criteria (7, 10). When including severe premenstrual syndrome (PMS) or sub-syndromal PMDD, this number can double (8). There are many theories that attempt to address and explain the gender differences in affective disorders; these include methodology of the research, and biological and psychosocial differences between men and women. The latter include victimization, social and life stress, as well as particular issues related to socialization (9).

Failure to treat to remission of illness is an additional problem in all individuals with depression or anxiety. Patients are either not offered care or are offered care and are treated with sub-therapeutic doses of antidepressants. At times, a therapeutic dose of a particular antidepressant fails to bring the patient to remission. Some studies have defined remission as a Hamilton depression score of 7 or less, the patient no longer meets the criteria for depression, displays minimal or no symptoms, and has had a return of psychosocial/occupational functioning (11). Impairment in work appears to normalize only with remission, with incomplete return of functioning when patient has a partial response (12).

The implications of depression, anxiety, and other affective disorders along with remission issues in those treated for female sexual dysfunction and desire are significant. For women, these issues affect willingness to engage in sexual activity through distractibility of female sexual desire, fatigue, situational stress, and mood. These untreated affective disorders result in decreased desire and arousal, and thus have a great impact on female sexual function (13).

Prevalence of FSD among affective and anxiety disorders

There is a limited literature on the prevalence of female sexual dysfunction (FSD) among women with untreated affective and anxiety disorders. Kennedy et al. found that "49% of depressed women and 26% of depressed men reported no sexual activity in the preceding month"(14). Casper et al. and Hamilton et al. found decreased libido in approximately 70% of depressed patients (15, 16). Zajecka et al. found a range of problems with arousal, lubrication or orgasm, with 65% of depressed women reporting some sort of sexual problem (17).

Untoward consequences of treatment for depression and anxiety: FSD with antidepressants

Since the advent of the serotonin reuptake inhibitor class of antidepressants there has been the consistent observation that for some patients these antidepressants have an adverse impact on the patient's orgasm and/or a decline in her libido as a result of these agents (18-20). Antidepressant Associated Sexual Dysfunction (AASD) is observed soon after treatment is initiated. Its impact and the course of AASD is highly variable with some patients having mild impairment while others have significant loss of orgasm or libido. These sexual side effects may improve for some and persist for others. The most common complaints in women are decreased orgasm and libido (21, 22). In the field of psychiatry, side effects, and particularly the side effect of AASD has important implications for successful treatment of this large population of women with depression because side effects are one of the main reasons for discontinuing antidepressants, with sexual dysfunction being a primary cause for discontinuation (23).

For the midlife to post menopausal woman, this issue is confounded by the fact that many women have orgasm and libido problems related to their major affective disorder and/or may have FSD related to gonadal hormone change with menopause and age. The dynamic relationship between these two are such that both conditions may need to be serially treated or concurrently treated so as to resolve the FSD. This treatment and the establishment of the etiology of the FSD is complicated by the onset in some patients of antidepressant-induced side effects. Improvement in the major affective disorder may result in resolution of their "appetitive" problems in the sexual realm but then be confounded by the occurrence of AASD (19, 24-26). The rates of sexual side effects secondary to antidepressants vary from a conservative 14% to the less conservative estimate of 73% (27). The degree of the problem, the persistence of the problem, and the degree of distress from the side effect are highly variable. The quality of these studies has also been questioned as many of these are observational and not prospective studies that have controlled for other pre-existing and contemporaneous variables (28). Additionally, many patients will have some degree of relief for their sexual side effects when the clinician diligently assesses pre-existing functioning, observes for new onset of FSD, and then either tries a different antidepressant, or uses some of the established augmentation strategies for amelioration of the AASD. Sildenafil has been a promising addition to these augmentation strategies (28, 29). More traditional approaches have been to augment the SSRI with buproprion or busparone (30).

CONCLUSIONS

Sexual dysfunction has been found in over 40% of the general population of women. Affective disorders, including anxiety and depression, are also highly prevalent, affecting roughly a third of all women. In many cases, sexual dysfunction accompanies affective disorders. While antidepressant therapy can relieve the sexual dysfunction caused by depression, this same therapy may cause Antidepressant Associated Sexual Dysfunction (AASD). The clinician should assess for baseline sexual function before providing antidepressant therapy, and watch for AASD. When AASD is present, the clinician should try switching to a different antidepressant, or augmenting the antidepressant with Sildenafil, buproprion or busparone. In addition, the clinician should assess whether or not any sexual dysfunction is related to gonadal hormone changes due to menopause or age, and treat accordingly.

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Sexual abuse and female sexual disorders: Clinical implications

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ABSTRACT. Patients that are seeking gynecological treatments for sexual dysfunctions are often likely to be sexual abuse survivors; it is therefore important for clinicians to conduct a thorough assessment that includes questions about sexual abuse history. Clinicians may not feel comfortable asking questions about sexual abuse history because of lack of experience and training on how to handle the difficult feelings associated with the topic. This paper aims at reviewing some of the most common health problems of women survivors of sexual abuse and provides a list of suggestions on how to handle disclosure of sexual abuse during the clinical interview.
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INTRODUCTION

Sexual abuse (SA) is a common problem often underestimated by clinicians. Although SA has a strong impact on the sexual functioning of survivors, questions about abuse are often not asked during assessment because health care providers may feel inadequately trained on the subject. This article aims at:
- providing suggestions on how to conduct interviews and assessments with women with a history of SA;
- providing information on psychosomatic, psychological and gynecological factors that may impact survivors' sexual functioning.

BACKGROUND

Women with a history of SA are more likely to utilize medical care than non-abused women (1, 2) and to report stress-related somatic and psychophysiological disturbances (3) including sexual dysfunctions. Becker et al. (4) found that in 371 assault survivors,

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sexual arousal dysfunction was highly prevalent in women with a history of rape and childhood SA, while low sexual desire affected women with a history of rape. Several factors make it difficult or uncomfortable for untrained clinicians to ask about past SA experiences: a) not knowing how to react to the patient's intimate disclosure, b) fear of invading the patient's privacy, c) confusion about what to do with the information given, and d) concern that talking about the event will make the patient feel worse. Studies in the area of trauma help address the answers to some of these concerns. For the clinician who is uncertain on how to react to a patient disclosing a history of SA, the best response is a warm and nonjudgmental one. At times the clinician may be tempted to investigate the accuracy of the patient's memories. Controversy surrounds the accuracy of SA recovered memories, which are defined as memories that have not been accessible to the patient for a period of time and begin resurfacing suddenly and often unexpectedly (5). Although researchers have not been able to determine the accuracy of these memories, from a clinical point of view this matter is of little importance (4). Treating all of the reported memories as valuable and reliable is the suggested approach taken by most therapists and clinicians who are conducting assessment and treatment interventions. Assuming an investigative role can create a hostile therapeutic environment and re-traumatization could occur if the patient were to feel doubted. At the same time, to prevent the formation of false memories, it is important not to imply or suggest that the patient may have been sexually abused.

When empathizing with a patient, the clinician should keep in mind that women vary in their responses to past SA. Some women have been able to cope effectively and although the memories of the abuse are still upsetting, they are no longer terrifying. For other women, the memories continue to be so disturbing that they are not ready to admit fear or anger toward the perpetrator. Reflecting the feelings expressed by the patient is a safe way to respond with empathy without making an assumption about the patient's current emotional state. The important message to convey in the initial moments of disclosure is complete acceptance with no judgment attached to what happened, and a genuine concern for the patient's safety and her feelings. Sympathy for the feelings of loss or for her anger towards the injustice of the situation can also be powerful tools for the development of a good relationship with the patient. Unless absolutely necessary for the assessment, it is not recommended that a clinician probe about details of the event. The patient may not be ready to disclose or focus on facts that could force them to delve into deeper feelings that they do not yet have the resources to control.

Clinicians often express concern that such questions may violate the patient's privacy, but survivors often report a sense of relief from disclosing a secret that was a source of guilt and shame. Additionally, including questions about a history of SA in the routine assessment helps dispel the myth held by some SA survivors that they are alone in their experiences. Clinicians should also keep in mind that the patient may have years of experience talking to therapists about the event and, consequently, talking about it may create little or no distress. Some clinicians may feel uncomfortable with the disclosure of the SA history because there is no immediate solution to the problem. These are feelings clinicians need to acknowledge, and this discomfort should not prevent them from including a useful and necessary part of the assessment.

Helpful procedures and recommendations for clinicians to offer patients who have disclosed a history of SA include assessing the patient's current safety, making a referral to a mental health professional when indicated, and ensuring the patient is not becoming overwhelmed with the memories. If the clinician suspects potential reoccurrence of the SA, the

patient needs to be referred to a mental care provider. It is important to keep in mind that the most intuitive advice (e.g., "leave your partner") may not be the safest or best solution for the patient. Clinicians should abstain from giving personal suggestions on what to do and should comply strictly with the ethical and legal guidelines of their affiliations. For those cultures in which therapy is not a common practice, the client may express some resistance to the referral. It can be useful to normalize the idea of therapy by explaining that often women report finding relief from being able to share these memories and feelings with someone who can help them work through the difficult emotions attached to these past events.

Conducting an invasive gynecological examination with SA survivors can be challenging. Patients' feelings of mistrust, anger, and pain may negatively interfere with the visit to the extent that they may not pursue further visits. Attention to key details can minimize the discomfort of the visit and increase the likelihood that the patient will return. First, conducting the interview prior to any physical examination can be helpful in establishing rapport. Second, the clinician should be cognizant of the patient's sensitivity to feeling out of control during assessment and invasive procedures. During the SA event, the survivor was deprived of the right to control what was happening, and this can be mirrored during the gynecological visit. The clinician should inform the client that she should feel free at any point to ask to stop or take a break. Giving the patient privacy when she undresses, asking for a female nurse to be in the room during the visit, and explaining the clinician's actions step by step are standardized procedures used in the United States that can be particularly useful with SA survivors.

CLINICAL APPROACH

Below are the three major areas of concern that would be helpful for the clinician to consider when assessing women with a history of SA:

1. Psychosomatic

Women with a history of SA often report having frequent headaches, weight change, and back pain. Weight change can have an impact on sexual functioning by making women feel unattractive (6). Often, a sense of nausea and gagging may be reported during sexual activity, particularly in women who were forced to perform oral sex. Cardiac arrhythmia and menstrual symptoms are also frequently reported.

2. Psychological

Because of the high comorbidity between psychological disturbances and SA, it is important to collect information regarding common psychological syndromes such as depression, post-traumatic stress disorder (PTSD), general anxiety, and dissociation. SA survivors may report a lack of interest in fun activities (sex may be one of the activities), lack of energy, and decreased self-worth. Feeling too tired to engage in previously enjoyable activities or feeling unattractive and unlovable are aspects of depression that can indirectly impact the patient's sexual functioning.

PTSD symptoms such as intrusive and unwanted memories, hypervigilance, or exaggerated startle reaction, and a sense of numbness or isolation from people may also negatively impact sexual functioning. Women often try to deal with these symptoms by avoiding situations that trigger memories, which sometimes means avoiding sex-related thoughts and behaviors (2). Women with PTSD often use drugs and alcohol to self medicate. This could put the woman at risk to engage in unwanted sexual behavior.

Dissociation (e.g., feeling like floating above one's body during sexual activity) is also a common experience among SA women who find sexual activity upsetting (7). Although the dissociation may have been an adaptive behavior during the SA experience since it allowed the woman to block out the pain and anguish,

Table 1 - Practical Message: psychosomatic, psychological and gynecological consequences of sexual abuse that may impact female sexual functioning.

Psychosomatic	Psychological	Gynecological
Headaches	Depression	Urinary tract infections
Nausea	Post traumatic stress disorder	STDs
Back pain	General anxiety	Pruritis
Cardiac arrhythmia	Difficulties trusting partner	Abdominal pain
Menstrual symptoms	Anger	Skin lesions and trauma
Weight change	Dissociation	Yeast infection
Gagging – Vomiting	Avoidance/Fear sex	Scars in posterior forchette, hymen, vagina

continuing to dissociate during consensual sexual activities may prevent the development of any type of sexual pleasure or sense of closeness. Feelings of anger towards sex in general, men, or one's partner, or a lack of trust in others (8) are often associated with a history of SA and can affect sexual functioning.

3. Gynecological

Lesions or sexually transmitted diseases that may have occurred as part of the SA can impact the survivor's current sexual functioning. In particular, physicians should pay attention to potential lesions and scar tissue in the hymen, posterior forchette, and inside and outside the vagina (9). Yeast infections are also common among women who have been sexually abused.

CONCLUSIONS

In summary, it is advisable for the clinician to question about a history of SA. If the patient starts disclosing a history of SA it is important to show empathy, assess for current safety, and make a referral in cases where the patient looks distressed or reports having difficulties dealing with the memories. To effectively assess sexual functioning, the clinician is advised to assess the potential psychoso-

matic, psychological and gynecological consequences of SA listed in Table 1.

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Hyperactive sexual desire in women: Myth or reality?

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ABSTRACT. Excessive sexual behaviour in women is viewed in many sociocultural contexts to be inappropriate, unacceptable, and perhaps even pathological. Clearly excessive sexual behaviour and desire are more easily managed and identified when they lead to distress in the individual. However, what about high sexual behaviour that is welcomed and linked to strong sexual desire, but which evokes significant distress in others? Here the issue of subjectivity and difficulty in determining normal from abnormal behaviour is an intrinsic problem that the provider faces. In this article we attempt to provide some historical background for conceptualizing hyperactive sexual desire, suggest etiological factors, and propose a clinical framework that would guide management of this difficult condition.
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HYPERACTIVE SEXUAL DESIRE IN WOMEN: MYTH OR REALITY?

When is excessive sexual desire a clinically significant syndrome versus a manifestation of the wide variability in individual differences and preferences? Due to a general lack of agreement upon objective criteria for defining when sexual behaviour is excessive, combined with the potential for a judgemental, moralistic attitude toward such behaviour in women, the possibility of diagnostic confusion and subsequent ineffective management in cases where true clinical syndrome exists, are high. Clearly, this issue is complicated by the fact that normal sexual behaviour itself is expressed along a continuum that is influenced by contextual and social factors. As clinicians, our charge is particularly difficult given the importance of recognizing and managing distressing behaviour within a context where our judgments are largely based

upon subjectivity in labelling normal versus pathological behaviour.

Definition

Whereas Kinsey (1) defined hypersexuality as the number of orgasms per week, here we define excessive sexual desire as a persistent or recurrent excess of sexual desire, expressed as constant and/or intrusive sexual thoughts and/or fantasies, or perception of a high/strong sexual drive. In some cases, such excessive desire leads one to seek sexual activity in the form of partnered or solitary behaviour, though not always. Such excessive desire causes personal and/or interpersonal distress. It may evoke frustration, anger and/or aggressive behaviour when the desire cannot be satisfied or is intentionally suppressed. It may also increase the vulnerability to less self-protective behaviours in the form of higher risk for unwanted pregnancies, sexually transmitted disease (STD), and the possibility of sexual victimization. It is estimated that at least 6% of the population experiences compulsive sexual behaviour (2). Some individuals have hypersexuality that is paraphilic (e.g., unconventional sexual behaviour involving disturbance in the object of sexuality) whereas for others it is nonparaphilic (e.g., conventional sexual behaviour that has become excessive or uncontrolled). Equally important is to differentiate desire or behaviour which is egosyntonic (behaviour, thoughts, or feelings viewed by oneself as acceptable) or egodystonic (those personally viewed as unacceptable or distressing). The former may nevertheless be the object of clinical consultation when it is considered socially inappropriate, causing distress in the partner, family, or social context. Some advocate that nonparaphilic hypersexuality, as distinct from paraphilic behaviour, should be included in the DSM-IV as a clinical disorder (3); however, this remains controversial.

The variability of social norms in defining what is the "normal" range of sexual desire and behaviour considered appropriate deserves special consideration, especially in societies that are rich in multicultural, multiethnic, and religious diversity. For the treating clinician, awareness of a judgemental approach and careful, ongoing self-monitoring of beliefs, personal norms, and values are key to avoid mislabelling of otherwise non-problematic behaviour.

Case example

A. Graziottin (4, 5) has compiled case descriptions of individuals who displayed overt, explicit, excessive sexual behaviour in the context of low sexual desire. She has also highlighted the link between excessive sexual desire and eating disorders, attributing this to up-regulation of the seeking system. "Sexual bulimia" is described as a possible sexual correlate of the eating disorder, Bulimia Nervosa, given that they share the characteristic compulsory seeking of a gratification either with food or sexual activity to manage unpleasant emotions. Quite important in both clinical pictures, the desire (be it for food or for sex) is low, despite the overt behaviour suggesting otherwise. Here we present the case of an 18-year old woman seen by the second author, referred for recurrent Papillomavirus infection and vulvar condilomata. The patient had already undergone three vulvar laser treatments and one terminated pregnancy. She reports regular sexual intercourse with men she meets at dance clubs though denies sexual desire. She acknowledges concern over the consequences of her unprotected sexual activity, but maintains that she cannot remain without sexual activity. For her, sexual activity helps to manage severe emotional instability that typically leads her to binge eat and purge. An understanding of the factors maintaining this hypersexual behaviour in the absence of desire serves to guide management. Here the clinical focus is on regulation of emotional instability and a recognition that, if left untreated, it will perpetuate the cycle of excessive eating and sex-

ual behaviour. Contraceptive suggestions were also given to protect against pregnancy and STDs while also empowering the patient to feel more in-control of her sexuality.

Etiology

There are a number of possible theories on the etiology of hypersexuality as outlined below:

1. *Substance abuse:* Excessive cocaine or amphetamine use has been linked to uncontrolled sexual behaviour (6). These and other substances likely act by disinhibiting the individual sufficiently to allow sexual activity, enhancing sexual pleasure, or decreasing guilt that usually ensues.

2. *Iatrogenic conditions:* Supraphysiologic androgen supplementation, chronic administration of cortisone with androgenic activity, dopaminergic drugs such as L-dopa used in the treatment of Parkinson's Disease, among other medications, have been linked to onset of hypersexual behaviour.

3. *Organic syndromes:* Some metabolic conditions may result in amygdala damage, affecting the centers or pathways involved in sexual inhibition and producing a "Kluver-Bucy syndrome" (7) in which patients display fearless and angerless placidity, in addition to hypersexual behaviour. There is a dramatic increase in the amount and variety of their sexual behaviours so that objects that would not previously have been attractive to them (e.g., members of the same sex, other species, non-living objects) now are. There have also been reports of a dramatic increase in masturbation, including in public, when the prefrontal cortex, key to the programming, regulation and verification of actions is damaged (8, 9). Organic factors damaging the amygdala and/or the prefrontal cortex, and leading to excessive desire, may be a) <u>endogenous</u>, e.g., metabolic syndromes; transient ischemic attacks (TIA); brain hemorrhage; brain thrombosis; epileptic foci; neurinomas or brain carcinomas; or b) <u>exogenous</u>,

e.g., traumatic insult, as in the famous case of Phineas Gage, described by Harlow in 1868, where a small part of the frontal lobe was damaged by a tamping rod shot through the head, leading to massive personality change and hypersexuality.

4. *Clinical syndromes:* Data show that approximately 2/3 of individuals with compulsive sexual behaviour meet criteria for an Axis I mental disorder (6). The Eating Disorders and Obsessive Compulsive Disorder (OCD) have specifically been implicated. In the latter, obsessions are similar to sexual fantasies, compulsions are similar to compulsive sexual behaviour, and there is clinical overlap between the two disorders with depression and anxiety common to both. There has been speculation that compulsive sexuality might be included as an OCD spectrum disorder. Conceptually, this poses a challenge for the clinician who must assess whether the hypersexual behaviour is related to excessive sexual desire, or rather, is a consequence of an underlying Axis I psychiatric condition.

5. *Idiopathic factors:* When no medical or psychosexual pathological findings are apparent, the egosyntonic behaviour may be attributed to idiopathic events. Clinical cases of Kluver-Bucy syndrome, in the absence of amygdala damage, have been reported (10).

Pathophysiology

To better understand the pathophysiology of excessive desire, we might turn to the literature on brain systems involved in sexual "appetitive" behaviours for clues (7-9, 11). Sexual desire or sexual drive may well be considered the sexual expression of the "seeking" system. Also known as the reward system, it has been associated with the terms "curiosity", "drive", "interest" and "expectancy", and is a non-specific motivational system that provides the arousal and energy that activates our interest in the world around us. This system generates perceptual notions that something "good" will

happen if we explore that environment. It is involved in motor behaviour such that it promotes exploration; in this way, it might be linked to masturbation focused on the pursuit of pleasure, or to courting, touching, caressing others, with sexual reward as a focus. The reward system is activated during sexual arousal and other appetitive states (e.g., hunger, thirst, and during substance cravings) (7).

The predominant neurotransmitter of the reward system is dopamine. The seeking system forms part of the mesocortical-mesolimbic dopaminergic system, which is the neurobiological correlate of basic "drives" in human as well as in other mammalians.

The seeking system is normally activated when the "need-detector" in the hypothalamus is switched on by changes in the internal milieu. A range of other inputs, both perceptual and cognitive, also likely activates the reward system. The system is non-specific (7). It is associated and intimately connected with the memory system, which provides the internal representations of objects that enable the organism to learn from experience and to build specific patterns of behaviours that may become object-oriented and therefore specific. One of the more basic tasks that these combined systems perform is to distinguish which objects in the outside world possess the specific properties that the internal milieu lacks when a particular need detector is activated. Like any system of learning, this requires a "reward" mechanism. Panksepp (11) labels a portion of this system the "lust system". Also known as the "pleasure", "reward" or "reinforcement" center, it is associated with gratification, that is, with consummation of the appetites that activate the seeking system (7). Perceptually, this system generates feelings of pleasurable delight: "I like it","That feels good". On the motor side, this system switches appetitive behaviours off and replaces them with consummatory behaviours. These instinctual behaviour patterns are automatically released when the object of an internal need is attained.

These rather crude basic mechanisms are subject to a wide range of higher cognitive influences that can modulate, modify or inhibit them and their associated behaviours. Given this basic understanding of the neural reward system, some speculations as to the underlying pathophysiological processes involved in excessive desire might be proposed:

a) it reflects a physiologic up-regulation of the seeking system, perhaps modulated by androgen levels. This may or may not be associated with a sustained feedback mechanism between seeking and consummatory phases. In its persistent form, excessive behaviour alternates with the rewards of the consummatory phase, leading to new urges for reward. Such a mechanism may be related to hyperactive sexual behaviour which is egosyntonic, where the behaviour is pleasurable and rewarding to the individual, regardless of interpersonal distress.

b) it reflects the reduced efficacy of inhibitory mechanisms, most of which are prefrontal. Although most frequent in male subjects, this behaviour has been described in women as well. In such cases it is the social context that requires control over "socially inappropriate" sexual behaviour, in spite of its possibly being egosyntonic to the individual.

c) in some cases, the hypersexual behaviour might reflect more complex damage of different amygdala systems involving fear and anger, as in the case of Kluver-Bucy syndrome. Because of impairments in the perception of risk, the individual might be at increased risk of sexual victimization.

Clinical approach

A careful, non-judgmental assessment should aim at clarifying the sexual behaviour as outlined below:

- Beginning with an open-ended question such as "How would you describe your sexual desire?" or "How is this desire expressed?" provides a neutral framework for discussing

behaviour that may be otherwise difficult to discuss.
- Follow-up questions might include "Does your sexual desire cause you any concerns?", "Does it lead to concerns in the lives of loved ones, friends, or co-workers?".
- Elucidate the temporal onset of the problem (lifelong vs acquired).
- Understand the context of the problem (generalized vs situational). Keep in mind that a behaviour that is perceived as normal with one partner/context might be received as abnormal in another.
- Assess the predisposing, precipitating, and perpetuating factors involved in etiology. For example, "When did this difficulty begin?" and "What are your thoughts about what might have triggered this problem?".
- Determine the comorbidity of psychiatric, sexual, and medical conditions. Research indicates frequent psychiatric comorbidity in a sample of individuals with excessive sexual behaviour who were not seeking treatment, and for nearly all of those who engaged in excessive behaviour, it was associated with particular moods, such as sadness and loneliness (6).
- Enlist the help of a physician in cases where there is the possibility of vascular, endocrine or other biologically relevant events.

CONCLUSIONS

Excessive sexual desire has been described in historical texts for centuries; however, a clear, pathophysiologically and clinically oriented understanding of it is lacking. Clinically it may be expressed quite differently across individuals. Support for a neurobiological basis is strong, though a precise pathophysiological understanding is still far from being complete. More research is needed to better define the syndrome, its etiology, and its social, religious and political correlates. In particular, sensitive and effective guidelines for management of this distressing condition are needed. Only after adequate clinical and empirical data are gathered can we effectively delineate when "hypersexuality" is a context-dependent judgmental label from that which is a really distressing personal and/or interpersonal problem.

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Sexual arousal problems in women: A clinical perspective

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ABSTRACT. *The objectives of this paper are 1) to review the latest recommendations for describing and diagnosing arousal disorders in women, 2) to describe a new and perplexing arousal disorder, namely that of persistent sexual arousal, and 3) to discuss psychological and physical treatment options for treating female arousal difficulties.*
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INTRODUCTION

In the last six years, disordered, diminished or absent female sexual arousal has become the focus of considerable clinical and research attention. Part of the increased interest may be attributed to the impressive success of sildenafil citrate, a phosphodiesterase-5 inhibitor, in treating male erectile problems, but the increased attention to arousal problems in women is also due to better understanding of the central role of arousal in the female sexual response cycle.

In order to appreciate the importance of sexual arousal for women, it is helpful to review Basson's proposed model (1) of womens' sexual response cycle (Fig. 1). Basson (2, 3) suggests that most women begin sexual activity from an initial stance of sexual neutrality and/or a wish for greater intimacy. With some motivation to be sexual, whether positive or negative, the woman either seeks out or becomes receptive to, and aroused by, sexual caress. It is the subjective awareness of pleasurable feelings, either mentally or physically, that helps launch sexual desire rather than internal sexual drive or feelings of genital tension for many women. This is especially true for peri or post-menopausal women or women in relationships of long duration where there is likely to be less intrinsic desire, decreased hormonal "prompting" for physical release and

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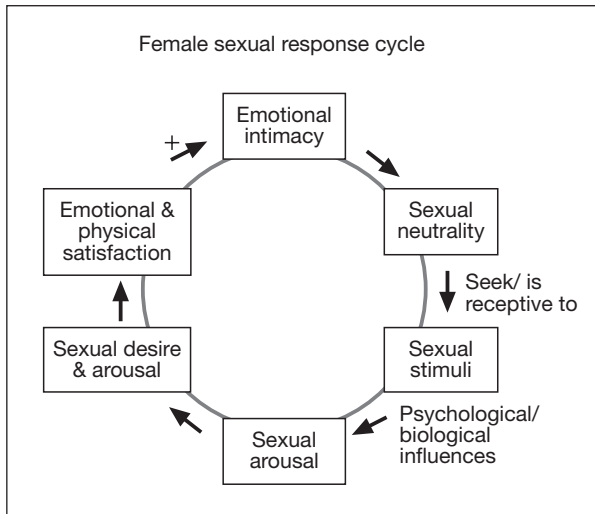
Figure 1 - Basson's model of womens' sexual response cycle. From (1).

less novelty. Rather, desire is activated by subjective feelings of sexual excitement which occur with sexual stimulation, whether self or partner induced. It is therefore the case that diminished or absent subjective awareness of sexual arousal is likely to interfere with the entire sexual response cycle.

PREVALENCE OF AROUSAL PROBLEMS IN WOMEN

The actual prevalence of arousal complaints is difficult to determine since there is tremendous overlap between arousal and desire problems in women (4). Furthermore, the criteria used to diagnose arousal problems tend to vary across samples and, until recently, there has been a paucity of research specifically focusing on arousal disorders. In a random population sample of post-menopausal women, Lindal and Stefansson (5) reported a lifetime prevalence of arousal problems to be 6%. Laumann et al. (6) reported a prevalence of 19% in a US sample. Fugl-Meyer (7) interviewed a large Swedish sample of women and reported the prevalence of arousal disorders to be 8%. Overall, it may be estimated

that, depending on the age and setting of the population studied, prevalence figures can range anywhere from 6-21% (8).

FEMALE SEXUAL AROUSAL DISORDERS: NEW DIAGNOSES

Recently, a group of invited experts in female sexuality recommended modifications and revisions in the DSM-IV description of women's sexual disorders in order to provide more refined and accurate diagnoses (9, 10). For example, one of the biggest shortcomings in the current definition of female sexual arousal disorder is the emphasis on genital lubrication as opposed to an emphasis on subjective feelings of sexual excitement, pleasure or satisfaction. This reliance on genital response ignores research evidence showing a lack of strong correspondence between women's subjective and genital awareness (11). For many healthy women, awareness of genital sensations of lubrication does not correlate with increased vaginal engorgement as measured by vaginal photoplethysmography. Furthermore, the complaint most upsetting to most women seeking consultation is that of diminished or absent subjective feelings of sexual arousal rather than complaints of insufficient genital lubrication.

In light of the etiological, clinical and research importance of distinguishing problems involving genital arousal from subjective arousal disorders, three sub-types of arousal disorder are described: genital arousal disorder, subjective arousal disorder and combined genital/subjective arousal disorder (see Table 1 for a description of the diagnoses).

In addition, it is important to recognize the existence of an arousal complaint that has been reported by a small minority of women but one which is greatly distressing, namely persistent genital arousal (12, 13). In this condition, feelings of genital vasocongestion occur without any feelings of conscious desire or actual sexual stimulation and persist despite one or more orgasms. The pulsating and

Table 1 - Subtypes of female sexual arousal disorders.

Subjective sexual arousal disorder

Absence of or markedly diminished feelings of sexual arousal (sexual excitement and sexual pleasure), from any type of sexual stimulation. Vaginal lubrication or other signs of physical response still occur.

Genital sexual arousal disorder

Complaints of absent or impaired genital sexual arousal. Self-report may include minimal vulval swelling or vaginal lubrication from any type of sexual stimulation and reduced sexual sensations from caressing genitalia. Subjective sexual excitement still occurs from non genital sexual stimuli.

Combined genital and subjective arousal disorder

Absence of or markedly diminished feelings of sexual arousal (sexual excitement and sexual pleasure), from any type of sexual stimulation as well as complaints of absent or impaired genital sexual arousal (vulval swelling, lubrication).

Persistent sexual arousal disorder

Spontaneous, intrusive and unwanted genital arousal (e.g. tingling, throbbing, pulsating) in the absence of sexual interest and desire. Any awareness of subjective arousal is typically but not invariably unpleasant. The arousal is unrelieved by one or more orgasms and the feelings of arousal persist for hours or days.

tingling sensations of genital arousal are typically experienced by the woman as being intrusive, insistent and unwanted. They result in frequent masturbation or sex with a partner in order to provide relief. However, orgasms do not quell the sensations of genital vasocongestion for very long. Arousal can reoccur quickly and persist constantly for days, weeks, or even months. Many women do not report this complaint to their physician because of feelings of shame or embarrassment so that the prevalence of this disorder is unknown at present.

ASSESSMENT

A careful assessment of all of the predisposing, precipitating and maintaining causes of the sexual complaint(s) is essential in arriving at an accurate diagnosis of the arousal disor-

der. Table 2 provides questions that may help guide assessment.

CLINICAL TREATMENTS
Pharmacological/ Physical approaches

For women who complain primarily of "genital arousal disorder" with an emphasis on impaired or absent lubrication, assessment of estrogen levels is important. For those

Table 2 - Assessing sexual arousal complaints.

When did your arousal problem begin? What was different then?

Has your "motivation" or interest in being sexual with your partner changed recently? What might have contributed to your change in sexual interest or desire?

Do you feel sexually excited "mentally" with sexual caress?

Do you feel sexually "turned on" in your genitals, e.g., with feelings of tingling or wetness?

Is there any kind of sexual material or touching that helps you feel sexually aroused?

If your partner provided more of the kinds of touching that you enjoyed, would you still have a problem with sexual arousal?

Do you have difficulty staying focused during sexual activity? If yes, what interferes? Distracting thoughts? Flashbacks? Memories?

Do you experience any alteration in your pulse rate and respiration when stimulated sexually?

Do you experience pleasurable sensations (feelings of warmth, tingling, increased sensitivity) in your clitoris and vagina with sexual stimulation?

Do you become lubricated or "wet" with sexual stimulation? How often is intercourse difficult or painful because your vagina feels dry and tight?

Do you need to use a vaginal lubricant for intromission?

What do you think would need to be different in order for you to be aroused?

Do you ever feel persistent feelings of sexual arousal despite being unaware of feelings of sexual desire?

Are you bothered by constant genital tingling that is unrelieved by orgasm?

Are there any other difficulties you are aware of that are interfering with your sexual interest or arousal?

women who are clearly estrogen-deficient, estrogen replacement or supplementation may be quite effective in the short-run (14). There are many estrogen delivery systems, including pills, creams, and vaginal rings. However, there are several counter-indications that should be considered with respect to the long-term administration of estrogen replacement therapy. Firstly, systemic estrogen replacement taken via the oral route may increase sex hormone binding globulin resulting in a reduction of bioavailable testosterone. This can have the unwanted effect of impairing sexual desire, further compounding the initial problem. Secondly, the recent results from the Women's Health Initiative study assessing the effects of combined HRT (conjugated equine estrogen 0.625 mg/d plus medroxyprogesterone acetate 2.5 mg) found a small increased risk of breast cancer and cardiovascular disease after five or more years of use (15). Consequently, although estrogen supplementation is very effective in alleviating vaginal atrophy and lubrication inadequacy, it is recommended that it be prescribed at the lowest possible dose and for the briefest possible time.

Fortunately, there are a variety of over the counter lubricants that are quite effective for relieving vaginal dryness as well as a variety of vibrators and/or devices that may facilitate bloodflow to the genitals, e.g. the EROS clitoral device.

Considerable research is also underway exploring the use of phosphodiesterase inhibitors, such as sildenafil, for the treatment of female arousal disorders. Although promising, recent research has not proven clear efficacy for PDE5 inhibitors, although these medications may be helpful for selected populations with the specific complaint of genital sexual arousal disorder (16). Vasoactive drugs may increase clitoral vasocongestion while adrenoceptor agonists such as phentolamine or yohimbine may help with generalized vasodilation. However, to date,

these approaches have not proven effective in increasing subjective excitement, the more common arousal complaint.

Psychological approaches

A variety of psychological and interpersonal factors can impede sexual arousal. These include lack of attraction, either sexual or emotional (or both) to the partner, sexual boredom, negative emotions such as guilt, shame, anxiety, anger and resentment, upsetting thoughts or feelings associated with arousal, and most significantly, distraction and/or inattention to the sexual context (17). Mothers of infants, for example, often report an inability to focus and/or attend to their partner or to their sexual sensations. Consequently, even though the woman's body responds appropriately to sexual caresses, she may be mentally disengaged and unaware of any sensations of arousal.

In these cases, it is important to determine the woman's motivation for treatment. A woman may be motivated to be sexually active in order to become pregnant, to avoid punishment or to satisfy a partner. On the other hand, she may be motivated to resist sexual arousal in order to thwart a partner, avoid flashbacks associated with past sexual abuse or to resist feelings of loss of control associated with sexual abandonment. Psychological treatment usually involves exploring the individual inhibitions and/or interpersonal factors that diminish arousal and increasing the conditions that can facilitate arousal, such as the use of erotica, fantasy and/or sexual aids. Therapy is sometimes indicated for resolving such intrapsychic inhibitions as fears of abandonment, loss of control, or feelings of undeserved sexual pleasure.

Treatment for persistent sexual arousal continues to be elusive. A careful and thorough pelvic examination is essential as well as evaluation of hormonal, neurological, anatomical and/or pharmaceutical contributions. Duplex ultrasound may be helpful in identifying abnormal clitoral blood flow. Some authors have reported success with cognitive reframing of

the arousal as a healthy response (18) while others have tried antidepressants, anti-androgenic agents and anesthetizing gels. To date, no single etiological cause has been identified, so no single treatment can be recommended. Most recently, Goldstein (unpublished material, 2002) described a case of PSAS in a 55 year old woman who complained of clitoral engorgement since the age of 18. An internal pudendal arteriogram revealed a 3 cm pelvic arterio-venous malformation with a single arterial link to the clitoral artery. Following embolization, the woman reported relief. This is the only case report of an obvious physical cause. While not a currently recognized arousal dysfunction, the complaint of persistent genital arousal should be taken seriously and etiological causes investigated since it can be quite distressing.

CONCLUSIONS

Female sexual arousal disorders constitute a varied spectrum of difficulties ranging from the total absence of genital or subjective pleasurable arousal to the absence of psychological arousal despite normal genital vasocongestion to feelings of persistent genital arousal in the absence of sexual desire. Much remains to be understood about the essential and overlapping etiological contributions to these complaints, but with the newest conceptualization of the female sexual response cycle, the importance of sexual arousal in women is undeniable. Research is required to better understand the potential role of vasomotor drugs, gonadal hormones and contextual factors in facilitating or inhibiting female sexual arousal.

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Vascular aetiology of female sexual arousal disorder (FSAD) in women: Evidence and diagnostic approach

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INTRODUCTION

The Report of the International Consensus Development Conference on Female Sexual Dysfunction (FSD) originally specified several types of difficulties regarding sexual arousability with the comprehensive definition of women's Sexual Arousal Disorder (1). This diagnosis could be further classified as lifelong versus acquired as well as generalized versus situational and, from an aetiological point of view, as organic, psychogenic, mixed or unknown (1).

Women's sexual arousal (SA) is a physiologic process primarily identified by genital vasocongestion, vaginal lubrication, enhanced local hyperaemia, increased vaginal length and vaginal pH, decreased vaginal luminal pressure as well as by the awareness of genital throbbing and tingling. SA involves the ability to attain and maintain adequate sexual excitement and it is gently modulated by psychosocial factors, hormonal milieu and several neurovascular inputs (2, 3).

Women's SA disorder is the persistent or recurrent inability to attain or maintain adequate sexual excitement causing personal distress. This disorder must consider the potential absence of coordination between an objective genital activation and/or extra-genital activation (i.e. skin sensitivity, mammary tension and increased scent perception towards pheromones) and the woman's subjective perception of the arousal itself (4).

Thus, due to these considerations, very recently a new classification system has been proposed, with the specific aim to subdivide the overall arousal disorder pattern into a) subjective SA disorder, b) genital SA disorder, c) combined genital and subjective arousal disorder as well as d) persistent SA disorder (5).

The aim of this section is both to distinguish few of the most frequent clinical vascular patho-physiological mechanisms of

genital FSAD and to suggest a practical specialized genital vascular diagnostic approach.

WOMEN'S SA DISORDERS: VASCULAR AETIOLOGY AND PATHO-PHYSIOLOGY

Physiological SA in women as well as in animals is strongly characterized by an increased autonomic activation. The latter seems to include both a parasympathetic blood flow component to genital and erectile tissues (namely, in the clitoris, labia and vaginal epithelium), and a sympathetic blood flow from the heart to striated and smooth muscles that participate in sexual responses. Moreover, during the last years the role of non-adrenergic, non-cholinergic (NANC) neurotransmitters/mediators [i.e. nitric oxide (NO)] in the arousal response have been studied with increasing interest. New in vivo models on rats, rabbits and dogs have made it possible to investigate vaginal and clitoral blood flow, vaginal oxygen tension, vaginal temperature and vaginal luminal pressure as markers of genital sexual arousal (6).

Genital hemodynamics results as the key point of the so-called women's genital arousal and normal hormonal milieu seem to represent a fundamental requisite to obtain a dynamic modification of the entire vasculature set throughout the arousal phase. Preclinical and clinical studies suggest that estrogens modulate genital hemodynamics and are critical for maintaining structural and functional integrity of vaginal tissues (7). Estrogen deprivation may lead to decreased pelvic blood flow resulting in diminished vaginal lubrication, clitoral fibrosis, thinning of the vaginal wall and decreased vaginal submucosal vasculature. Not many studies concern the effect of androgens over the genital blood flow and vasocongestion. Clinical studies have indicated that androgens modulate SA responses (8). While estrogens seem to strongly regulate the vascular components of genital tissues, androgens markedly facilitate genital blood flow in estrogenized animals. Thus, it has been also suggested that androgens can contribute to genital arousal independently from a pure hemodynamics response to the clitoris and the vagina (8).

Women's SA is therefore also a hemodynamic process, involving increased arterial inflow, coordinated with clitoris smooth muscle relaxation, but it may be better defined as the final expression of a complex process involving sexual stimulation, ascending/descending steady control by the central nervous system (both supraspinally and spinally), a peripheral neurovascular pathway, and an important hormonal balance.

DIABETES MELLITUS AS A POTENTIAL GENITAL VASCULAR RISK FACTOR

A few manuscripts have underlined the significant role of diabetes (DM) in promoting women's sexual disorders (9). Neuropathy, vascular impairment and psychological problems have been showed as closely implicated in high rate of decreased libido, slow arousability, decreased vagina lubrication, orgasmic dysfunction and dyspareunia in women complaining of DM.

Recently, Enzlin et al. (10) reported data of a case-control study concerning prevalence and characteristics of sexual dysfunction in women suffering from type 1 DM, as compared with an age-matched control group of healthy women, demonstrating that significantly more women with diabetes (27%) than age-matched controls (15%) reported sexual dysfunction (χ^2=4.5, df=1; p=0.04). Moreover, patients presented a higher prevalence of overall SA dysfunction (χ^2=3.8, df=1; p=0.05) and of decreased lubrication (χ^2=6.5, df=2; p=0.04) than healthy women. Interestingly, sexual problems were not isolated in occurrence; indeed, 11% in the studied group reported 2 or 3 sexual problems. Patients complaining of sexual disorders were not significantly differ-

ent in age (p=0.13), BMI (p=0.08), length of disease (p=0.36) or HbA$_{1c}$ values (p=0.47) as compared with those without sexual complaints. Interestingly, this analysis did not show any statistically significant correlation between sexual complaints and peripheral neuropathy, autonomic neuropathy, nephropathy and retinopathy. In addition to what said before, the statistical analysis did not demonstrate any significant evidence due to the menopausal status (p=0.59) as well as the use of hormone replacement therapy or oral contraceptive pill (p=0.37).

Erol et al. (11) reported a reduced libido (77%), a diminished clitoral sensation (62.5%), while 37.5% complained of vaginal dryness and 41.6% described vaginal discomfort also in DM type 2 women.

We recently reported some preliminary results of a cross-sectional study aiming at evaluating prevalence and predictors of sexual dysfunction in both DM type 1 (58.3%) and type 2 (41.7%) women as compared with a control group of healthy age-matched controls asking for a yearly routine check-up visit at the Ob/Gyn clinic (12). While no significant differences have been found regarding the Female Sexual Function Index (FSFI)-arousal phase domain score, a direct comparison demonstrated that DM patients had worse score for the desire (p<0.001), the lubrication (p<0.001), and the orgasm (p<0.001) domains of the FSFI, as compared with the control group. The Beck's Inventory for Depression (BDI) showed that 48% of these patients had some degree of depression. The BDI score was significantly correlated with the arousal domain (r= -0.54; p=0.003), the orgasm domain (r= -0.39; p<0.05) as well as the satisfaction domain of the FSFI (r= -0.48; p=0.04).

A further analysis has been performed regarding the hormonal profile of the normal cycling women among the type 1 DM patients enrolled in the trial. Due to the potential significant role of the oestrogen balance in promoting a normal genital blood flow, we considered the so-called "estrogenic basal tone" thus subdividing the patients into a group with estradiol (E2) ≥40 pg/ml (namely, women with a normal ovulatory cycle) and another one with E2 <40 pg/ml (namely, not-ovulatory cycles). The direct comparison analysis demonstrated that DM women had lower E2 than controls both in the normal ovulatory and the not-ovulatory group. Moreover, DM women showed significantly (p<0.05) lower values for total and free testosterone, as well as for DHEA-S and delta 4-androstenedione. While the biologic role of these decreased values should be better defined, the reduction of circulating hormones might have a significant impact over the genital blood flow and the vaginal lubrication.

SEXUAL DYSFUNCTION IN WOMEN WITH CORONARY ARTERY DISEASE

While ED is a common and well known problem in men suffering from coronary artery disease (CAD), and may herald a systemic vasculopathic state, such as ischemic heart disease (IHD), at our knowledge investigations of sexual function and dysfunction in women with CAD are fewer and rarely complete.

To try to better evaluate both chronological, epidemiological and aetiological correlations between women's sexual dysfunction and CAD, from February 2001 we have enrolled 60 consecutive women presenting with angina pectoris at the emergency unit of our institution (13). A total amount of 30 (50%) out of the 60 patients [mean±SE age: 56±1.66 years] were ultimately enrolled in this still ongoing cross-sectional study and underwent a morphological and functional evaluation of the coronary arteries with a coronary angiography. Their FSFI results were thus compared with those of 102 age-matched consecutive women assessed for a yearly routine check-up at the Ob/Gyn clinic.

The overall prevalence of sexual dysfunction (SD) among these CAD women was 30% (9/30). 70.9% (7/9) of the CAD women complained of FSAD while a low lubrication score was reported by 8 (88.9%) out of these 9 women.

The direct comparison of the FSFI scores showed that the total-FSFI value was significantly higher (p=0.02) for controls than for women suffering from CAD. Patients also reported a significant higher amount of SA (p=0.002) as well as lubrication (p=0.10) disorders. Moreover, patients also had significantly lower (p=0.01) scores regarding the orgasmic phase domain of the FSFI. The BDI demonstrated that 33% (10/30) suffered from mild depression while severe depression interested 3 (10%) of the patients. Beck's score was significantly correlated with the FSFI-desire domain [p=0.008 (r= -0.48)] as well as with the arousal domain [p=0.0005 (r= -0.64)], the lubrication domain [p=0.0008 (r= -0.63)], the orgasm domain [p=0.0004 (r= -0.66)] and the overall sexual satisfaction domain [p=0.0007 (r= -0.63)]. Interestingly, FSD became evident prior to symptoms of ischemic heart disease in 7 (23%) out of the 30 patients. Therefore, 7 (78%) out of 9 patients in this series developed sexual disorders prior (median of 51 months; range: 12-96 months) to angina or a myocardial infarction. Although these findings need to be confirmed in a larger patient population, this preliminary report suggested that SD is an important health issue in women with CAD.

VASCULAR SPECIALIZED DIAGNOSTIC TESTING: A BRIEF COMPOUND

Diagnostic modalities such as vaginal photo-plethysmography, duplex Doppler ultrasound, vaginal and clitoral temperature and vibration sensory testing, and selective pudendal arteriogram expand the physician and patient understanding of the pathophysiologic mechanisms of FSAD, but, unfortunately, lack of normative data may limit the use of these specialized testing.

From a practical point of view, non-invasive vascular testing of women with SD, clinically useful in the everyday practice, includes vaginal photo-plethysmography and genital duplex Doppler ultrasound. Vaginal photo-plethysmography measures the vaginal pulse amplitude (VPA), reflecting phasic changes in vaginal engorgement with each heart beat providing quantitative data on the extent of vaginal vasocongestion (14). Several studies have already addressed its significance in a research setting; very recently, for instance, Basson and Brotto (15) elengantly demonstrated that women with photo-plethysmographic evidence of impaired genital arousal might also objectively benefit from sildenafil. Similarly, Laan et al. (14) conducted an objective study to demonstrate the effectiveness of tibolone in postmenopausal women by means of a vaginal photo-plethysmographic device. The authors showed that tibolone was effective in increasing VPA values when compared to placebo, that is to say to improve the vaginal hemodynamics during erotic stimulation. Likewise, the same study confirmed that tibolone increased both sexual desire in women, and frequency of excitement and vaginal lubrication compared to the placebo group.

The role of duplex Doppler ultrasonography in the management of women with SD remains to be determined. Historically Lavoiser et al. (16) reported data about the potential usefulness of the method and some practical suggestions. More recently a few investigators reported small patient series using duplex doppler ultrasound before and after stimulation (i.e., visual and vibratory, even in combination with topical application of 2% alprostadil) as a diagnostic tool in women with SD (17, 18). Nappi et al. (19), for instance, very recently used this diagnostic technique to objectively demonstrate that oral tibolone seemed to increase clitoral blood flow in post-

menopausal women complaining of both desire and genital arousal disorders. However, a standard technique is not yet available to maximize diagnostic information obtained by duplex doppler ultrasonography.

CONCLUSIONS

Genital women's sexual arousal dysfunction represents an important health issue and includes a broad spectrum of etiological disorders. As a parallel with the ED disorder in men, it might say that sometime FSAD should be considered as a symptom of clinically significant disease and life-threatening situations. Thus, sexual medicine absolutely needs a larger amount of clinical trials in this fascinating field.

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Female orgasm disorders: A clinical approach

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ABSTRACT. *Female orgasmic disorders are a prevalent problem that can affect quality of life. This article provides a review of the biopsychosocial factors affecting female orgasm and a review of the assessment and treatment of female orgasmic disorders. Clinical assessment and treatment should be multidisciplinary, involving biomedical, psychosocial, and sexual aspects. Currently available therapies that have received clinical research attention include cognitive-behavioral therapy and pharmacotherapy. The importance of female orgasmic functioning as a quality of life issue warrants ongoing controlled biopsychosocial research.* Urodinamica 14: 99-104, 2004

INTRODUCTION

Female orgasmic disorders are a prevalent problem that can affect couple relationships and generate emotional distress (1, 2). It has been estimated that from 5% to 30% of women in community- and population-based studies and from 18% to 76% of women in clinic-based studies report difficulty in reaching orgasm or dissatisfaction with orgasm frequency (3-5). In one American study, orgasmic difficulties were the second most common sexual complaint reported by women (24%) (5).

BACKGROUND

Diagnosis

The Diagnostic and Statistical Manual of Mental Disorders-IV-TR (DSM-IV-TR) (6) defines Female Orgasmic Disorder as the "persistent or recurrent delay in, or absence of, orgasm following a normal sexual excitement phase" that causes personal distress or interpersonal problems (i.e., the partner is distressed). A recent consensus-

development committee on defining sexual dysfunctions further recommended that the diagnosis be applied only when the presenting individual reports distress; distress reported by the partner, but not the presenting individual, does not merit the diagnosis (1). In addition, the majority of women are unable to attain orgasm through intercourse alone (e.g., 4, 7); clitoral stimulation appears essential to trigger orgasm, even during intercourse (7). Hence, the capacity to have masturbatory orgasm but not coital orgasm, even though it may cause personal distress, is viewed as a normal aspect of female sexual functioning (e.g., 8).

Etiological factors

A formal DSM diagnosis of Female Orgasmic Disorder includes categorizing the etiology of the disorder and ruling out organic factors (i.e., medical conditions, substance use, medications) and other Axis I psychopathologies (6). However, the Consensus Committee proposed that the etiological categories for sexual disorders should include organic factors (1); accordingly, Female Orgasmic Disorder can be attributed to organic, psychogenic, mixed, or unknown factors. Numerous biopsychosocial factors have been investigated for their impact on female orgasm functioning and orgasmic dysfunction. Table 1 summarizes some of these factors. A detailed review of these factors is beyond the scope of this article; interested readers are directed to the many comprehensive reviews available (e.g., 4, 7, 9). Because research concerning orgasmic disorders typically entails observational studies rather than controlled experiments, few of these factors can be considered definite or direct determinants of female orgasm functioning and orgasm disorders (4).

CLINICAL APPROACH

Assessment

In assessing the presenting problem, the DSM-IV-TR subcategories of female orgasmic

disorder (lifelong vs acquired; generalized vs situational) (6) provide one useful organizing structure. Maurice (8), for example, discussed the lifelong/generalized ("anorgasmia"), lifelong/situational, and acquired/generalized orgasmic disorders as the three most common clinical presentations of female orgasmic dysfunction. This structure reflects the core content and contextual issues to be assessed: a) duration (e.g., "Have you been able to have orgasms before?", "When did you first notice the problem?"); b) partner-related sexual activities (e.g., "Have you ever had orgasm during intercourse? With manual or oral stimulation from your partner?", "Do you or does your partner stimulate your clitoris during intercourse?"); c) masturbation activities (e.g., "Have you ever masturbated? With a vibrator?", "Have you ever had orgasm this way?"); d) level of arousal (e.g., "On a scale of 1-10, how sexually excited do you get during intercourse? During non-coital stimulation from your partner? During masturbation?"); e) qualitative changes (e.g., "Have you noticed changes in your orgasm experience?", "Has orgasm become noticeably less intense or less pleasurable? Do you have pain during orgasm?"); and f) reactions to and attitudes about the problem (e.g., "What do you think or feel when orgasm doesn't occur?", "What does your partner say when you don't have orgasm?") (8).

In accordance with the Consensus Committee's proposed etiological subtypes (organic, psychologic, mixed, unknown) (1), assessment of contributing factors should include both a physical examination, to identify or rule out organic factors, and a thorough review of medical, psychological, relationship, and sexual and psychosexual functioning. Reviewing multiple domains besides the biomedical is important given that female sexuality may be significantly influenced by psychosocial factors. Table 1 lists many of the biopsychosocial factors that should be assessed. More pertinent factors include the fol-

Table 1 - Factors reported to be associated with female orgasm.

Biological factors	Psychosocial factors
periperal nervous system - hypogastric, pelvic, and pudendal nerves (+) - vagus nerve (?)	*sociodemographic characteristics (+)* - age - marital status (with partner) - educational status
central nervous system (+) - T10-L2 and S2-S5 spinal levels - various cortical and subcortical structures (e.g., prefrontal cortex, frontal-temporal cortex, septum, amygdala, cingulate, basal ganglia, hypothalamic structures)	*psychological adjustment factors (-)* - self-blame attributional style - repressed emotions - need for control - conservative attitudes - dependency - apprehensiveness, negativity - psychiatric conditions

neurotransmitter systems
- cholinergic (?)
- adrenergic, noradrenergic (+)
- dopaminergic (+)
- serotonergic (-)
	sexual behaviours (+)
	- triggers of orgasm
	  - clitoral and mons stimulation
	  - vaginal, cervical, and G-spot stimulation
	  - pubococcygeal muscle strength
	  - breast stimulation
	  - mental imagery, fantasy
	- initiation of sexual activity by woman
	- frequency of masturbation, intercourse, and overall sexual activity
	- use of sexual fantasy
	- varied sexual activity, extended foreplay, sexual experimentation
	- uninterrupted genital stimulation

neuroendocrine systems - steroid hormones (e.g., androgens [+], estrogens [?]) - oxytocin (+) - prolactin (-) - neuropeptides (e.g., vasoactive intestinal peptide, opioids) (?)	
psychotropic medications (-) - antidepressants (e.g., SSRIs, tricyclics, MAOIs) - benzodiazepines - neuroleptics (especially prolactin-elevating drugs)	
other medications - antihypertensive medications (-) - anti-epileptic drugs (-) - drug treatments for orgasm disorders (e.g., amantadine, buproprion, cyproheptadine, ephedrine, gingko-biloba, mirtazapine, olanzapine, vasoactive drugs [e.g., sildenafil], yohimbine) (?)	*psychosexual factors* - premarital sexual experiences (+) - sexual responsiveness (+) - attitudes about masturbation (+) - awareness of physiological arousal (+) - sexual compatibility with partner (+) - partner involvement in sexual activity (+) - sexual abuse history (-) - sex guilt (-) - low sexual desire or arousal (-)
substance use - moderate alcohol intake (+) - heavy alcohol use (-) - substance use (e.g., cocaine, amphetamines) (-)	
medical conditions with neurological, vascular, or other physiological involvement - multiple sclerosis (-) - diabetes (?) - spinal injury (-) - neuroanatomical damage from surgical procedures (e.g., pelvic surgeries) (-)	*interpersonal factors (+)* - marital stability, happiness, and satisfaction - emotional closeness to partner - early relationship quality with parental figures *cultural factors (-)* - sociocultural control of sexual expression

These factors are listed without considering either the methodological quality of the studies in which they were investigated or whether the reported relationship is direct vs indirect. The following symbols denote the direction of the relationship reported in studies between a factor(s) and higher female orgasm frequency, strength, or satisfaction or improvements in orgasmic disorders: (+) = positive relationship, (-) = negative relationship, (?) = relationship unclear.

lowing: knowledge about orgasmic and sexual functioning, sexual repertoire, functioning across the sexual response cycle, and comorbid sexual dysfunctions such as lack of sexual desire, sexual arousal, or premature ejaculation in the partner; quality of the couple relationship; historical review of relationships and sexual functioning, including sexual abuse or trauma; recent stressors; comorbid psychopathologies; medical conditions and medications; and alcohol and substance use.

Empirically investigated treatment strategies

<u>Cognitive-behavioral therapy (CBT).</u> The goals of this multi-faceted therapy include a) promoting changes in sexual knowledge, beliefs, and attitudes, b) decreasing anxiety about sex, c) expanding the sexual repertoire, and d) increasing connections between positive feelings and sexual behaviors (4, 10). Behavioral exercises form a core component of CBT. Depending on assessment findings, sex education, communication-skills training and couple therapy, self-help components (bibliotherapy), and other exercises to promote cognitive and interpersonal changes are typical adjuncts (10). With conflictual relationship issues, for example, couple therapy to improve communication and negotiate conflicts may be helpful for some, in addition to sex therapy (11, 12). For couples concerned about being unable to attain coital orgasm, normalizing strategies involving sex education and referral to published sources, indicating that the majority of women cannot attain coital orgasm without additional clitoral stimulation, should be employed (e.g., 8).

Directed masturbation (DM) is the most frequently prescribed treatment for lifelong/generalized orgasmic difficulties (4, 10). DM typically begins with sex education. Individuals then engage in private visual exploration of their body, including the genitals, to attain familiarity and comfort with the body and genitals. Finally, individuals stimulate their genitals to discover the stimulation needed to trigger orgasm. Controlled studies have shown that DM is effective: success rates for achieving masturbatory orgasm with DM range from 47% to 100% for lifelong anorgasmia and from 10% to 75% for acquired anorgasmia (4, 10).

Orgasmic consistency training (OCT) involves a structured sequence of exercises (13) to address lifelong/situational difficulties (e.g., orgasm achieved through masturbation but not coitus). First, the couple engages in sensate focus, a sequence of body-touching exercises that begins in a non-sexual manner and then progresses in an increasingly sexual manner. This includes non-demand genital touching by the partner, followed by manual and then penile stimulation of the woman's genitals, and finally intercourse. Sensate focus helps couples shift away from goal-focused orgasm and more towards awareness of sexually sensitive bodily areas, pleasurable sensations, and freer sexual communication (4). The couple then learns the coital alignment technique (CAT), a variant of the missionary position (2, 13). The man rests on top of the woman but farther forward, and then both partners move their pelvis in a rocking motion. The resulting penile-clitoral contact theoretically provides clitoral stimulation to trigger orgasm. Studies of OCT have shown that women who completed DM training and were assessed prior to CAT training were more likely to report achieving orgasm during intercourse than those who completed both DM and CAT training and were assessed after CAT training (13). This difference may be attributable to the fact that DM advocates additional clitoral stimulation during intercourse, whereas CAT does not (13). However, these findings require replication (cf. 2).

Some have argued that these procedures work by reducing sexual-performance anxiety (e.g., 4, 10). For example, sensate focus might be a form of systematic desensitization: It involves a hierarchy of touching exercises that removes the imperative of achieving or-

gasm and reduces self-monitoring ("specta-toring") and performance anxiety (e.g., 4). The effectiveness of other anxiety-reduction techniques like relaxation training can be difficult to evaluate because such techniques are typically part of a multi-component treatment plan. Anxiety-reduction techniques alone, however, have not shown great promise for orgasmic difficulties when evaluated in controlled studies (4, 10).

Pharmacological therapy. Pharmacological treatments attempt to facilitate the neuro-physiological mechanisms underlying orgasm or to counteract the sexual side effects of medications. Of recent interest in the treatment of female sexual dysfunctions has been the drug sildenafil. Its vasoactive properties may help increase physiological arousal and in turn the likelihood of achieving orgasm. However, this mechanism of action, as well as the efficacy of sildenafil in treating female sexual dysfunctions in general, still needs to be evaluated with placebo-controlled studies (10). Many psychotropic medications and other pharmacological agents have sexual side effects, including inhibition of orgasm (Table 1). On the whole, findings from controlled studies of pharmacological agents are mixed or suggest little benefit beyond placebo in treating both medication-induced female orgasmic dysfunction and female orgasmic dysfunction in general (e.g., 10).

CONCLUSIONS

Because female orgasm is widely viewed as essential to sexual satisfaction, female orgasmic disorders should be addressed within the context of individual quality of life and couple satisfaction. The complex factors underlying female orgasmic disorders suggest a multidisciplinary approach to assessment and treatment. Considering the impact of psychosocial factors on female orgasm, this should include expertise in sex and couple therapy.

Clinical practice would further benefit from continued investigation of the subjective characteristics and physiological mechanisms of female orgasm and how they interact to produce the orgasm "experience". Female orgasm, especially its physiological aspects, is less well understood than male orgasm (e.g., 7, 10). To advance knowledge about its primary characteristics and functional mechanisms, controlled studies should incorporate both physiological and subjective measures. While measures of genitopelvic (e.g., vaginal blood volume, vaginal and anal muscle contractions) and extragenital changes (e.g., heart rate, blood pressure) during orgasm exist, imaging technology (e.g., fMRI) may provide more precise data on such changes. There is also a need for a standardized self-report measure of the psychological experience of female orgasm. We are engaged in the ongoing evaluation of an adjective checklist, the Orgasm Questionnaire, to assess the components of the subjective orgasm experience (7). Finally, other research directions include placebo-controlled trials of substances reported in case or uncontrolled studies to alleviate female orgasmic disorders (10), and controlled studies comparing the relative treatment efficacy of individual components of multi-faceted treatment programs like cognitive-behavioral therapy. Findings from such efforts would help advance the effective treatment of female orgasmic disorders.

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Sexual pain disorders: Clinical approach

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ABSTRACT. *Sexual pain disorders include dyspareunia and vaginismus. They may affect 10 to 15% of women between 18 and 59 years of age. Vulvar vestibulitis is the leading cause of dyspareunia in the fertile age. Etiology includes recurrent vaginal infections; hyperactivity of the mastcells; myalgic contraction of the pelvic floor; hyperactivity of the pain system, with shift from nociceptive to neuropathic pain, and neurogenically mediated inflammation. Iatrogenic factors may cause acquired dyspareunia. Loss of estrogens and related genital arousal disorders are the leading etiology of dyspareunia in the postmenopause. Special attention wll be dedicated to the strong association between urinary tract symptoms and dyspareunia − RR= 7.61 (4.06-14.26) − and genital arousal disorders − RR= 4.02 (2.75-5.89) − respectively. Psychosexual factors may contribute to sexual pain disorders. Inadequate coping modalities may worsen pain perception over time. A careful clinical approach, aiming at understanding and treating all the causes of sexual pain disorders, is mandatory if sexual pain is to be effectively addressed.* Urodinamica 14: 105-111, 2004
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INTRODUCTION

Dyspareunia is a comprehensive word, used when intercourse is characterized by pain, of different etiology (1-4). Vaginismus focuses on the muscular component of the disorder, namely the defensive contraction of the pelvic floor, that is usually psychogenically triggered by fear of penetration of whatever conscious or unconscious etiology (5). Vaginismus is still considered the clinical expression of fear of penetration, the muscular involvement being a more variable and inconsistent finding (see Graziottin et al., this issue). When severe, vaginismus interferes with penetration. It is the leading female cause of unconsummat-

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ed marriage. Lifelong vaginismus, when not severe enough to prevent penetration, may cause introital dyspareunia. Considering the main interest of the readers, this paper will focus on dyspareunia and associated urinary tract symptoms. Evidence of the increasing role of the pain system in the maintenance of the local inflammatory response (6), in the hyperalgic genital perception and in the lowering of the central pain threshold has dramatically changed the clinical approach to dyspareunia in the recent years. Implications for management will be reviewed.

DEFINITION AND PREVALENCE

"Dyspareunia defines the persistent or recurrent pain with attempted or complete vaginal entry and/or penile vaginal intercourse. Vaginismus indicates the persistent or recurrent difficulties of the woman to allow vaginal entry of a penis, a finger, and/or any object, despite the woman's expressed wish to do so. There is often (phobic) avoidance and anticipation/fear of pain. Structural or other physical abnormalities must be ruled out/addressed" (7). The "non coital sexual pain disorders", described as the "recurrent or persistent genital pain induced by non coital sexual stimulation", i.e. foreplay evoking or worsening clitoralgia or vestibular pain, formerly included in the classification of FSD, has been deleted from the latest version (8)

Ten to 15% of coitally active women in the fertile age (9), and 22.5-33% of postmenopausal women complain of various degrees of dyspareunia. Vaginismus is reported in average 0,5-1% of fertile women.

THE PATHOPHYSIOLOGICAL SCENARIO

Vaginal receptiveness is a prerequisite for intercourse. This ability requires anatomofunctional integrity of the many tissue com-

ponents, both in resting and aroused state. Normal trophism, mucosal and cutaneous, adequate hormonal impregnation, lack of inflammation, particularly at the introitus, normal tonicity of the perivaginal muscles, vascular, connective and neurological integrity, and normal immunitary response are credited to be the necessary conditions to guarantee the vaginal "habitability" (2, 3). Vaginal receptiveness may be further modulated by psychosexual, mental and interpersonal factors: the woman's motivation to intercourse is key. Etiology of dyspareunia may be biological, psychosexual and context-dependent (1-8, 10-12) (Table 1). Usually multiple causes are present in the individual patient. Poor arousal, with vaginal dryness, may be a predisposing factor of biological etiology, or the consequent sign, of poor psychosexual arousal (13, 14). Fear of penetration, with a variable defensive pelvic floor contraction and general muscular arousal secondary to anxiety, may lead to vaginismus. It may be so severe as to prevent penetration at all. The defensive pelvic floor contraction may also be secondary to genital pain, of whatever cause. It may be triggered by pain in the introital area associated with: vulvar vestibulitis (1-3, 6, 14); recurrent vaginal infections (12); vulvovaginal atrophy, secondary to loss of estrogens and/or androgens (10); iatrogenic factors, such as poor outcome of episiorrhaphy, vulvar lasertherapy; overzealous colporrhaphy; posterior colporrhaphy, radical surgery for cervical carcinoma, pelvic radiotherapy (2, 3). Vulvar vestibulitis has three major symptoms: acute burning pain, most at 5 and 7, when loooking at the vaginal introitus like a clockface; reddening of the vestibular mucosa and dyspareunia (1). An almost constant finding is the associated contraction of the pelvic floor muscles (2, 3). Non-genital, nonsexual causes, such as anorectal problems (anismus, hemorrhoids, ragads) or urological factors (in association with urinary tract symptoms, cystitis first, urge incontinence

Table 1 - Etiology of dyspareunia. Many causes may overlap or be associated with coital pain with complex pathophysiologic interplay. The relative weight of each cause in the individual woman may change with chronicity of pain and progressive involvement of other pelvic organs.

A) Biological

  1) *superficial/introital and/or mid-vaginal dyspareunia*
    - infectious: vulvitis, vulvar vestibulitis, vaginitis, cystitis
    - inflammatory, with mastcell's up-regulation
    - hormonal: vulvo-vaginal atrophy
    - anatomical: fibrous hymen, vaginal agenesis
    - muscular: primary or secondary contraction of levator ani muscle
    - iatrogenic: poor outcome of genital surgery; pelvic radiotherapy
    - neurologic, inclusive of neuropathic pain
    - connective and immunitary: Sjogren's syndrome
    - vascular

  2) *deep dyspareunia*
    - endometriosis
    - pelvic inflammatory disease (PID)
    - pelvic varicocele
    - chronic pelvic pain and referred pain
    - outcome of pelvic or endovaginal radiotherapy
    - abdominal nerve entrapment syndrome

B) Psychosexual

    - co-morbidity with desire and /or arousal disorders, or vaginismus
    - past sexual harassment and/or abuse
    - affective disorders: depression and anxiety
    - catastrophism as leading psychologic coping modality

C) Context or couple related

    - lack of emotional intimacy
    - inadequate foreplay
    - couple's conflicts; verbally, physically or sexually abusive partner
    - sexual dissatisfaction and consequent inadequate arousal
    - poor anatomic compatibility (penis's size and/or infantile female genitalia)

Modified from Graziottin, 2004, with permission.

second) are often associated to the levator ani contraction (13). Latent classes of sexual dysfunctions by risk factors in women indicate that urinary tract symptoms have a RR= 4.02 (2.75-5.89) of being associated with arousal disorders and a RR=7.61 (4.06-14.26) of being associated with sexual pain disorders, accord-

ing to the epidemiological survey of Laumann et al. (9). Endocrine, infectious, muscular, vascular, nervous (particularly pain associated) and psychosexual factors may variably contribute to the individual sexual pain disorder. In chronic dyspareunia, particularly when associated with vulvar vestibulitis or interstitial cystitis (IC), pain becomes prominent in 90.3% of patients with vulvar vestibulitis and 93.6% of classic IC patients report various degrees of pain. Of those with pain, 80.4% have pain in the lower abdomen, 73.8% in the urethra, 65.7% in the lower back and 51.5% in the vestibular/vaginal area. (13). Intermittent flares may occur premenstrually, both in IC and VV patients. Hormonal modulation of the mastcell's hyperactivity associated with chronic pain is the most plausible factor. Hormones may trigger the release of histamine, substance P, bradichynine, and other pro-inflammatory substances from the vesicules packed in the mastcells. Whatever the agonist stimulus – infectious, inflammatory, neurogenic, mechanic, hormonal or chemical – that triggers the mastcell's release and up-regulation, the common outcome is the maintenance and worsening of local inflammation and tissue damage, with parallel up-regulation of the pain system, mediated by the mastcell's production of Nerve Growth Factor (NGF). Current understanding of the pathoplasticity of the pain systems indicate that the shift from nociceptive pain (indicator of threatened or ongoing tissue damage) to neuropathic pain (generated in up-regulated fibers and centers of the pain system) is the common denominator of most of pelvic pain syndromes, inclusive of dyspareunia (2, 3, 6, 11, 13). Three major steps have been described: 1) neurogenic inflammation, as a result of prolonged noxious stimuli, with afferent nerves firing antidromically (backward down the sensory nerve); 2) "cross-talk" of pelvic viscera with shared innervation, together with the increasing recruitment of usually "silent" unmyelinated fibers (A-delta and

C-fibers), the most important carriers of pain signals. This recruitment may explain the increasing hyperalgesia whilst the cross-talk seems to be a further contributor of the progressive involvement of different pelvic organs in the increasing pain perception; 3) development of viscero-muscular reflex, which results in muscular instability and a hypertonic contracted state within the muscles of the pelvic floor (13). This results in a decrease in muscle function and in the development of myofascial trigger points and myofascial pain with the development of new pain generators (13).

Medical ("organic") factors – too often underevaluated in the clinical setting – are therefore the most frequent and important causes of dyspareunia and chronic pelvic pain. They may interact with psychosexual factors. A thorough medical evaluation is therefore mandatory.

THE DIAGNOSTIC WORK-UP

Clinicians should investigate sexual pain disorders with an empathic attitude, respect and kindness. Women suffering from sexual pain disorders have usually been neglected for years, treated as neurotic, referred to mental health providers, and/or substantially denied of having something deserving medical attention other than psychiatric. For many of them, to be understood in the reality of pain is the first key step to begin a constructive, effective and rewarding relationship with the physician (11). The clinical history and diagnostic work-up in sexual medicine, unfortunately unaddressed in the formal medical training as well as in the specialty one, will be presented in detail, to ease the clinical approach of the caring physician (2, 3, 11).

1) "Was the coital pain you are experiencing present from the very beginning of your sexual life ("lifelong") or did it appear after months or years of sexual well being ("acquired")? If lifelong, were you afraid of feel-ing pain before your first intercourse? If lifelong, dyspareunia might usually be caused by vaginismus and/or coexisting, life-long low libido and arousal disorders. Do you remember urinary tract symptoms (enuresis, urge incontinence, giggle incontinence, cystitis) preceding your sexual pain disorders? Or did such symptom(s) appear in concomitance of, or after, the beginning of the coital pain (dyspareunia)" (11, 13-15)?

2) "If the sexual pain is acquired, do you remember the situation or what happened when it started?"

3) "Is it present in any situation and/or with different partners ("generalized"), or is it limited to specific situations ("situational")?"

4) "Where does it hurt? At the beginning of the vagina, in the mid vagina or deep in the vagina?" Ask again the question while you are gently examining the patient to record her "pain map" (2, 3, 11). Location of the pain and its onset within an episode of intercourse are the strongest predictors of presence and type of organicity:

- Introital dyspareunia may be more frequently caused by poor genital arousal (of biological and/or psychosexual etiology), vulvar vestibulitis, vulvar dystrophia, painful outcome of vulvar physical therapies, perineal surgery (episiorrhaphy, colporrhaphy, posterior perineorrhaphy), pudendal nerve entrapment syndrome and/or pudendal neuralgia, Sjogren syndrome or painful outcome of female genital mutilation (FGM) (2, 3).

- Mid vaginal pain, acutely evoked during physical examination by a gentle pressure on the bilateral sacro-spinous insertion of the elevator ani muscle, is more frequently due to levator ani myalgia, the most frequently overlooked biological cause of dyspareunia, either primary (and possibly concomitant to vaginismus) or secondary to persistent coital pain and/or recurrent or chronic cystitis or anorectal painful syndromes (2, 3, 11-15).

- Deep vaginal pain may be caused by or associated with: endometriosis; pelvic inflammatory disease (PID; chronic pelvic pain; varicocele; adhesions, referred abdominal pain, outcomes of radiotherapy and abdominal cutaneous nerve entrapment syndrome (2, 3).

5) "When do you feel pain? Before, during or after intercourse?"

- Pain before intercourse suggests a phobic attitude towards penetration, usually associated with vaginismus, and/or the presence of chronic vulvar vestibulitis.
- Pain during intercourse is more frequently reported. This information, combined with the previous – "where does it hurt?" – proves to be the most predictive of the organicity of pain.
- Pain after intercourse indicates that a mucosal damage was provoked during intercourse, possibly because of poor arousal, contributing to or secondary to the pain associated with vulvar vestibulitis, pain and defensive contraction of the pelvic floor.

6) "Do you feel other accompanying symptoms, vaginal dryness, pain or paresthesias in the genitals and pelvic areas? Or do you suffer from cystitis symptoms 24-72 hours after intercourse or from other urinary symptoms?"

- Vaginal dryness, either secondary to loss of oestrogen and/or to poor genital arousal may coincide with dyspareunia.
- Clitoralgia and/or vulvodynia, spontaneous and/or worsening during sexual arousal may be associated with dyspareunia and hypertonic pelvic floor muscles.
- Post coital-cystitis should suggest the presence of a concomitant bladder vulnerability, a subclinical interstitial cystitis, a hypertonic pelvic floor muscles and/or a hypoestrogenic condition: it should specifically be investigated in fertile patients complaining of bladder symptoms first, and/or of dyspareunia (13, 14). It deserves to be investigated and treated in the post-

menopause and senium as it may benefit from vaginal Estrogen Replacement Therapy (14, 16) and a specific rehabilitation of the pelvic floor aimed at relaxing the myalgic perivaginal muscles.
- Vulvar pruritus, vulvar dryness and/or feeling of a burning vulva should be investigated, as they may suggest the presence of vulvar lichen sclerosus, that may worsen the introital dyspareunia. Neurogenic pain may cause not only dyspareunia but also clitoralgia. Eye and mouth dryness, when accompanying dyspareunia and vaginal dryness, should suggest Sjogren's syndrome, a connective and immunitary disease.

7) "How intense is the pain you feel?" Focusing on the intensity and characteristics of pain is a relatively new approach in addressing dyspareunia issues. A shift from nociceptic to neuropathic pain is typical of chronic dyspareunia, as briefly indicated above; treatment may require a systemic and local analgesic approach (see Vincenti and Graziottin, this issue).

The accurate clinical history will help the physician to focus his/her following diagnostic steps.

1. Physical accurate examination to define the "pain map", inclusive of pelvic floor trophism, muscular tonus, signs of inflammation, elicited pain in the urethral and/or trigonal area, poor outcome of pelvic surgery, associated urogenital and rectal pain syndromes, myogenic or neurogenic pain, vascular problems (11). All medical factors contributing to dyspareunia in the individual patient should be described, explained to the woman (and partner!) and addressed with a multimodal approach (see Vincenti and Graziottin, this issue). Intensity of pain elicited in each point during the medical examination should be scored with an analogic scale, from 0 to ten (worst ever) and recorded in the medical chart.

2. Hormonal profile should be tested, if amenorrhea, of whatever etiology, is re-

Table 2 - Treatment of dyspareunia.

- Address predisposing, precipitating and maintaining etiologic factors, either biological and/or psychosexual, taking a collaborative approach where possible

- Treat recurrent vaginitis and/or cystitis or other associated urinary tract or proctologic symptoms

- Restore normal vaginal trophism with topical estrogens first (always record the vaginal pH!)

- When a defensive contraction of the pelvic floor is diagnosed, teach relaxation techniques, focused on the pelvic floor muscles, inclusive of local vaginal self-massage.

- When myalgia of the pelvic floor is diagnosed with tender and/or trigger points on the levator ani, either physiotherapy and/ or electromyographic vaginal biofeedback may significantly reduce both the contraction and the associated muscular pain.

- If VVS is diagnosed, treat the pertinent predisposing, precipitating and maintaining factors

- Depending on the nature of pain (nociceptive or neuropathic), address the pain disorder with topical electroanalgesia or specific systemic and local antalgic treatments; vestibulectomy is to be reserved to chronic VVS that is not responsive to the above treatments

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ported (10). The recording of the vaginal pH during the medical examination may immediately give a measure of vaginal estrogenization and associated ecosystems (12). Increase pH is likely in post-menopausal years, from the normal pH 4 typical of the fertile age, to pH 7 of the late menopause (12). This shift may be associated with both genital arousal disorders with vaginal dryness and/or dyspareunia and recurrent vaginal and bladder infections by colonic germs. Different estrogenic preparations may improve vaginal and bladder symptoms. Controlled prospective randomized trials show that topical vaginal estrogens (17 beta-estradiol vaginal tablets, twice a week) may significantly improve symptoms of vaginal dystrophy, dyspareunia and urinary tract symptoms as well (16).

3. Psychosexual factors, poor arousal first, should as well be investigated (see Leiblum, this issue).
4. Marital issues, particularly in chronic dyspareunia, deserve special attention.

A multimodal approach aimed at curing different causal factors is mandatory to address dyspareunia and associated co-morbidities, both with other FSDs and/or other medical conditions, urological first. Relaxation of the contracted pelvic floor is a common step in most dyspareunia cases (17). Key steps of the multimodal treatment are summarized in Table 2 (2, 3, 10, 11, 14, 16-19). (See also Vincenti and Graziottin, this issue, for the specific intervention in chronic neuropathic pain associated with Vulvar Vestibulitis and dyspareunia).

CONCLUSIONS

Pain is rarely purely psychogenic. Dyspareunia is no exception. Like all pain syndromes, usually it has one or multiple biological etiological factors. Psychosexual factors, mostly low libido, lifelong or acquired, because of the persisting pain; lifelong vaginismus, when a phobic component is prominent; and genital arousal disorders, lifelong or acquired, due to the inhibitory effect of pain and/or loss of estrogens, should be addressed in parallel, in order to give a comprehensive, integrated and more effective treatment. Urinary tract symptoms, either preexisting or secondary to dyspareunia and/or genital arousal disorder, should be addressed in parallel, to cure the complex co-morbidity, both between FSD and between FSD and associated medical conditions, urological first.

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Neuropathic pain in vulvar vestibulitis: Diagnosis and treatment

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ABSTRACT. *Patients affected by vulvar vestibulitis syndrome (VVS) suffer from symptoms typical of neuropathic pain such as allodynia and hyperalgesia. Because of the severe pain on vestibular touch or attempted vaginal entry, intercourse is increasingly avoided. Pathophysiology of physical symptoms is related to the microscopic findings of proliferation of pain fibers which are also superficialized within the vestibular tissue. Current non-invasive treatment may be useful in a number of patients, but the most severe cases need a stronger approach, such as anaesthetic nervous blocks. Monthly repeated nervous anaesthetic blocks with bupivacaine of the impar ganglion, sacral roots and pudendal nerves, completed by ancillary therapy including antidepressant and anticonvulsant (as gabapentin) drugs, may progressively reduce intensity of pain and its extension. Both decreased ending fibers sprouting induced by periodic anaesthetic blocks sessions and secondary changes of forebrain activity seem to be a rational pathophysiologic explanation of the efficacy of this new and original therapy for VVS' pain.* Urodinamica 14: 112-116, 2004
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INTRODUCTION

Recent findings of histologic and biochemical features of vestibular tissues of patients affected by vulvar vestibulitis syndrome (VVS) (1-3) have stimulated a new and more effective therapy of the cases defined as intractable.

Anaesthetic nervous blocks mainly of the impar ganglion and ancillary therapy with gabapentin have modified the general approach to the treatment of these patients, who were before scheduled for an ablative surgery of the vestibulus, i.e. vestibulectomy. Pathophysiologic considerations are necessary to elucidate the rational basis of our therapeutic approach.

PATHOPHYSIOLOGIC SCENARIO

An acute aggression to the vulvar vestibulus due to bacterial, fungal or viral infection, to chemical irritants, to coital rubbing when lubrication is lacking, as well as iatrogenic procedures may cause an acute pain, lasting from some days to a few months. This cause an inflammatory response with a typical nociceptive pain, which a correct symptomatic and etiologic approach may resolve (4). When such an irritation becomes chronic, the mastcells become up-regulated. Their production of Nerve Growth Factors (NGF) promotes nerve pain fibers proliferation, which correlates with hyperalgesia, and superficialization of them which causes "allodynia", the perceptive shift from tactile to burning pain (1-4). This explains why pain becomes persistent in spite of every current non-invasive treatment. When nerves work in an abnormal fashion, as they signal pain without an apparent peripheral damage, the term "neuropathic pain" may be used. This pain also describes the process by which the neurons involved in pain transmission are converted from a state of normosensitivity to one in which they are hypersensitive.

Initially, pain is only due to peripheral mechanisms, but later central mechanisms are progressively recruited. The pathophysiology of peripheral neuropathic pain is therefore based both on abnormal peripheral inputs and an abnormal central processing (1-5). Peripheral mechanisms include (a) nociceptors sensibilization, (b) spontaneous activation of primary afferent fibres ectopically firing from the site of lesion and, in addition, (c) the so called "neurogenic inflammation". The latter is characterized by algogenic substances release which may move backwards along the sensory nerves and/or be released by the up-regulated mastcells through a neurogenic activation of their de-granulation. A close interaction between mastcells and pain nerve fibers, with reciprocal potentiation, seems to be a key feature of peripheral neuro-pathic pain. As far as the central mechanisms are concerned, wind up phenomenon occurs due to the progressive increase of cellular firing following repeated identical electrical stimuli (6). Also, spinal and supraspinal propagation of abnormal local changes caused by peripheral nervous lesion is responsible for an aberrant central elaboration. In the biochemical field, excitatory aminoacids and NMDA (n-methyl-d-aspartate) receptors play a crucial role in the genesis of chronic neuropathic pain (6).

The dorsal horn of the spinal cord seems to be extremely important in the beginning and maintenance of neuropathic pain. Very recently, Tsuda et al. (7) have demonstrated that activation of p38 mitogen-activated protein kinase (p38MAPK), in spinal hyperactive microglia of the dorsal horn contributes to pain hypersensitivity to innocuous stimuli (tactile allodynia) following peripheral nerve injury. In fact, intrathecal administration of a specific p38MAPK inhibitor (SB203580) suppresses the development of the nerve injury-induced tactile allodynia. Other investigations (8) show that galectin-1 (one of the endogenous galactoside-binding lectins, involved in a variety of functions, such as neurite outgrowth, synaptic connectivity, cell proliferation and apoptosis) increases in the dorsal horn at 1 to 2 weeks after axotomy and that intrathecal administration of anti-recombinant human galectin-1 antibody partially but significantly attenuates the upregulation of substance P receptor (SPR) in the spinal dorsal horn and the mechanical hypersensitivity induced by the peripheral nerve injury. These data suggest that endogenous galectin-1 may support neuropathic pain after the peripheral nerve injury at least partly by increasing SPR in the dorsal horn.

Tissue injury of almost any kind, but especially peripheral or central neural tissue injury, can lead to long-lasting spinal and supraspinal re-organization that includes the forebrain (9). These forebrain changes may

be adaptive and facilitate functional recovery, or they may be maladaptive, preventing or prolonging the painful condition (9, 10). In an experimental model of heat allodynia, functional brain imaging showed that: (a) the forebrain activity during heat allodynia is different from that during normal heat pain, and (b) during heat allodynia, specific cortical areas, specifically the dorsolateral prefrontal cortex, can attenuate specific components of the pain experience, such as affect, by reducing the functional connectivity of subcortical pathways. The forebrain of patients with chronic neuropathic pain may undergo pathologically induced changes that can impair the clinical response to all forms of treatment.

CLINICAL DIAGNOSIS

Neuropathic pain arising from VVS may clinically be associated with a complex regional pain syndrome (CRPS) (6), early recognized as reflex sympathetic dystrophy. Burning pain, tenderness, sometimes itching, psychological involvement are the main complaints of patients suffering from VVS. Persistent vulvar allodynia and hyperalgesia lead to the avoidance of intercourse, which causes dyspareunia (4). In the absence of appropriate treatment pain tends to worsen and widen in the perineal and bladder area.

Patients with VVS have an increased innervation and/or sensitization of thermoreceptors and nociceptors in their vestibular mucosa. In patients with VVS Bohm-Starke et al. (2) found presence of allodynia to mechanical testing with von Frey filaments (14.3±3.1 mN in the symptomatic posterior area as compared with 158±33.5 mN in healthy subjects), as well as to the pain threshold to heat (38.6±0.6°C in patients and 43.8±0.8 in controls); in addition, pain threshold to cold was 21.6±1.2°C in patients whereas cooling down to 6 °C was usually not painful in controls.

The VVS classical definition of Friedrich (11)

about the constellation of symptoms and findings involving, and limited to, the vulvar vestibule that consists of (a) severe pain on vestibular touch or attempted vaginal entry, (b) tenderness to pressure localized within the vulvar vestibule, and (c) physical findings confined to vulvar erythema of various degrees, seems to be always valid only for (a) and (b), since many patients suffering from neuropathic pain may present an apparently normal mucosa without signs of erythema. In fact, according to Bergeron et al. (12) erythema does not appear to be a useful diagnostic criterion; in addition, no active inflammation was seen by biopsies obtained from the vestibular mucosa by analysing cyclooxygenase 2 and inducible nitric oxide synthase (indirect immunohistochemistry method).

THERAPY FOR SEVERE NEUROPATHIC PAIN

A basic therapeutic approach to the VVS is always mandatory (4). Hygienic and behavioural recommendations should be given in order to avoid chronic irritation and maceration of the fragile tissues and improve perineal care. Prevention of yeast's infection recurrences should be maintained with antimycotic oral treatment (4). Food intake should be qualitatively controlled as well, to reduce vestibular irritation during micturition, and to reduce candida's recurrences. Relaxation of the pelvic floor should be obtained through self massage, physiotherapy and/or electromyographic feed-back (13). In fact, treatment of underlying causes but especially of etiologic specific factors (organic and psychologic) must be done before performing an effective anthalgic therapy. The Authors have suggested specific guidelines for management of neuropathic pain due to VVS (Table 1) (14).

As a rule, patients with intractable (to conventional therapy) neuropathic pain from VVS need the 2a (invasive, non-surgical) stage of

Table 1 - Guidelines for management of neuropathic pain due to vulvar vestibulitis syndrome.

Stages of treatment (a multimodal interdisciplinary treatment approach)

1. CONVENTIONAL, NON-INVASIVE

    a. Pharmacological

    b. Electromyographic biofeedback of pelvic floor musculature (13)

    c. TNS (transcutaneous nerve stimulation)

2. INVASIVE, NON-SURGICAL

    a. Peripheral anaesthetic blocks (impar ganglion, sacral nerves, pudendal nerves) (14)

    b. Sacral nerves stimulation by implantable catheters (15)

3. SURGICAL (vestibulectomy)

treatment. The pathophysiologic basis of this approach should be looked for in the histologic alterations of vestibular innervation which appears intraepithelially increased in the mucosa of VVS patients. If chronic aggressive factors can transform a normal mucosa into an altered histologic picture (Figure 1), a correct and ad hoc pathophysiologic treatment with periodic anaesthetic blocks can restore the normal innervation.
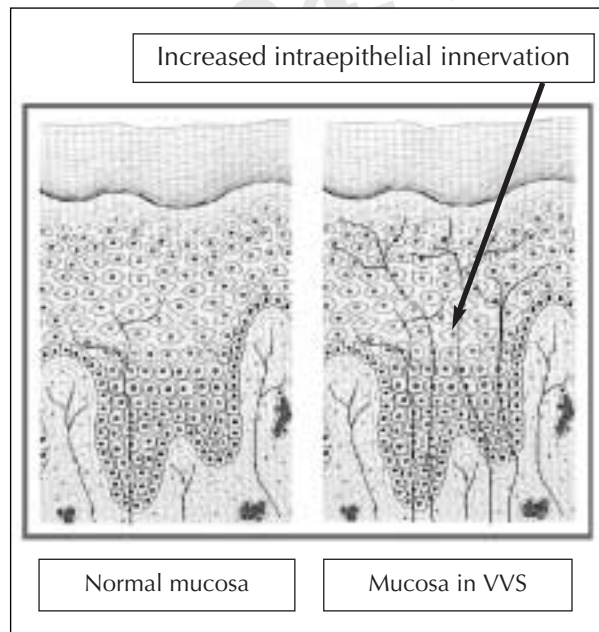

Figure 1 - Schematic pictures of healthy mucosa and mucosa of VVS patients.

The persistent efficacy of nervous block therapy may be explained as follows. The anaesthetic block of specific afferent fibres, especially neurovegetative, from an area involved in neuropathic transmission might induce a progressive self-reduction (neuroplasticity) of the hyperplastic peripheral nervous arborization in the intraepithelial field, with a parallel reduction of the neurogenically induced degranulation of the up-regulated mast-cell. In fact, even a transient but repeated anaesthetic deafferentation should be sufficient to modify an altered (excessive) supply of nervous endings, functionally producing allodynia and hyperalgesia as a result of reduced pain threshold. Therefore, we have employed repeated anaesthetic nervous blocks of the impar ganglion (4, 14) which is the last ganglion of the sympathetic chain, with the task of transmitting sympathetic information to and from the perineal area.

RESULTS

As far as materials and methods are concerned, every session of blocks is currently composed of anaesthetic blocks of sacral nerves, pudendal nerves (through perineal way) and finally the impar ganglion (under the guidance of a finger rectally introduced), which is the main target. Plain 0.25% bupivacaine is used in a total volume of no more

than 30 ml per session. 23G needles from 30 to 90 mm are employed.

The correct use of these anaesthetic blocks has offered a dramatic improvement of the clinical conditions by controlling burning pain immediately (onset time less than 2 min). Following the first sessions of anaesthetic blocks, the duration of pain relief is limited to a few hours or some days. After some months, pain-free time becomes longer and longer up to a duration of some weeks. Within 6 months about 80% of patients affected by intractable pain from VVS obtain persistent pain relief rating more than 90% in comparison with the pre-block period.

In order to offer additional comfort when pain relief by block therapy is still not complete, gabapentin and tricyclic antidepressant (amitriptyline) drugs are utilized. Dosage is adjusted to the principle of minimum effective dose or of the dose allowing acceptable minor side effects.

CONCLUSIONS

The anaesthetic nervous blocks monthly performed in the perineal region, including the impar ganglion, seem to be the most effective answer to women affected by severe neuropathic pain due to VVS and resistant to current non-invasive therapy.

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Vaginismus: A clinical and neurophysiological study

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ABSTRACT. *Former studies on vaginismus failed to prove any specific levator ani's muscular activity that could differentiate it from other conditions such as dyspareunia. Eighteen women, suffering from lifelong, generalized vaginismus of severe degree, were examined with concentric needle electromyographic (EMG) recordings from the levator ani muscle (LA) at rest, during voluntary activation and straining. Fourteen out of 18 (77.7%) examined patients showed an increase in tonic basal activity. In 13 out of 18 patients a correct attempt of straining did not inhibit this basal activity showing, conversely, a paradoxical activation with an increased motor unit potentials firing. This is the first study documenting an abnormally increased basal tonic activity of the LA muscle associated with a lack or reduced ability to inhibit it with straining in vaginismic women.*
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INTRODUCTION

Vaginismus is a controversial sexual disorder (1-3). Most of the controversy depends on its elusive nature (1), the difficulty in substantiating a common physical denominator of the disorders (1, 2), the partial overlapping with dyspareunia (1, 2, 4).

Vaginismus is the leading female cause of unconsummated marriages.

DEFINITION

The fourth edition of the Diagnostic and Statistic Manual of Mental Disorders (DSM-IV-TR) defines vaginismus as "recurrent or persistent involuntary spasm of the musculature of the vagina, which prevents sexual intercourse" (5). The first International

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Consensus Conference on Female Sexual Disorders modified the definition as "Recurrent or persistent involuntary spasm of the musculature of the outer third of the vagina that interferes with vaginal penetration"(6). In a further revision of vaginismus's definition, the "muscle spasms" part was deleted, for the lack of empirical evidence supporting it (2, 3, 7). The last published definition therefore refers to vaginismus as: "The persistent or recurrent difficulties of the woman to allow vaginal entry of a penis, a finger, and/or any object, despite the woman's expressed wish to do so. There is often (phobic) avoidance and anticipation/fear of pain. Structural or other physical abnormalities must be ruled out/addressed" (8).

THE PATHOPHYSIOLOGIC SCENARIO

Vaginismus is a sexual disorder with a spectrum of severity, clinically well described by Lamont in 1978 (9) and unfortunately omitted in the last classifications. Two characteristics contribute to the individual scenario: a) the intensity of the contraction of the levator ani ("perivaginal muscles"), at any attempt of vaginal penetration; and b) the severity of associated phobia, which may be associated to a variable increase of systemic muscular tension and neurovegetative arousal. In the more severe cases, the combination of a tight contraction of the pelvic floor's muscles, with a severe phobic attitude and a parallel systemic arousal – with all the neurovegetative signs it implies – prevents any genital touch and can make the individual vaginismus very difficult to treat. The least severe cases, where the reflex contraction is limited to the moment of the attempted penetration and the phobia is minor or absent, may allow penetration and may indeed overlap with and/or contribute to lifelong dyspareunia. The continuum of sexual pain disorders may therefore have at one end the lifelong severe vaginismus, with a possible (neuro)myogenic component, at the opposite end the acquired transient dyspareunia of variable etiology (like short-living vaginitis, or post-partum dyspareunia which spontaneously resolves when ovulation resumes and estrogens restore vaginal lubrication).

Indeed, although there is a longstanding tradition to distinguish the female sexual pain disorders into vaginismus and (superficial) dyspareunia, recent research has demonstrated persistent problems with the sensitivity and specificity of the differential diagnosis of these two phenomena. Both complaints may comprise, to a smaller or larger extent (2, 3, 7, 8, 10):

a. problems with muscle tension (voluntary, involuntary, limited to vaginal sphincter – pubococcygeus' median fibers and bulbocavernous superficial muscles – or extending to the whole pelvic floor, adductor muscles, back, jaws, or entire body) (9-12);

b. pain upon genital touching, which may be superficially located at the vaginal entry, the vulvar vestibulum and/or the perineum; either event-related to the duration of genital touching/pressure, or more chronic, lasting for minutes/hours/days after termination of touching and/or ranging from unique association with genital touching during sexual activity to more general association with all types of vulvar/vaginal/pelvic pressure (e.g., sitting, riding horse or bicycle, wearing tight trousers) (1-4, 7-12);

c. fear of sexual pain (either specifically associated with genital touching/intercourse or more generalized fear of pain, or fear of sex) (1-4, 7-12);

d. propensity for behavioral avoidance of intercourse, that shows a full spectrum of attitudes, from the maximal avoidance at the extreme end of severe vaginismus to the acceptance of intercourse in spite of coital pain in dyspareunia;

e. co-morbidity with lower urinary tract symptoms (most in dyspareunia) (Graziottin,

this issue) and constipation (more frequent in severe vaginismus), the common pathophysiology being a tighten contraction of the anterior or posterior portion of the pelvic floor.

The only difference that would maintain the separation between the two clinical entities, although in a continuum of clinical presentations, would be the evidence of a spontaneous hyperactivity of the pelvic floor muscles in vaginismus, which was clinically described but previously never substantiated in empirical studies.

AIM OF THE STUDY

Objective of the study was the neurophysiological evaluation of the pelvic floor muscles in lifelong vaginismic women, with a generalized, severe disorder, aiming at documenting the muscular pattern of contraction of their levator ani.

PATIENTS AND METHODS

Eighteen young women were studied at the Department of Neurology, University of Verona, Italy from January 11th 2004 to April 30, 2004. Age ranged from 19 to 47, (mean 32.9±2 DS). They were selected among vaginismic women attending the private office of the first Author (AG), a referral center for dyspareunia, vaginismus and unconsummated marriages. They accepted to undergo this examination, with an informed consent, to test the hypothesis that their vaginismus could be not only "psychogenic" but could have as well a primary muscular component.

Inclusion criteria were the lifelong nature of their vaginismus, its persistence with any partner and in any situation (inclusive of vaginal examination), i.e. a generalized disorder, its severity (4th degree, according to Lamont) and their informed consent to undergo an invasive exam. Other etiologies other than vaginismus, that could have prevented penetration, were excluded. They all

reported unconsummated relationship, 14/18 (77.7%) were married, 4/18 (22.2%) living common law. Duration of the relationship ranged from 2 to 15 years (mean 7±2 DS). No penetration of any kind had ever been accepted. Five patients, fulfilling the above mentioned criteria of severity, were excluded: 2 because their fear of needles would have prevented the neurophysiological exam, 3 because the idea of an invasive exam was unacceptable.

At the clinical history, 15/18 (83.3%) reported comorbidity with constipation (less than 4 evacuation per week). 6/18 (33.3%) comorbidity with lower urinary tract symptoms (LUTS), urgency, frequency, and/or recurrent cystitis (3/18). 2/18 had sexual harassment (genital foreplay) during childhood with no attempts of penetration. 12/18 had already experienced previous psychotherapies of variable duration (from two months to five years, average two years), which failed at curing their symptom. They were all extremely motivated to resolve their problem, mostly for desire of motherhood (14/18). Five preliminary sessions were scheduled, both to initiate a pharmacologic treatment to reduce their phobic response (10) and make them comfortable with commanding the pelvic floor and accepting the contact of the examining hand.

A neurophysiological examination was then scheduled. Concentric needle electromyographic (EMG) recordings from the levator ani muscle (LA), midway between the vaginal fourchette and the anal opening was performed at rest, during voluntary activation and straining in all patients. Unlike peripheral skeletal muscles, the majority of pelvic floor muscles show an involuntary activity at rest in order to maintain a certain tonus. Recruited involuntary motor units fire at low rate and frequency varying with subject changing position. The normal basal tonus is typically inhibited during attempted defecation and then tonus inhibition could be elec-

tromyographically tested by asking patient to strain. Muscle contraction, either voluntarily or reflexively, is characterized by a full interference pattern, with a duration range from 5.5 to 7.5 ms and an amplitude range from 200 to 500 uV.

RESULTS

Fourteen out of 18 (77.7%) examined patients showed a spontaneous increase in tonic basal activity. In 13 out of 18 patients a correct attempt of straining did not inhibit this basal activity showing, conversely, a paradoxical activation with an increased motor unit potentials firing. In all patients during anal sphincter maximal contraction, a full interference pattern was registered by the concentric needle. Motor unit firing was normal and the EMG pattern did not show significant differences with normal women. Polyphasic motor unit potentials were present in a normal percentage. Anal reflex was normal.

DISCUSSION

The current diagnostic criterion of vaginismus, based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR), includes the presence of recurrent or persistent involuntary spasm of the musculature of the outer third of the vagina that interferes with intercourse. However, there are few studies which tried to prove this involuntary spasms, and debate still exists about which vaginal pelvic or vaginal muscle is involved in vaginismus. A recent study (7), in which vaginal/pelvic spasms were tested using intravaginal EMG surface electrodes, during relaxation, sustained and alternate contraction, found no significant differences in muscle EMG activity in patients with vaginismus, dyspareunia or no-pain women. Authors concluded that vaginal/pelvic spasms do not appear to be a critical clue in vaginismus diagnosis.

In our study, in a carefully selected population of women affected by severe vaginismus, an EMG recording with concentric needle from the levator ani muscle, was performed. This is the first study documenting an abnormally increased basal tonic activity of the LA muscle associated with a lack of, or reduced ability to inhibit it with straining. These finding may explain the severity of the vaginismus, its possible neuro(myogenic) etiology, and the co-morbidity with constipation reported by 15/18 of the examined patients. These clinical and neurophysiological patterns seem to be the expression of a generalized pelvic floor involuntary and sustained hypercontraction and dyssynergia, as seen in other neurological conditions characterized by involuntary and sustained muscular contractions due to a wrong motor programming, i.e. focal dystonia, such as writer's cramp or spasmodic torticollis.

We hypothesize that severe vaginismus, and constipation which is reported in co-morbidity, or generally speaking, pelvic floor hypertonia, could derive from an erroneous central motor programming that could be triggered by abnormal sensory input. This may lead to a completely different pathophysiologic and interpretative model.

CONCLUSIONS

This is the first study documenting an abnormally increased basal tonic activity of the LA muscle associated with a lack of, or reduced ability to inhibit it with straining, in women affected by severe vaginismus. These findings may explain the severity of the vaginismus, its pathophysiologic difference from dyspareunia with other etiologies, and the high co-morbidity reported with constipation. Further studies are needed to confirm our hypothesis, which could have important nosographic and therapeutic consequences.

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Role of the pelvic floor in female sexual dysfunction: Diagnosis and treatment

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ABSTRACT. Disorders of the pelvic floor may have an important role in the etiology of female sexual dysfunction (FSD). Urinary incontinence may increase sexual distress and decrease total sexual function. With pelvic organ prolapse, sexual function complaints are more prevalent amongst women with higher grades of prolapse. As corrective pelvic surgery may also affect sexual function and response, it is important to access baseline sexual function including presence of vaginal pain, arousal or orgasmic difficulties, alteration in genital sensation and low libido. All women who present with voiding dysfunction or prolapse should be questioned about their sexual function as well.
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INTRODUCTION

Female sexual dysfunction (FSD) is age-related, progressive, and highly prevalent, affecting 30-50% of American women. While there are emotional and relational elements to female sexual function and response, female sexual dysfunction can occur secondary to medical problems and have an organic basis. The same disease processes and risk factors that are associated with erectile dysfunction in men such as aging, hypertension, cigarette smoking, and hypercholesterolemia, can also be associated with sexual dysfunction in women. Unlike men, many women undergo drastic anatomical changes to their pelvic floor throughout their lifetime as a result of pregnancy, delivery, hysterectomy and menopause. Disorders of the pelvic floor are multifactorial and include stress incontinence, overactive bladder and urge incontinence, pelvic floor prolapse and pelvic pain syndromes. Although there has been a great deal of focus on the role of hormones in the etiology and treatment of FSD, the pelvic

floor may have an equally important role, and as such is the topic of this discussion which includes the following teaching points:
- To review the pathophysiology of female sexual dysfunction due to changes in the pelvic floor,
- To discuss the sexual function complaints associated with disorders of the pelvic floor and the effects of treatment,
- To gain a better understanding of the current clinical research on pelvic floor disorders and female sexual dysfunction.

BACKGROUND – PATHOPHYSIOLOGY

The pelvic floor is a collection of tissues that span the opening within the bony pelvis. In addition to supporting the abdominal and pelvic organs and maintaining continence of urine and stool, the pelvic floor allows for intercourse and parturition. The pelvic floor musculature, in particular, the pelvic diaphragm that is formed by the levator ani muscles, the urogenital diaphragm, and the perineal membrane, is important for pelvic support. The perineal membrane that consists of the ischiocavernosus, bulbocavernosus, and superficial transverse perineal muscles, is closely related to the vestibular bulbs and clitoris, and plays a role in sexual response. These muscles, when voluntarily contracted, can intensify orgasm of both the female and her male partner.

The levator ani muscle has two different parts, the pubococcygeus and the iliococcygeus. These muscles can be palpated during pelvic examination as a distinct ridge just above the hymenal ring along each lateral wall of the pelvis. The function of this group of muscles is to pull the rectum, vagina, and urethra anteriorly toward the pubic bones to compress the lumens closed. Non-voluntary pelvic floor spasm associated with vaginal penetration or even examination with a speculum, is referred to as vaginismus. This disorder prevents sexual intercourse and is associated with dyspareunia and other sexual pain disorders. If the opposite problem exists, consisting of laxity and hypotonia of the pelvic floor musculature due to aging, menopause, or childbirth, for instance, symptoms of vaginal hypoanesthesia, coital anorgasmia, as well as incontinence during sexual intercourse or orgasm can develop. In addition, altered anatomy with changes in vaginal convexity can affect orgasmic capacity and dyspareunia, revealing the importance of vaginal anatomic angles in sexual satisfaction and the need to maintain vaginal axis and depth during surgery. Clearly, women with pelvic floor disorders often have co-existing urologic and sexual dysfunction complaints. Due to this overlap, all women who present with voiding dysfunction or prolapse should be questioned about their sexual function as well.

CLINICAL RESEARCH UPDATE
Urinary incontinence

Studies have revealed a relationship between urinary incontinence and sexual function complaints. Incontinence affects emotional well-being, and is associated with feelings of shame, depression, anger, guilt, loss of self-esteem or preoccupation with urine control (1). A study of patients with stress incontinence found more than 40% had sex life impairment due to their incontinence. Specifically, the respondents reported pain with intercourse and/or incontinence with intercourse and felt that their sex life overall was "spoilt" by their incontinence (2). Loss of urine during intercourse or orgasm, which occurs in up to 24% of sufferers, may be a significant contributing factor to sexual dysfunction. Another study found a significantly higher incidence of sexual dysfunction in patients complaining of idiopathic detrusor instability (3). In a prospective study of patients with urodynamic diagnoses, total sexual function (TSF) score was significantly lower

in patients with detrusor instability (DI) than in those with genuine stress, sensory urge or mixed incontinence (3). Similarly, other studies have found urinary incontinence to impact on sexuality. In one study, symptoms of urinary incontinence significantly correlated with high levels of sexual distress and low sexual desire (4). However, other studies have not found a relationship between incontinence and sexual dysfunction (5). In the past, psychiatric factors were thought to play a causative role in incontinence, specifically in detrusor instability (6). However, more recent research supports that these psychiatric associations may be a result of, rather than a cause, of the disorder.

Pelvic organ prolapse

The precise relationship between prolapse of the pelvic organs and sexuality has not been well documented. The work of Kegel and Graber supports the theory that a nonfunctional pelvic floor impairs the contractions and response of the pelvic muscles to orgasm. Currently, studies are ongoing to evaluate the effects of these disorders on sexuality and response to surgical correction.

Data suggests higher rates of sexual dysfunction in patients with pelvic floor prolapse (7). One study compared sexual function in women with and without uterovaginal prolapse and urinary incontinence. The authors found overall that sexual function in women with prolapse and urinary incontinence did not differ from continent women without prolapse. Age of the population appeared to be the only predictive factor (8). Occurrence of dyspareunia in their sample did not vary significantly with grade of prolapse; however, women with more advanced prolapse were more likely to be symptomatic. Increasing grade of prolapse in this group predicted interference with sexual activity but did not affect frequency of intercourse or satisfaction (8). In another study, comparisons of sexual function in women with urinary incontinence and pelvic organ prolapse were made to determine the effects of therapy on sexual function (9). While prolapse was found to be more likely to be perceived as affecting sexual function, overall sexual satisfaction was found to be independent of diagnosis of, or therapy for, urinary incontinence or prolapse. Of course, these results may be affected by the nature of the study population, as the study subjects were women who chose to be sexually active despite symptoms of prolapse or incontinence. Additionally, women who agree to participate in a study of sexual function may be somewhat different from those who refuse to participate, and this may affect their attitude towards sexual activity.

Pelvic surgery

Pelvic surgery to correct prolapse and incontinence may affect sexual function and response. Hysterectomy has been associated with impaired sexual satisfaction, which may be a result of either destruction of vital nerves in the area of the lower uterus and cervix or removal of organs which contribute to orgasm *via* contraction (10). Dissection of the upper and anterior vaginal wall during sling procedures may affect the abundant nerve fibers that course through this area and have resultant effects on sensation and arousal (11). While pelvic surgery has been found to cause sexual dysfunction, an increase in sexual arousal with episodes of spontaneous orgasm after rectocele repair has recently been reported (12).

Weber et al. evaluated sexual function in women before and after surgery for prolapse, incontinence or both. Eighty-one women who were sexually active before and after surgery were identified. Sexual function improved or did not change for most patients. It was not possible to correlate symptoms after surgery with objective changes in the vaginal anatomy (13). Vaginal dimensions of introital caliber and length

were significantly lower after surgery, although this was not clinically significant. Dyspareunia occurred in 8% of women before surgery and 19% of women after surgery. Pain was most often found in conjunction with posterior colporrhaphy with or without Burch colposuspension.

Some studies suggest that 20% of women have sexual function complaints following surgery for incontinence and prolapse (14, 15). Other studies have demonstrated that pelvic floor surgery involving vaginal dissection produces neuropathy of the pudendal nerve as measured by terminal motor latency. This neuropathy can affect vaginal sensation and orgasm (11). Thus, prior to surgical or medical intervention, it is important to access baseline sexual function including presence of vaginal pain, arousal or orgasmic difficulties, alteration in genital sensation and low libido.

PRACTICAL MESSAGES

- Women undergo drastic anatomical changes to their pelvic floor throughout their lifetime as a result of pregnancy, delivery, hysterectomy and menopause, which can have devastating effects on urologic and sexual function.
- Disorders of the pelvic floor include stress incontinence, overactive bladder and urge incontinence, pelvic floor prolapse and pelvic pain syndromes.
- Urinary incontinence may increase sexual distress, decrease total sexual function, and have a negative effect on emotional well-being overall.
- Pelvic organ prolapse is associated with female sexual dysfunction, with sexual function complaints more prevalent amongst women with higher grades of prolapse.
- As pelvic surgery to correct prolapse and incontinence may also affect sexual function and response, it is important to access baseline sexual function including presence of

vaginal pain, arousal or orgasmic difficulties, alteration in genital sensation and low libido.
- All women who present with voiding dysfunction or prolapse should be questioned about their sexual function as well.

CONCLUSIONS

Women with pelvic floor disorders often have co-existing urological and sexual complaints. These diseases likely affect women's sexual well-being through both physical and emotional effects. Patients who present with these urological problems should be questioned about their sexual function. Surgical treatment in these patients may be curative of some aspects of their sexual dysfunction (e.g. repairing incontinence), but may also have undesired effects on sensation, blood flow and anatomy. This results in disorders of arousal, orgasm or pain. A better understanding of the functional anatomy of the pelvic floor will guide us in a more targeted approach to management of these conditions.

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The clitoris: A unified structure. Histology of the clitoral glans, body, crura and bulbs

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ABSTRACT. *A series of detailed dissections and histological observations were performed on clitoral and bulbar tissues from both fresh and embalmed cadavers. The clitoral body, crura and bulbs all contained cavernous tissue. The clitoral body and crura, but not the bulbs, were invested in a dense layer of connective tissue, which extended to divide the body sagitally. Around the clitoral body, most prominent anteriorly, lay large neurovascular bundles. The glans of the clitoris contained minimal spongy tissue but many prominent nerve trunks. The bulbs were intimately associated with the Bartholin's glands and ducts. Histologically, the clitoral body, crura and bulbs were cavernous structures containing trabeculae of smooth muscle around sinusoidal spaces. Clitoral and penile histology appears to be very similar.*

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BACKGROUND

Recent gross anatomical studies of the clitoris have provided new insight into the structure of the clitoris and the shortcomings of typical illustrations in anatomical textbooks (1). The clitoris appears to be a complex of erectile structures consisting of the corpora, crura and bulbs surrounding the urethra and flanking the distal vaginal wall. We were not able to find a previous report describing and comparing the histology of each clitoral component: bulbs, crura, as well as the corpora and glans.

Greater interest in female sexuality and female sexual dysfunction has been evident in recent years with a significant increase in anatomical investigation in the last 7 years. A number of studies have investigated the clitoris, using modern techniques, with the aim of understanding normal clitoral structure and function. The conclusions of some of these studies, while valu-

able, have been limited by the source material, collected during gender re-assignment surgery, surgery to remove clitoral tumours or from fetuses (2-6). A recent report (7) presented histological findings from a series of 15 fresh cadavers and 3 patients undergoing clitoral surgery. The younger patients whose tissue was analysed had pathological conditions of the clitoris, namely congenital adrenal hyperplasia and genital lymphangioma. The effects of ageing on the clitoral histology were investigated, the majority of the patients being studied having major systemic illness (cardiovascular disease, hepatic cirrhosis, advanced malignancy). In each of these studies, the relationship to normal clitoral anatomy is unclear.

Histological study of the clitoris has been limited typically to investigations of the glans clitoris or the body of the clitoris. Lack of recognition of the clitoral (vestibular) bulbs as part of the clitoris has compounded the issue. Specific investigation of the bulbs has also been limited although a description and diagrams without histological photographs of the related structure, the corpus spongiosum, has been reported (5).

Herein we report on structural and histological studies on a series of fresh and fixed cadavers in whom no clitoral pathology was present. We have compared the histology of the cavernous tissue of each of the clitoral components.

RESEARCH APPROACH

Methodology

Tissue samples were obtained from 11 fresh female cadavers, age range 10 weeks to 51 years. Tissue from two adult embalmed cadavers was also obtained. Ethics approval for this study was obtained from the Institutional review boards of the Royal Melbourne Hospital, Royal Children's Hospital and the Victorian Department of Forensic Pathology.

Tissue taken from fresh cadavers, or cadavers embalmed in 2% formaldehyde in a mixture containing ethanol, glycerol and phenol in saline, was processed for routine paraffin-embedded histology. This tissue was further fixed for a minimum of 24 h in 10% neutral formalin before embedding in paraffin and sectioning at 5 μm. Sections were stained using haematoxylin and eosin.

Results

The clitoris is a tri-planar complex composed of several conjoined structures, the body, crura, glans and bulbs (Fig. 1A). The body up to 4 cm in length comprises paired corpora which lie in the sagittal plane and project externally from the undersurface of the pubic symphysis outward in a curved shaped, convex superficially to reach the glans. The glans clitoris is a superficial structure, projecting as the external tip of the clitoral body. The crura are the internal continuation of the corpora. At the pubic symphysis the corpora bifurcate and then each corpus descends adherent to the ischiopubic rami for up to 9 cm. The bulbs lie ventral to the urethra, and descend on either side lateral to the vaginal introitus on the lateral wall of the distal vagina. They extend posteriorly to a variable extension but always flank at least as far dorsally as the urethra. They are straddled by the crura and lie dorsal to the clitoral body. An extensive connective tissue suspensory ligament secures the clitoris to the labia, fascia of the mons pubis and the pubic symphysis (8).

Figure 1B-F demonstrates the histology of each of the clitoral components. A dense connective tissue sheath, the tunica albuginea, surrounds the body of the clitoris (Fig. 1B-C), which is made up of cavernous sinuses and smooth muscle trabeculae. The tunica albuginea has an incomplete midline septum dividing the clitoral body into two corpora that run in a sagittal plane (Fig. 1C). Superficial to the tunica albuginea lie the ventral clitoral

neurovascular bundles. The bulk of the nerve trunk appears to enter the glans clitoris intact (Fig. 1B) although branching is observed along the length of the clitoral body. Pacinian corpuscles are clearly seen in association with the nerve trunks and in the glans. Large arteries and veins run with the nerve trunks along the length of the body. The cavernous tissue of the clitoral body within the tunica is highly vascular, composed of vascular sinuses surrounded by smooth muscle trabeculae and connective tissue. The sinuses have an endothelium but no obvious smooth muscle in their walls. A moderately large artery (cavernosal artery) is present medially bilaterally in the clitoral body close to the septum. The cavernous tissue and its surrounding tunica albuginea extend into the proximal aspect of the glans (Fig. 1C). The midline septum continues into the glans but the cavernous tissue does not reach the tip of the glans. Hairless thin skin overlies the glans while deep to this is a dense, vascular dermis.

The bulbs of the clitoris are also composed of cavernous tissue. The vascular spaces are larger than those of the body and crura and the trabeculae appear to be thicker than in the other clitoral cavernous tissues (Fig. 1E). Large vascular and neural channels are not a feature. The greater vestibular glands lie between the vaginal wall and bulbs (Fig. 1D). The bulbs are not surrounded by a dense tunica. The bulbs in every specimen examined, and most obviously in the fixed specimens, were a different colour than the other clitoral components i.e. blue-purple versus red, which appears to relate to the presence of the dense capsule overlying the body and crura being absent over the bulbs.

The crura (Fig. 1F) are also composed of cavernous tissue strongly resembling male cavernous tissue. The crura are not completely surrounded by a tunica, it being absent laterally where the crura attach to the bone and where the ischiocavernosus skeletal muscles insert. Large nerve and vascular trunks do not appear within the crura.

PRACTICAL MESSAGES

To achieve orgasm women require either direct or indirect clitoral stimulation (9). Anatomical research including gross and histological studies may help to further knowledge of normal female sexual function and the ways it can be preserved during surgical procedures. Research into female sexual anatomy and physiology is in its infancy though considerable progress has occurred in recent years.

We showed, in agreement with others, the presence of cavernous tissue in the clitoral body and crura. However, while both structures are associated with Pacinian corpuscles, their neurovascular patterns do differ, the body being surrounded by large neurovascular trunks external to the thick fibrous tunica. Baskin (6) observed that the glans is anatomically distinct from the corpora and reported "large bundles that fanned out laterally" on the ventral surface of the clitoral bodies. The cavernous tissue of the bulbs has a different character again, the sinusoids being larger and the trabeculae thicker but without any obvious presence of large neurovascular bundles.

Histological analysis of a series of clitoral specimens of varying ages showed significant changes with increasing age. In the more elderly specimens studied and particularly those with known cardiovascular disease-related mortality, significant fibrosis was observed. This type of analysis may be useful if a simple biopsy technique becomes available for the investigation of female sexual function.

The only other existing histological study of the bulbs and their relationship to the urethra recently suggested an important role in urethral sphincteric function (10). The study also revealed the junction of the bulbs directly caudal to the clitoral body; tissue that van Turnout et al. (5) refer to as the "corpus spongiosum". We were not able to verify that finding with this study, although several of the dissections of cadavers had tissue consistent with this anatomical structure.
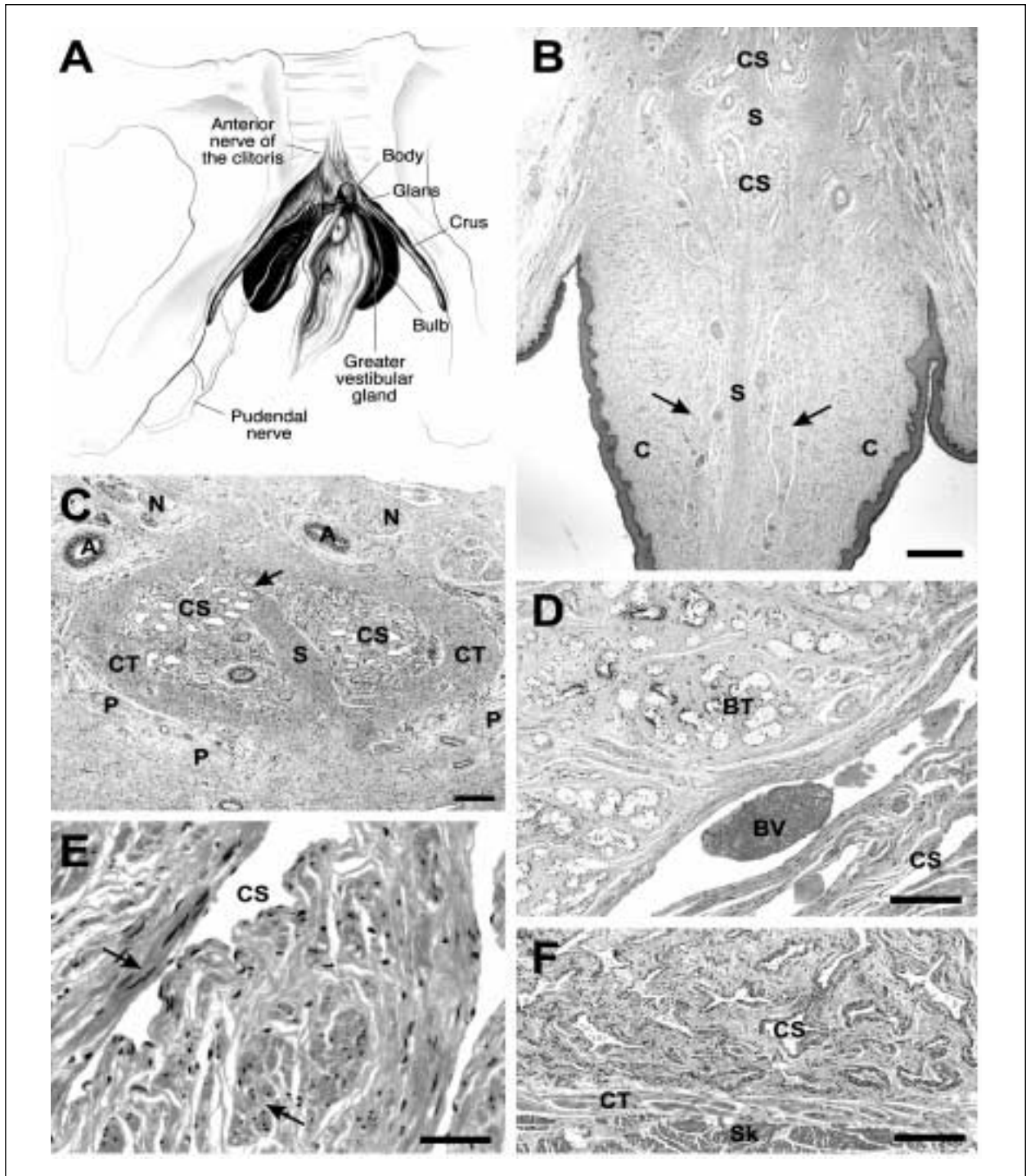
Figure 1 - All micrographs are stained with haematoxylin and eosin.
A. Artist's rendition of anatomy of clitoris from oblique view. This anatomy is based on dissections of fixed tissue and therefore may not truly represent the anatomy in the live state and does not represent the aroused state. It shows the relationships between structures, the approximate size of the anterior clitoral nerves and the structure of the clitoris as a whole including its components: glans, body, crura and bulbs (*Continued*).

Figure 1 (*Continued*) - B. Coronal section through the glans clitoris of a 23 year old. Inferior is to the bottom of the image. The tissue forming the core of the glans (C) is vascular connective tissue, with no sign of the abundant sinuses that characterize cavernous tissue. The only cavernous sinuses visible (CS) are deep to the glans, where the distal part of the body of the clitoris can be seen, surrounded by a layer of dense connective tissue that is also present as a septum (S) that divides the body in two. The septum continues beyond the body into the glans. Note also the major bilateral nerve trunks that are the continuation of the dorsal nerves (arrows). Scale bar= 500 µm.
C. Transverse section through the body of the clitoris from a two year old. Anterior is to the top of the micrograph. The mid-line is slightly twisted due to post mortem compression of the tissue. The body is divided into two corpora by a septum that is incomplete anteriorly (arrow). The tissue of the body consists of prominent cavernous sinuses (CT) with occasional arteries present, surrounded by a thick dense connective tissue layer (CT). Anterior to the body are a pair of prominent arteries (A) and also very large nerve trunks (N) that descend towards the glans. Present in the connective tissue surrounding the body are Pacinian corpuscles (P). Scale bar= 250 µm.
D. Section from the medial boundary of the bulb from an 80 year old showing the intimate contact between Bartholin's gland (BT) and unencapsulated cavernous tissue of the bulbs (CS). Note that a large blood vessel (BV) lies on the boundary between the bulb and Bartholin's gland in this section. The mucous tubules and ducts of Bartholin's gland are embedded in connective tissue located between the bulbs and vestibule of the vagina. Scale bar= 200 µm.
E. Section showing cavernous sinuses (CT) in the bulb. The smooth muscle bundles (arrowed) are cut both longitudinally and transversely in this section. Scale bar= 50 µm.
F. Section of crus from a two year old along the boundary with skeletal muscle (Sk). The cavernous sinuses of the crus (CS) are separated from the skeletal muscle by a layer of connective tissue (CT). The cavernous tissue contains abundant trabeculae of smooth muscle and occasional arteries. Scale bar =200 µm.

Pacinian corpuscles are associated with the body of the clitoris. Pacinian corpuscles are sensory receptors normally associated with the dermis. They are rapidly adapting receptors sensitive to vibration. Krantz (11) has previously commented on their association with large nerve trunks in the female genitalia and reported that they are more prevalent in association with the clitoris than with surrounding skin. In that study, the exact part of the clitoris examined was not described. The presence of Pacinian corpuscles surrounding the clitoral bodies may indicate a role in generating clitoral sensation when the clitoris is engorged. The clitoris is midway in sensitivity between the skin of the fingers and feet in response to a classical vibratory stimulus to assess Pacinian corpuscle sensitivity (12).

The glans is composed of hairless thin skin, a vascular dermis and nerve trunks. The structure of the clitoral body and crura, being composed of erectile tissue and surrounded by a dense fibrous capsule, is likely to result in "erection" when engorged with blood. Thus the term "erectile" appears valid for these structures although word better applies to the pendular structure of the penis than the curved and fixed structure of the clitoris. The bulbs are composed of typical cavernous tissue, but with only a thin capsule. This suggests that during engorgement they are likely to expand and become turgid rather than "erect".

Toesca et al. observed that the clitoral body architecture differs from the penis in having a regular anterior tunical surface with no internal venous plexus (2). This plexus is believed to be required for penile rigidity.

The number of specimens available for study is very limited because of the restrictions on access to tissue for the purpose of human research. In a number of specimens we were only permitted to sample internal tissues, so that structures such as the glans were not accessible for study. In future research accurate delineation of histology from specimens would permit observation of the changes associated with ageing, parity, hormonal and other factors. It should be technically feasible to biopsy the bulbs through the anterior vaginal wall under ultrasound guidance. Biopsy of the bulbs via the labia would be expected to be associated with a significant bleeding risk.

CONCLUSIONS

The corpora, crura and bulbs are composed of cavernous tissue and form an almost completely internal structure. The glans is a densely innervated, non-cavernous structure. The corpora, glans and neurovascular bundles are associated with significant numbers of Pacinian corpuscles, indicating that deep sensation is part of their physiology. On the basis of recent research, clitoral pharmacology and physiology is expected to be very similar to penile tissue.

ACKNOWLEDGEMENTS

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Urge incontinence and female sexual dysfunction: A life span perspective

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ABSTRACT. *Co-morbidity between urological disorders, overactive bladder and urge incontinence first, and female sexual dysfunctions (FSD) is still underdiagnosed in clinical practice, in spite of data indicating an extremely high association between the two conditions. Latent class analysis of sexual dysfunctions by risk factors in women indicate that lower urinary tract symptoms have a RR= 4.02 (2.75-5.89) of being associated with arousal disorders and a RR=7.61 (4.06-14.26) of being associated with sexual pain disorders. Clinical history focusing on prepubertal signs and symptoms of overactive bladder (enuresis, nocturia, daily symptoms) indicate that 2.3% of women currently suffering of urge incontinence do report these early symptoms when actively asked for. Pathophysiological factors underlying co-morbidity between urge incontinence and FSD may begin in early infancy or adolescence. Estrogens may attenuate bladder' vulnerability at puberty. Their loss at menopause may re-trigger bladder overactivity, which remains borderline across the fertile age. Higher clinical and research attention is needed to further substantiate this preliminary finding and improve life-span designed preventive and therapeutic measures.*
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INTRODUCTION

The overactive bladder (OA) is a frequent and underreported condition affecting 11.4 to 17% of women over 40 years, with increasing incidence paralleling increasing age (1). It is characterised by uncontrolled contractions during the bladder-filling phase. Symptoms include an increased frequency of micturition, a strong and sudden desire to void and, if involuntary contraction is not suppressed, urge incontinence (UI).

Co-morbidity between urological disorders, OA and UI first, and female sexual dysfunctions (FSD), is still underdiagnosed in clinical practice, in spite of data indicating an extremely high association between the two conditions. Latent class analysis of sexual dysfunctions by risk factors in women indicate that lower urinary tract symptoms have a RR= 4.02 (2.75-5.89) of being associated with arousal disorders and a RR=7.61 (4.06-14.26) of being associated with sexual pain disorders (2).

Clinical history focusing on prepubertal signs and symptoms of OA (enuresis, nocturia, daily symptoms) well indicate that women currently suffering of urge incontinence do report these early symptoms when actively asked for (3). Pathophysiological factors underlying this co-morbidity may well begin in early infancy or adolescence (4, 5).

Unfortunately, a persisting communication failure still separates the pediatric world from the gynecological/urological one, puberty being a sort of invisible wall that separates the two clinical domains. The aim of this paper is to suggest a life span approach to urge incontinence. This could improve our understanding of different modulating factors (estrogens first) across the life span and incourage a more investigative approach to early pathophysiological factors that may increase co-morbidity between OA/UI and female sexual dysfunctions in adults.

THE EARLY PATHOPHYSIOLOGIC SCENARIO IN OA

2.3% of incontinent adults report to have had urge incontinence and/or nocturnal enuresis in their infancy (3, 6). Unfortunately prospective data on the percentage of girls who continue to display urge incontinence in adult life are scanty (6). In particular, in these patients, information about the so-called "toilet training period" is not available, underestimating the complexity of steps required to achieve the continence skill.

Between 1 and 3 years, the maturation of the cortical inhibitory pathways to the pontine micturition centre parallels the child's ability to increase his/her continence competence. A progress that is mirrored in progressively fewer episodes of leakage. In parallel with the bladder expanding its size and filling capacity, the ability to completely suppress voiding at socially inappropriate times is progressively acquired. The child's perception of this overactivity and his/her understanding of how to suppress it is determined by different factors. They depend on gender (3), individual ability and motivation to control (6), socially determined attitudes about continence (3-7), impulse control (9) and appropriate age to reach it (3-9). Genetically determined factors are increasingly recognized as contributors (10-12). When the cortical pathways between the parietal lobe and brainstem mature, the child finally learns to initiate voiding when the bladder is not full.

If during this "toilet training" critical period coercive methods are used, an overactivity of the external urethral sphincter may result. When a girl experiences urgency during childhood, she may increase the compensatory pursuit of a better continence through the contraction of the levator ani, as an adjunct strong sphincter controller. When active for years in childhood and adolescence, this coping muscular behaviour may contribute to a hypertonic pelvic floor, predisposing the young girl to vaginismus, dyspareunia and constipation (4, 5) with unexpected consequences on the urinary and genital area, considering the contiguity between them. The hypertonic muscle may then become a further contributor of the vicious circle that increases the detrusorial hyperactivity.

In a recent survey on 38 adolescent girls with persistent nocturnal enuresis and diurnal urge incontinence (8), 21% reported lifelong dyspareunia (coital pain) during intercourse, likely due to vaginismus. This disorder indicates the recurrent or persistent invol-

untary spasm of the musculature of the outer third of the vagina, which interferes with vaginal penetration, and which causes personal distress (13). In over 16% of these patients there is a gap between parental sphincter control requests and voiding competence achievement. Constipation was reported in 37%, well addressing the medical comorbidity underlined by pelvic floor dysfunctions. Patients who report a positive clinical history for early pressure to bladder control and/or had former enuresis are at increased risk of developing a transient urgency and frequent urination. Most of them, and women with UI, express a fear of losing urine during intercourse, a concern that may become a humiliating experience when leakage is during the orgasm, in adulthood. Recurrent vaginal and vulvar infection and inflammations may complicate the co-morbidity of a persisting OA and UI in infanthood (4). Recurrence of vestibulitis and vulvovaginitis in girls and adolescents with urge incontinence may be related to an incorrect position of the legs adopted during micturition that gives rise to "vaginal micturition", that would be more appropriate to call "vestibular micturition" (5). Urine may therefore irritate and cause chemical inflammation of the mucosa on the external side of the hymenal opening. The frequent observation in the same girls of a partial fusion of the labia minora (7) may explain the persistency of urine loss during urgency in the vestibular vaginal area and its irritating effect on the delicate vestibular tissue. Mastcell hyperactivation may follow, triggering the up-regulation of local immunitary-inflammatory response (14). Upregulation of the mastcell production of Nerve Growth Factor may precipitate and maintain the shift from nociceptive to neuropathic pain (see Graziottin, and Vincenti and Graziottin, this issue). This complex upregulation of local immunitary and pain-related responses may be a cofactor in the early onset of vestibular pain, even before the first intercourse, predisposing

to vulvar vestibulitis syndrome and associated lifelong dyspareunia (5, 14).

When urge incontinence is associated with nocturnal polyuria, two different symptoms, probably accounted for by different sleep architecture and/or different threshold sensitivity to bladder signals, may be complained of (3, 4, 6-8, 15, 16):
- nocturnal enuresis (NE), when the girl and the woman cannot wake up,
- nicturia when appropriate night awakenings maintain the bladder competence.

A new emphasis on the pathophysiology of nocturnal enuresis has become essential for treating girls with this problem for two reasons, medical and psychosexual (4, 8, 15, 16).

The first one is that NE is not a self-limiting condition as traditionally expected, the prevalence in adult women varying from 0.5 to 2.3%. The second one is that the persistence of childhood enuresis is associated with a maturation delay of basic psychosexual needs: attachment, autonomy, sex identity, self-esteem and self-confidence (17, 18) which may impair adult sexual competence in a complex way. Indeed, feelings of inadequacy and incompetence, depression, loneliness, sadness, shame, anger and aggressiveness, guilty feelings and disappointment with parents, poor perception of locus of control, self limitations like living overnight outside home with friends or schoolmates, the search for perfection as frequent compensatory coping mechanisms, more in girls, are frequently reported (4, 6, 9, 17).

At puberty, the estrogen rise may indeed increase the bladder threshold to increasing filling volumes, acting both as a control enhancer and threshold stabilizer, through central and peripheral mechanisms. It therefore may seem that puberty "cures" the disorder, whilst it is just reducing one of key contributing factors, which remains borderline. This protective "estrogenic window" may show some clinical failures, with reappearance of

Table 1 - Therapy of postmenopausal urogenital atrophy. Efficacy of treatment with 25 micrograms of 17- beta-estradiol applied vaginally twice a week, after 12 months, in a multicentric, randomized, double-blind, placebo controlled study (N=828 treated vs N=784 controls). From (19).

Lower urinary tract symptoms and signs	*p* at 12 months
Dysuria	<0.003
Urinary frequency and nocturia	<0.001
Cystitis	<0.034
Urinary incontinence	<0.002
Urinary atrophy	<0.001

higher frequency and urgency, coherent with the underlying hormonal changes, during persisting amenorrhea in adolescent and/or during the amenorrhea in peurperium. After menopause, the exhaustion of ovarian production of estrogens, deprives women – who suffered from early OA and/or UI – of the estrogen-dependent protective help. Indeed, and in positive, a recently published multicentric, randomized, double-blind, placebo controlled study (level I of evidence) well indicate that 25 micrograms of estradiol applied topically to the vagina twice a week may significantly improve urogenital and sexual co-morbidity (19) (Table 1). They significantly improve bladder capacity, bladder volume at first stimulus and bladder volume at strong need to void, a finding of special relevance as it is documented by cystometry at baseline and after 12 months (Table 2) (19).

The parallel improvement of OA, UI, and the cohort of symptoms – nicturia first – and FSD with vaginal estrogen treatment after the menopause (19) again stresses the importance of a closer attention to the complex pathophysiology of this disorder and the powerful impact different levels of sexual hormones may have on its severity across the life span.

CLINICAL APPROACH

Investigating childhood habits may help to identify a continuity between urge incontinence in girls and women. A well focused case history is mandatory in all women with this disorder. During the interview the doctor should be aware that a number of psychological factor may prevent reporting on this embarrassing topic. Indeed only 1/3 of affected women discuss their problem with a doctor or a nurse. Of these, 2/3 had suffered from OA and/or UI symptoms for two years.

Fear of rejection, shame, embarrassment, loss of self-esteem, all contribute to the difficulty a woman has in consulting her physician and asking for help (17, 18).

Active investigation on the part of the clinician is key in easing communication and avoiding the "collusion of silence" that conceals both bladder and sexual problems in a common denial. Specific questions for a correct assessment are also suggested in order to identify whether the urge incontinence appeared in adult life or was also present in childhood. In case urge incontinence is associated with enuresis or nicturia some more fo-

Table 2 - Improvement of bladder capacity and urgency. Efficacy of treatment with 25 micrograms of 17- beta-estradiol applied vaginally twice a week, on bladder capacity and overactive bladder' symptoms. Multicentric, randomized, double-blind, placebo controlled study (N=828 treated vs N=784 controls). Cystometric evaluation was performed at baseline and after 12 months of treatment. From (19).

Maximal cystometric capacity	from 200 ml to 290 ml, *p*=0.023
Bladder volume at first urgency	from 140 ml to 180 ml, *p*=0.048
Bladder volume at strong need to void	from 130 ml to 170 ml, *p*=0.045

cused questions are asked to complete the picture.

Emotional and sexual intimacy has also to be investigated, as sexual identity, sexual function and sexual relationship may all be crippled by urge incontinence. Up to two thirds of affected women report they are less confident in courting and less willing to start a new relationship. One third prefers not to have orgasm for fear of leakage. More than half report their feeling of being less feminine and less sexually attractive: the smell of urine instead of the "scent of a woman" is difficult to accept for both men and women. Focusing on sexual function, an increasing number of women report a progressive loss of sex drive, more likely when this disorder is complicated by hormonal loss in the menopause. The quality of an intimate relationship may be impaired both in and outside the bedroom and may become a real challenge, particularly for newly formed couples. Even body image may change because of the depressing perception of a "bladder dominated" life.

Last but not least, urge incontinence may affect all dimensions of women's life and self-esteem' basis: few jobs can be sustained when a woman has to leave her place frequently and rush to the toilet to avoid the major humiliating disaster of an urge incontinence episode. Sexual identity, sexual function and sexual relationship may all change for the worse because of troublesome bladder symptoms: a concept that deserves the highest medical attention.

CONCLUSIONS

A life span perspective towards overactive bladder and urge incontinence may prove rich of new inspiration for a better understanding of underlying pathophysiology, to design more effective preventive and terapeutic measures. Increased awareness of complex co-morbidity between urogenital

and sexual symptoms and their modulation by sexual hormones should further encourage physicians to break the "collusion of silence" by actively investigating both OA related symptoms and FSD in every consulting woman. A parallel evaluation of signs and symptoms of urovaginal dystrophy should encourage a pragmatic therapeutic approach to relieve the hormone-dependent component of OA and UI. A detailed interview on the style and timing of toilet training, on the presence of recurrent lower urinary tract infection during childhood, constipation, and/or persistence of nocturnal enuresis over 6 years is mandatory in all adult women with urge incontinence. Indeed, unaddressing dysfunctional voiding habits in childhood and adolescence and associated medical and psychosexual comorbidity may have a wide range of late consequences, impacting on sexuality, quality of emotional intimacy, and overall quality of life.

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