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MANAGEMENT OF SEXUAL PROBLEMS IN WOMEN: THE ROLE OF ANDROGENS

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Please note these guidelines are summarised from the following journal articles (dual publication):

Wylie K., Rees M, Hackett G, Anderson R, Bouloux PM, Cust M, Goldmeier D, Kell P, Terry T, Trinick T, Wu F. (2010) Androgens, health and sexuality in women and men. Maturitas. 67, 275-89 Wylie K., Rees M, Hackett G, Anderson R, Bouloux PM, Cust M, Goldmeier D, Kell P, Terry T, Trinick T, Wu F. (2010) Androgens, health and sexuality in women and men. Human Fertility, 13, 277-297.

Separate guidelines are issued with regard to the management of sexual problems in men.

BACKGROUND

- An active and satisfactory sex life is beneficial for health, but there is often a reluctance on the part of professionals (in primary and secondary settings, including gynaecology, urology, psychiatry and endocrinology) to enquire about sexual symptoms.
- Reduced androgen levels (a feature of ageing in both sexes) may have somatic, psychological and sexual effects, sometimes severe enough to compromise a patient's general well-being or sex life in particular. Androgen replacement is used in the treatment of sexual disorders, in both women and men. The principal androgen is testosterone; its precursors include dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA-S) and androstenedione. Testosterone itself is a precursor of estrogens; in women it is produced by the ovaries and adrenals.
- Health-care professionals need to be careful that they use terms such as sexual 'problems', 'concerns', 'difficulties' and 'dysfunctions' appropriately. Labelling the patient as suffering from a dysfunction may lead to over-medicalisation, whereas classifying a severely distressed patient as having a 'concern' may be equally unsatisfactory.

WOMEN

- The role of androgens in maintaining well-being in women is not fully understood. Between a woman's mid-30s and early 60s, adrenal androgen production reduces by about two-thirds. After a natural menopause, ovarian production continues to a variable degree. After bilateral oophorectomy, ovarian production of androgens and precursor sex hormones is lost.
- Contraceptive and sexual health clinics, cervical screening, postnatal and menopausal assessments represent useful opportunities for patients and clinicians to mention the possibility of sexual problems. Less than 30% of female patients with sexual problems discuss treatments with their general practitioner and only a third of these are likely to accept medication. Fewer than 10% of patients are asked about their sexual health during a routine visit to their doctor. Consideration should be given to routinely asking women if they have any sexual concerns, especially those at high risk. These include women who have premature surgical menopause, urogenital atrophy, depression or a history of sexual abuse.
- Natural and surgical menopause and endocrine disorders that alter estrogen and androgen precursors may affect female sexual function. However, hormones are only one component of the many factors that contribute to normal sexual function in women.
- Biochemistry assays of testosterone are of limited value and are not routinely recommended in women. Assay results will vary with the time of day, and other steroids can interfere with them. Age- and gender-corrected normal ranges are lacking. Testosterone largely circulates bound to at least two plasma proteins, sex hormone-binding globulin (SHBG) and albumin. SHBG levels can fluctuate, and are reduced in obesity and hypothyroidism, and raised in women taking exogenous estrogens, those with hyperthyroidism and women of increasing age.

EPIDEMIOLOGY

- The common sexual disorders in women are categorised as:
 - sexual desire disorders hypoactive sexual desire disorder (HSDD) and sexual aversion disorder (SAD)
 - sexual arousal disorders
 - orgasmic disorder
 - sexual pain disorders dyspareunia, vaginismus and non-coital sexual pain disorders.
- Each of the categories is subtyped on the basis of the medical history, physical examination and laboratory tests as:
 - lifelong versus acquired
 - generalised versus situational
 - of organic, psychogenic, mixed or unknown aetiology.
- The four main categories are not exclusive and can overlap, and one may cause another. For example, dyspareunia is likely to lead to avoidance of sexual activity, and anticipation of pain leads to lack of arousal, loss of orgasm and an increased chance of pain recurring.
- Interest in sex declines in both sexes with increasing age, but this change is more pronounced in women. The prevalence of 'low sexual desire' is around 30%. The figure for sexually related personal distress is lower, at around 20%; it is lowest in elderly women (under 15%), and higher (25%) in middle-aged and younger women. Similarly, the age-stratified prevalence of any distressing sexual problem is highest in women aged 45–64 years (15%), lowest in women 65 years or older (9%), and intermediate in women aged 18–44 years (11%). The prevalence of true HSDD in women is around 10%; the prevalence of arousal and orgasmic disorders is approximately 5% each. Although sexual difficulties are more prevalent in older women, the distress and relationship difficulties they cause are generally greater and more frequent among younger women (the older women are more accepting of these difficulties than are their younger counterparts).

RISK FACTORS

- Risk factors for female sexual dysfunction may be non-hormonal or hormonal (estrogen and androgen deficiency).
- Non-hormonal factors include conflict between partners, insomnia, inadequate stimulation, life stress and depression. Concomitant medical disease such as hypothyroidism or diabetes may also be involved. In addition, sexual problems in the woman's partner for example, loss of libido or erectile difficulties should not be overlooked.
- No level of a single androgen is predictive of low sexual function in women and there appears to be no
 important independent role for androgens in various aspects of sexual functioning. However, postmenopausal
 estrogen deficiency does cause atrophic changes: the vaginal mucosa becomes thinner, and the vulva and the
 vaginal walls become pale and thin and lose their elasticity. Vaginal secretions also decrease, leading to reduced
 lubrication.

• The effect of hysterectomy and oophorectomy on sexual function depends on several factors, such as age, preoperative mental health and preoperative sexual function, the indications for surgery, whether the woman chose to have the procedure, the specific procedure performed and whether or not estrogen was used postoperatively. There seem to be improved psychological well-being and sexual function after hysterectomy for benign disease, but women with depression or sexual problems preoperatively are at increased risk of experiencing a worsening of mood and libido postoperatively.

DIAGNOSIS

- Assessment may be undertaken over several consultations and may involve the use of validated questionnaires, such as the DSDS (Decreased Sexual Desire Screener), BISF-W (Brief Index of Sexual Functioning for Women) or PFSF (Profile of Female Sexual Function).
- The sexual history assessment should cover:
 - localisation of any pain or discomfort
 - current sexual functioning and practices
 - whether there is a disparity of desire between partners
 - whether there are stressors, such as relationship or family problems, exacerbating the problem
 - whether there are sexual problems in the partner
 - whether the woman has a history of physical, emotional or sexual abuse.
- The medical history will consider co-morbid medical conditions that affect sexual desire and arousal, in particular: bilateral oophorectomy, postpartum complications, premature ovarian failure (POF); cardiovascular disease; diabetes; depression; thyroid disease.
- Laboratory testing is indicated to rule out diabetes and thyroid disease. This should include a full blood count, fasting glucose, thyroid function, urea and electrolytes, creatinine and liver function tests. Hormone assays (total and free testosterone levels, SHBG, FSH, LH, prolactin) may be indicated in women with amenorrhoea or oligomenorrhoea to establish a diagnosis. Routine testing of testosterone levels is not recommended.
- In addition, various medications can affect sexual function, such as antidepressants, antipsychotics, antihypertensives, corticosteroids and hormones (including oral contraceptives and hormone replacement therapy).

TREATMENT

- All patients reporting a problem of a sexual nature should be offered the opportunity for psychosexual and/or couples counselling or sex therapy. In addition, pharmacological options are evolving which may form part of the treatment plan alongside any 'talking therapy' recommended to a woman.
- The generalised use of testosterone by women has been advised against, because of inadequate indications and lack of long-term data. However, postmenopausal women who are distressed by their decreased sexual desire and who have no other identifiable cause (e.g. physical and psychosocial factors, medications, bilateral oophorectomy) may be candidates for testosterone therapy. Androgens may also be used by those women who are hypogonadal as a result of pituitary problems in the premenopause. However, women with a SHBG level above 160 nmol/l are unlikely to benefit from testosterone therapy.
- Although there is no consistent correlation between sexual functioning and levels of androgens (free and total testosterone, androstenedione, dihydroepiendrosterone and SHBG) across a wide age range, in some women testosterone therapy can improve sexual desire. In any one woman, changes in androgens may or may not be relevant to her sexual functioning.
- Transdermal patches and topical gels or creams are preferred over oral products because of first-pass hepatic effects documented with oral formulations.
- Monitoring should include subjective assessments of sexual response, desire, and satisfaction as well as evaluation for potential adverse effects.
- The major side-effects of androgens are hirsutism and acne. These are related to both the dose and the duration of treatment but are generally reversible when the androgen is discontinued. No safety concerns with regard to testosterone implants have been reported in the UK. There is, thus, no indication for increased frequency of breast screening. Neither is there a need for increased frequency of cervical cancer screening.
- It is good practice to measure fasting lipid and glucose levels after six months of therapy, if clinically indicated (e.g. by diabetes or hyperlipidaemia). If these are abnormal, a decision should be made regarding to how to improve them. If lifestyle changes or lipid-lowering drugs are inadequate, it may be prudent to consider stopping testosterone therapy.

MANAGEMENT ALGORITHM (WOMEN)

	Yes	No
Proactive enquiry about a woman's satisfaction with her sex life in, for example, contraceptive and sexual health clinics, cervical screening, postnatal and menopausal assessments.		
2. Is distress with some aspect of sexual functioning reported?	More detailed assessment is indicated, possibly involving the use of a validated questionnaire, such as the DSDS, BISF-W or PFSF.	
3. Is the sexual distress associated with a problem secondary to any of the following: a disparity of desire between partners; stressors such as relationship or family problems; sexual problems in the partner; a medical condition; medication?	Advise referral of partner, or advise some form of relationship counselling. Treat primary medical condition. Review medication. Offer follow-up appointment.	If the sexual problem is of a primary nature, the woman should be offered the opportunity for psychosexual and/or couples counselling or sex therapy. Pharmacological options may form part of the treatment plan alongside any 'talking therapy'.

	Yes	No
4. Does the medical history suggest the involvement of a co-morbid medical condition that might affect sexual desire and arousal? Notable examples are: bilateral oophorectomy; postpartum complications; premature ovarian failure (POF); cardiovascular disease; diabetes; depression; thyroid disease. Laboratory testing is indicated to rule out diabetes and thyroid disease.	Treat condition and refer for follow-up.	As above.
5. Is the patient taking any medication that might affect sexual function, such as antidepressants, antipsychotics, antihypertensives, corticosteroids and hormones (including oral contraceptives and hormone replacement therapy)?	Consider if there are alternative medications which may have a different sexual side effect profile whilst maintaining effect	As above.
6. Is the patient a postmenopausal woman distressed by decreased sexual desire and with no other identifiable cause or hypogonadal as a result of pituitary problems in the premenopause?	Offer psychosexual and/or couples counselling or sex therapy. Pharmacological options may form part of the treatment plan.	The generalised use of testosterone by women is not advised.
7. Is the woman's SHBG level above 160 nmol/l?	Testosterone therapy is inappropriate.	The woman may be a candidate for testosterone replacement.
8. If testosterone treatment is initiated for sexual dysfunction, monitor for subjective symptomatic improvement as well as sideeffects such as hirsuitism.		

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Mike Cust - Previous member of P&G advisory board on transdermal testosterone patches

Frederick Wu - FCWW served on advisory boards and acted as consultants for the following companies: GSK, Organon bv, Bayer-Schering Pharma, Ferring, TAP, Eli-Lilly, Proctor & Gamble, Ardana Biosciences, Pierre Fabre Medicaments in the last 10 years. He has been awarded research grants from Organon bv, Bayer-Schering Pharma

Phillip Kell - Worked for Bayer/Prostrakan as an advisor and have done research trials

Geoff Hackett - No conflicts. Occasional speaker for Lilly, Bayer and Boehringer-Ingleheim

Tom Trinick - No conflicts of interest

Pierre-Marc Bouloux - No conflicts of interest

Richard A Anderson – Served on advisory boards for Organon/Schering Plough and Roche

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