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Female Sexual Dysfunction: Principles of Diagnosis and Therapy

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Female sexual dysfunction is a common health problem, affecting approximately 43% of women. Female sexual dysfunction is defined as disorders of libido, arousal, orgasm, and sexual pain that lead to personal distress or interpersonal difficulties. It is frequently multifactorial in etiology, with physiological and psychologic roots. Approaching female sexual dysfunction involves an open discussion with the patient, followed by a thorough physical examination and laboratory testing. Therapy consists of patient and partner education, behavior modification, and may include individualized pharmacotherapy. Ultimately, as awareness and research in the field grows, it is hoped that a better understanding of the physiology and pharmacology of the female sexual response will be achieved.

Target Audience: Obstetricians & Gynecologists, Family Physicians

Learning Objectives: After completion of this article, the reader should be able to list the classifications of female sexual dysfunction, to outline the evaluation of a woman with female sexual dysfunction, and to summarize the various therapies for female sexual dysfunction.

Sexual dysfunction is defined by the World Health Organization as “the various ways in which an individual is unable to participate in a sexual relationship as he or she would wish” (2). Female sexual dysfunction (FSD) is characterized by problems with sexual desire, arousal, orgasm, or dyspareunia that cause personal distress (2).

The advent of new therapies for male sexual dysfunction has led to widespread attention to these problems in women. Patients are becoming more

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comfortable with turning to their physician for assistance with sexual problems. A recent study showed that 42% of women with sexual complaints sought help from their gynecologist. Of those who did not seek help for their problem, 54% stated they would like to (3). Unfortunately, most texts and journals have little information on the subject, and good clinical data are lacking for both diagnosis and treatment. The objective of this review is to provide a framework for the diagnosis and treatment of female sexual dysfunction.

EPIDEMIOLOGY OF FEMALE SEXUAL DYSFUNCTION

Although it is recognized as a widespread health problem, some controversy exists regarding the prevalence of FSD. This may be the result of variation in assessment techniques or an overly broad description of what defines FSD. Prevalence rates in clinic pop-

TABLE 1
Classification of female sexual dysfunction (FSD)* (2)

Disorder	Definition	Potential etiology
Hypoactive sexual desire disorder (HASDD)	Persistent, recurring deficiency of sexual fantasies/thoughts and/or receptivity to sexual activity, which causes personal distress	Menopause, aging, endocrine abnormality
Sexual aversion disorder	Persistent or recurring phobic aversion to, and avoidance of, sexual contact with a sexual partner, which causes personal distress	Trauma, sexual assault
Sexual arousal disorder (FSAD)	Persistent or recurring inability to attain or maintain sufficient sexual excitement causing personal distress	Menopause, surgery, diabetes, neurologic disease, vascular disorder, hypertension
Female orgasmic disorder (FOD)	Persistent or recurrent difficulty, delay in, or absence of attaining orgasm after sufficient sexual stimulation and arousal, which causes personal distress	Muscle weakness, endocrine abnormality, surgery, neurologic disease
Sexual pain disorders Dyspareunia	Recurrent or persistent genital pain associated with sexual intercourse	Inadequate lubrication, atrophy, infections, endometriosis, vestibulitis, cystitis, sexual trauma, abuse
Vaginismus	Recurrent or persistent involuntary spasms of the musculature of the outer third of the vagina that interferes with vaginal penetration and which causes personal distress	
Other sexual pain disorders	Recurrent or persistent genital pain induced by non coital sexual stimulation	

*This table provides a guideline for diagnosis and possible etiologies of FSD and may assist in guiding the management of these disorders.

ulations vary, with estimates in women of 40% to 50% (4,5). Population prevalence data are more scarce. A recent study in Britain found 53.8% of women had a minimum of one sexual problem lasting at least one month over a 2-year period (6).

The most widely cited study is based on the U.S. National Health and Social Life Survey of 1992. This was published in 1999 and evaluated a National Probability Sample of 1749 women and 1410 men, aged 18 to 59 years (1). The authors reported that sexual dysfunction occurs more often in females (43% prevalence) compared with males (31%). Low libido was the most common complaint (51%) followed by problems with arousal (33%) and pain disorders (16%). Increasing sexual dysfunction was noted with younger age (18–39 years), less education, unmarried status, and poor physical and emotional health. Importantly, it can lead to negative relationship experiences and significantly impact quality of life. Unfortunately, this study does not provide information about prevalence rates in women over the age of 59 and does not include in the definition an element of personal distress caused by the dysfunction (1).

CLASSIFICATIONS OF FEMALE SEXUAL DYSFUNCTION

In 1988, The Sexual Function Health Council of the American Foundation for Urologic Disease (AFUD) devised the first consensus-based definition and classification system for FSD (Table 1). The purpose was to create a classification system for FSD that would include psychogenic and organically based disorders. The final system uses the 4 major categories as described in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) and the International Classification of Diseases, 10th Revision, but the definitions of several disorders have been changed to reflect current clinical and research practice and a new category of sexual pain disorder has been added (2). This system is widely accepted by healthcare providers and provides a guideline for diagnosis and treatment (2). The classifications, which may coexist, are subtyped as life-long versus acquired, generalized versus situational, and organic versus psychogenic or mixed (2).

HORMONAL MEDIATORS OF SEXUAL FUNCTION

Estrogens

The precise impact of estrogen deprivation on female sexual function is controversial. In 1966, Mas-

ters and Johnson reported altered sexual function associated with menopause. They described a delay in reaction time of the clitoris, delayed or absent vaginal lubrication, decreased congestion of the vagina, and reduced duration of contractions with orgasm (7). These changes were attributed to declining estrogen levels. Sarrel et al. correlated improved libido and orgasm with replacement of estrogen in postmenopausal women (8). Others have shown improvement in vaginal lubrication, blood flow, and vaginal compliance in menopausal women on systemic estrogen replacement (9,10), but these were not correlated with subjective improvements in sexual function. Additionally, many studies have documented that systemic estrogen alone is insufficient to cure symptoms of sexual dysfunction (11–13).

Androgens

Androgen synthesis in women occurs by the ovary (25%), the adrenal (25%), and tissue sites in the periphery (50%). Dehydroepiandrosterone (DHEA) is produced by the ovaries and adrenals, DHEAS solely by the adrenals. The existence of an androgen insufficiency (AI) syndrome in women has been postulated recently. As yet, normative ranges of androgen levels in women have not been established (14), and insensitivity of many assays to androgen measures hinders the study and diagnosis of this condition (15).

Although there is a gradual decline in testosterone levels starting before the age of 30 and continuing to menopause (16), the postmenopausal ovary remains an androgen-secreting organ (17). Despite this, by the time a woman is menopausal, levels may be half what they were in her 30s or 40s (18). Loss of estrogen levels may exacerbate this deficiency (19). Thus, postmenopausal women are more frequently diagnosed with AI than premenopausal women (18), and most data on androgen replacement is based on this population. Recognized causes that may affect premenopausal women include hypopituitarism, Addison's disease, corticosteroid therapy, ovarian failure or oophorectomy, oral estrogen replacement or oral contraceptive pills and idiopathic (14). Clinical signs of insufficiency include a diminished sense of well-being, persistent unexplained fatigue, and sexual function changes such as decreased libido, sexual receptivity, and pleasure (15). These symptoms are similar to depression and environmental factors, which make it difficult to recognize the diagnosis (20).

EVALUATION

Patients, especially those who are elderly or are bound by cultural convention, are unlikely to volunteer this information without being asked. Often the physician can begin the conversation by commenting on the frequency of sexual problems in the population or associations with diseases or treatments (21). Universality as a questioning technique suggests that the patient is not alone and may be helpful in initiating the discussion. Questions that are open-ended or nondirective are often helpful. Examples include, "Many people in your situation may feel a certain way, I wonder what you think about that?," using listening and silence. Another technique, which may be preferred, is to use a standardized intake form to identify patients with concerns. After identification of a problem, a comprehensive evaluation should be performed. This includes a medical history, psychosocial history, physical examination, and laboratory testing. Often the etiology of sexual dysfunction is multifactorial, with both biologic and psychological factors playing a role. If necessary, the patient may need to schedule a second appointment, because the process can be time-consuming.

Medical History

The medical history should include medical, surgical, obstetric, gynecologic, psychiatric, sexual, and social information. Important factors in sexual function include intimacy, past experiences, level of knowledge, and availability of partner. The impact of the dysfunction on the patient's personal well-being and its significance should be quantified. Sexual orientation may be addressed. Uses of cigarette smoking, alcohol, and/or drugs are important. Overall, general health and well-being are evaluated.

All concurrent medical disorders must be delineated. Psychiatric disease such as depression, anxiety, and other common conditions are part of the differential diagnosis of sexual dysfunction and important comorbidities. Neurologic disease such as multiple sclerosis, spinal cord injury, or diabetes can affect sexual function by impairing both arousal and orgasm (22). Cardiovascular disease has been linked to female arousal disorder as a result of atherosclerosis of the vessels supplying the vagina and clitoris (23). Gynecologic conditions such as endometriosis, fibroids, infections, prolapse, or incontinence should be addressed. Obstetric history, specifically related to previous operative delivery, tears, or episiotomy, may outline sites for potential denervation or dyspa-

TABLE 2
Some medications with sexual side effects (28–30)

Medication	Mechanism of action	Sexual side effects
Antihypertensives	Effects on sympathetic and vascular system, dose-dependent Uncertain Uncertain, may be effect on vascular smooth muscle	Diminished libido, ejaculatory dysfunction Sexual dysfunction unspecified, ejaculatory dysfunction Impotence, impaired ejaculation, decreased libido
Beta-blockers		
Alpha-blockers		
Diuretics		
Psychotherapeutic agents	Anticholinergic side effects Seritonergeric effects In conjunction with benzodiazepines Increased prolactin levels and testosterone antagonism	Impotence Diminished desire, arousal, orgasm Erectile dysfunction Erectile dysfunction, priapism
Tricyclic antidepressants		
Selective serotonin receptor inhibitors		
Lithium		
Neuroleptics		
Anticonvulsants	Affect cytochrome P-450 pathway and increase metabolism of androgens	Sexual dysfunction unspecified
Carbamazepine, phenytoin, phenobarbital, primidone		
Hormonally active agents	Effects on estrogen and androgen levels	Decreased libido, sexual dysfunction unspecified
Oral contraceptives, antiestrogens, antiandrogens, estrogens	Presumed the result of gonadal suppression	Sexual dysfunction unspecified
Chemotherapeutic agents	Possibly the result of antiandrogen effect	Impotence and painful erections
Gastrointestinal agents		
Cimetidine, ranitidine, famotidine, omeprazole		
Cardiovascular agents	Uncertain Decreased testosterone levels, increased estrogen levels, related to sex hormone-like structure	Diminished libido, erectile dysfunction Erectile dysfunction
Lipid-lowering agents		
Digoxin		

reunia. A history of pelvic trauma or injury (eg, motor vehicle collision) may be an important etiology for diminished sensation or pain.

Previous surgery should be ascertained. The effects of pelvic surgery on sexual function are controversial. Although most reports suggest improvement of sexual function after hysterectomy (24,25), there are some patients who report diminished sensation, impaired lubrication, and vaginal changes postoperatively. Removal of the ovaries may lead to FSD secondary to estrogen or androgen depletion. Certain surgical repairs such as Burch bladder suspension with posterior colporrhaphy may be associated with increased rates of dyspareunia postoperatively (26). Postoperative vaginal stenosis, although rare, may result from levatorplasty at the time of posterior colporrhaphy or aggressive trimming of the vaginal mucosa at the time of colporrhaphy and result in dyspareunia or apareunia (27).

Several medications may impact libido, arousal, and orgasm (28–30) (Table 2). Attention should be paid to these as possible contributors to sexual dysfunction. However, available information on sexual side effects often minimizes these consequences, and accurate incidence data is difficult to obtain (31). Much of the available information is based on data from male subjects, and it is unknown whether dysfunctions noted in males will also exist in females.

Psychologic History

The physician must establish the nature of the disorder. Several validated instruments are available for assessment of sexual function. These produce scores and delineate the source of the problem with questions that address libido, arousal, orgasm, pain, and relationship factors. The results provide a baseline to follow response to intervention. Examples include the Brief Index of Sexual Function for Women, the Female Sexual Function Index, and the Sexual Distress Scale (32,33). The Female Sexual Function Index (www.fsfi-questionnaire.com) is easy to use, relatively short, and validated based on DSM-IV diagnoses of arousal disorder, orgasmic disorder, and hypoactive desire disorder (32,34).

Lastly, it is important to try to screen patients for the need for psychotherapy in conjunction with medical treatment. Relationship problems and potential stressors should be outlined. Concurrent psychiatric diagnoses should be delineated (eg, depression, anxiety, anorexia). A history of sexual assault or trauma is a potential contributor to sexual dysfunction. Patients with these features should undergo assessment

by a therapist who can address sexuality issues for potential treatment.

Physical Examination

On physical examination, attention should be given to assessing the external genitalia, including the clitoris and vestibular glands. The pelvic floor should be examined and any evidence of prolapse or pelvic floor disorders evaluated. The strength of the pelvic muscles can be graded based on degree of contraction during pelvic examination. Neurologic screening should be performed to assess sensation. Signs of atrophy or infection should be noted.

If the patient complains of pain, it is important to try to reproduce the complaint. Pain mapping may be achieved using a cotton swab on the vestibule. While the labia are held apart, the vestibule, vulva, hymen, and minor vestibular glands are touched gently with the swab. Tenderness and erythema may suggest vulvar vestibulitis, which may require treatment (35). An assessment of the levator muscles for spasm and pelvic organs for masses or tenderness can be performed by a digital internal examination. At this time, the presence of vaginismus may also be noted as an involuntary contraction of the outer third of the vagina, which may be severe enough to preclude speculum insertion. Episiotomy scars and previous surgical incisions may be sites of tenderness as a result of vaginal narrowing, scarring, or nerve entrapment.

Laboratory Assessment and Specialized Testing

Laboratory studies may be performed if a hormonal deficiency is suspected. If menopausal status is uncertain, estradiol, follicle-stimulating hormone, and luteinizing hormone may be obtained. DHEAS reflects adrenal androgen secretion and may highlight an adrenal insufficiency. Thyroid-stimulating hormone may identify a thyroid dysfunction. Assessment of androgen production can be obtained with measures of total and free testosterone, total testosterone and sex-hormone binding globulin (SHBG), or free testosterone and SHBG (14). Androgen levels are highest in the morning and middle third of the menstrual cycle (days 8–18) and should be measured at these times, if possible (36). Because of the paucity of research on normal levels of androgens in women, levels in the lowest quartile are thought to require treatment in patients with clinical signs of AI (14). In addition, a complete blood count, liver func-

tion tests, and lipid profile may be helpful, especially if treatment with medications is anticipated.

Specialized diagnostics such as duplex Doppler ultrasonography, vaginal pH measurements, and vaginal/clitoral sensory perception thresholds are not widely available and require expensive equipment (30). Although useful for study purposes, this equipment is not essential to evaluate and diagnose patients with sexual dysfunction.

Once the history, physical, psychologic interview, and diagnostic testing are complete, the patient should return to the office for discussion with or without her partner. Using the AFUD classification system (Table 1), she may fall into 1 or more categories (ie, libido, arousal, orgasm, or pain disorders). It is important to ascertain the most distressing symptom because complaints often overlap. At this visit, therapeutic options may be addressed.

THERAPY

General

An open discussion should take place with the patient and her partner. Patient and partner education about the diagnosis and physiological basis is important, and goals and expectations of treatment should be established. Patients should be educated that not having orgasms with each sexual encounter does not mean that the experience was a failure, and clitoral stimulation may be more likely to lead to orgasm than coital intercourse (37). Behavioral modification and nonpharmacologic therapies are the first emphasis.

Patients may begin by informing themselves about their situation. Reading books or articles about sexual function can establish that others have had similar experiences and may validate patients' feelings. Experimentation with different sexual practices and encouraging women to familiarize themselves with their anatomy may be helpful (37). Lifestyle changes are also important. Modification of known risk factors such as hypertension, hyperlipidemia, diabetes, cigarette smoking, or drug and alcohol abuse is part of the treatment process. Exercise, a healthy diet, and adequate sleep will promote physical and sexual well-being.

Intimacy is a powerful motivator in the female sexual response. Women often initiate sexuality to enhance emotional closeness, and this impetus may drive libido. Further willingness to experience arousal arises from the need to increase intimacy (38). Lack of intimacy may need to be addressed as

a contributor to FSD. Often patient and partner counseling can improve communication and reduce relationship strains, if present.

Topical lubricants and vaginal moisturizers aid with vaginal dryness and dyspareunia and must be emphasized. Medication adjustments may be helpful. Antidepressants, in particular, are a common medication that may have a negative impact on libido and arousal. Strategies to manage antidepressant-induced sexual dysfunction include initiating treatment using an antidepressant with a favorable profile (bupropion, nefazodone) (29,39), waiting for adaptation, reducing the drug to the minimally effective dose, switching to another antidepressant, drug holidays, and pharmacologic antidotes (39). There has been some reported success with sildenafil treatment of selective serotonin reuptake inhibitor (SSRI)-associated sexual dysfunction (31,39,40). Another option is to add bupropion or buspirone (31,41). Switching antidepressants to one with a favorable sexual side effect profile like bupropion or nefazodone may be effective in alleviating complaints and treating depression (42), but it is possible for a reduced antidepressant response to occur (31).

Many experts feel that clinicians should start with estrogen replacement when treating domains of FSD in postmenopausal patients (14,43). However, studies have documented that systemic estrogen alone is insufficient to cure symptoms of sexual dysfunction (11–13). Additionally, estrogen treatment increases SHBG levels and depletes levels of bioavailable testosterone, potentially exacerbating androgen insufficiency. Recent shifts in attitude to estrogen replacement have led to reluctance of patients to start treatment unnecessarily. Therefore, for complaints of dyspareunia resulting from atrophy (burning, dryness, and soreness), our clinic uses a vaginal preparation (cream, tablet) with limited systemic absorption (44). In menopausal patients with diminished libido or orgasm, systemic estrogen replacement is used before or in conjunction with androgens. Appropriate counseling of the patient regarding risks and benefits of treatment is a prerequisite to starting therapy.

Hypoactive Sexual Desire Disorder

Androgen replacement in women is a controversial topic. Although studies have documented an association between androgen replacement and improvement in sexual desire, large quality trials with long-term follow up are needed. Shifrin and colleagues

demonstrated women who underwent surgical menopause with hysterectomy and oophorectomy and on systemic estrogen had improved sexual function and psychologic well-being after treatment with 300 μg transdermal testosterone (11). However, there was a strong placebo response in this study, and many subjects had evidence of borderline high androgen levels. Lobo and colleagues evaluated postmenopausal women to assess effects of 0.625 mg oral estrogen with or without 1.25 mg methyltestosterone on hypoactive sexual desire. At the 16-week follow up, therapy with methyltestosterone increased bioavailable testosterone and improved sexual interest/desire, and frequency of sexual interest/desire in most subjects (13). Other studies have shown a correlation with low androgen levels and decreased libido in both pre- and postmenopausal subjects (45). DHEA supplementation in these subjects improved sexual dysfunction (46).

Patients who have symptoms of androgen insufficiency (diminished sense of well-being, persistent fatigue, sexual function changes) and have low levels of serum-free testosterone may be offered replacement. It is important to inform patients that the majority of androgen replacement therapy is “off-label” and not U.S. Food and Drug Administration (FDA)-approved. Most of the available data is based on short-term studies and long-term safety and efficacy are unknown. Therapy should be performed under close physician supervision. As stated earlier, levels in the lowest quartile are thought to require treatment as a result of insensitivity of the assays at lower ranges and paucity of research on normal levels of androgens in women (14). Early effects of androgen therapy include acne and hirsutism, with a recent study reporting a 2.9% increased rate of acne in the testosterone therapy group (13). Long-term side effects such as male pattern baldness, voice changes, and hypertrophy of the clitoris are infrequent within normal androgen ranges. Androgen therapy may adversely affect the lipid profile, and knowledge about long-term effects on cardiovascular risk is unknown (20). Potential benefits of androgens include increased muscle mass and stimulation of bone formation (47,48) as well as improvement of hot flashes. After initiation of therapy levels of androgens, lipids and liver enzymes should be performed at 1- to 2-month intervals (16). Restoration to the upper half of the normal range is necessary to ensure a good therapeutic response (46).

The majority of testosterone preparations are not well studied in women, and many are not approved for use in North America. Currently, the only FDA-approved testosterone preparation for women is

TABLE 3
Therapy for arousal disorder

Medication/therapy	Mode of delivery	Data available	Negative effects	Cost	Available
L-arginine: ArginMax	Oral	Ito et al., 2001 (51)	Potential systemic effects	Approximately \$35/month	Online, no prescription needed
L-arginine: Vigel, Viacreme, Femore, Sensua	Topical	No published studies	Local irritation	Approximately \$4.00/application	Online, no prescription needed
L-arginine plus yohimbine	Oral	Meston, Worcester, 2002 (61): improvement with L-arginine plus yohimbine in objective arousal	Unknown	Unknown	Under development
Zestra for women	Topical	Ferguson et al., 2003 (52)	None	Approximately \$3-4/use	Online, no prescription needed
Alprostadil: Femprox	Topical	Islam et al., 2001 (53)	Local itching, burning, soreness	Unknown	Under development
Avlirmil	Oral	No published studies	Potential systemic effects	Approximately \$30/month	Online, no prescription needed
Sildenafil	Oral	Kaplan et al., 1999 (54) Caruso et al., 2001 (55) Basson et al., 2002 (56) Nurnberg et al., 2003 (40)	Potential systemic effects, contraindications with heart disease	Approximately \$90/10 tabs	Prescription required
Eros therapy	Mechanical therapy	Billups, 2002 (58) Billups et al., 2001 (59) Wilson et al., 2001 (60)	Local irritation	Approximately \$350 cost of device	Prescription required

methyltestosterone combined with esterified estrogen, suitable only for postmenopausal patients. It is also possible to have a pharmacist compound methyltestosterone tablets in 1.25-mg and 2.5-mg strength for patients who do not want to have estrogen replacement. Phase II trials are being carried out for a testosterone gel for use in women (49), and a testosterone patch is likely to be available in early 2005.

DHEA is an intermediate in the biosynthesis of androgens. It is available as a nutritional supplement. This is not FDA-regulated and quality of formulations vary (50); hence, follow-up androgen levels are required approximately 6 weeks after medication adjustments. A proposed initial dosage is 50 mg daily but may be modified based on androgen levels and side effects. Reported improvements in libido, arousal, and orgasm have been found in patients with low androgen levels before treatment (46,47); however, these are small studies and not placebo-controlled. Thus, long-term risks and benefits are unknown. This may be an option for patients who are premenopausal who do not require estrogen replacement. For postmenopausal patients presenting with androgen insufficiency, our clinic begins with estrogen and methyltestosterone with additional DHEA supplementation as needed. In premenopausal patients, we generally begin with DHEA at a dose of 50 mg and monitor patients' androgen levels and side effects. Appropriate patient counseling about the experimental nature of the therapy is essential before initiating treatment.

Female Sexual Arousal Disorder

Treatments for female sexual arousal disorder (FSAD) have received much attention, and various formulations are available without a prescription that have undocumented safety and efficacy for FSD (Table 3). Therapies that report benefits often base their claims on small studies with short-term follow up. Similar to therapies used in males for erectile dysfunction, many of these focus on increasing blood flow as a mechanism for improving sexual arousal. However, in women subjects, improved blood flow, lubrication, and engorgement do not necessarily correlate with improved subjective arousal.

L-arginine is a precursor in the formation of nitric oxide, a mediator of vaginal and clitoral smooth muscle relaxation. ArginMax (Daily Wellness Co., Sunnyvale, CA) is a daily nutritional supplement containing L-arginine, ginseng, ginkgo, damiana, calcium, iron, and several vitamins. A recent study evaluated 77 women, 34 treated with ArginMax and

43 with placebo. Findings were improved sexual desire, satisfaction, frequency of orgasm, and clitoral sensation in 4 weeks in the treated group (51). Systemic long-term side effects are not known.

Topical L-arginine is marketed widely for treatment of arousal disorder. Several over-the-counter topical creams have been developed. They are designed to be applied to the vulva before sexual activity. Often these contain menthol, which may be irritating to the patient. There are no published studies on the effectiveness of these treatments and side effects are unknown.

Another topical agent is Zestra for Women (Qualilife Pharmaceuticals, Charleston, SC) marketed as a feminine massage oil. The ingredients are borage seed oil, evening primrose oil, special extract of angelica, special extract of coleus, and the antioxidants ascorbyl palmitate, alpha-tocopherol, and natural fragrances. Approximately 0.4 to 1 mL is to be applied to the vulva before activity. A study of 20 women showed improvement in level of desire, arousal, sensation, pleasure, and ability to have orgasms in both normal and FSAD patients using Zestra compared with placebo (52).

Topical alprostadil (PGE₁) is a vasodilator being developed by NexMed (Femprox; NexMed, Robbinville, NJ). A similar substance is marketed for use in males. A study of 8 women showed improved subjective and physiological arousal compared with placebo. Adverse events included vaginal itching, burning, and soreness (53). The product is still in phase II trials (49).

Avlimil (“salvia rubus”; Warner Health Care, Inc., Cincinnati, OH) is a once-daily tablet for treatment of FSD that has been marketed in women’s magazines and television. The ingredients include sage leaf, red raspberry leaf, kudzu root extract, red clover extract, capsicum pepper, licorice root, bayberry fruit, damiana leaf, valeriana root, gingerroot, black cohosh root, and some stabilizers. A study published on the web site cites improvements in desire, arousal, and orgasms with Avlimil compared with placebo; however, this is not published in a peer-reviewed journal. Systemic side effects are possible as well as potential interactions with other medications.

Sildenafil is a selective type 5 phosphodiesterase inhibitor, which decreases the metabolism of cGMP, the second messenger in NO-mediated relaxation of clitoral and vaginal smooth muscle. Currently, it is only approved for use in males. Results of studies in women have been conflicting. Kaplan and colleagues evaluated 33 postmenopausal women with FSD treated with sildenafil. Of these, only 21% had a

significant response, similar to the 25% placebo response rate seen in studies done on males (54). Caruso et al. studied 53 premenopausal women in a double-blind, crossover, placebo-controlled study. Improvements were noted in arousal, orgasm, enjoyment, frequency of intercourse, and fantasies with sildenafil, and 70% were willing to continue treatment (55). Most recently, a randomized, controlled trial of 781 women showed no significant effect on subjective assessment of lubrication, sensation, or sexual enjoyment with sildenafil in women with sexual arousal disorder (56).

The conflicting data suggest that sildenafil does not clearly benefit women with FSAD. The female arousal response is complex. Women are not always aware of changes occurring in their genitals or do not equate these changes to improved arousal. Basson et al. postulate that women who may benefit from sildenafil include those with absent genital engorgement rather than absent subjective arousal (56).

Tibolone is a synthetic steroid with estrogenic, progestogenic, and androgenic properties. It is not currently available in the United States but has been used in Europe for 20 years. Studies have suggested a positive effect on sexual function with use (57). This may be a future option for treatment of FSD, and a randomized, controlled trial is currently being conducted (57).

The Eros Therapy (Urometrics Inc., St. Paul, MN) is the first FDA-approved nonpharmacologic device for treatment of female sexual dysfunction. It is a battery-operated handheld device, which is placed over the clitoris. The device provides a gentle adjustable vacuum suction and a low-level vibratory sensation. It is designed to be used 3 or more times a week for approximately 5 minutes at a time. Use of the Eros Therapy has been shown to increase blood flow to the clitoral area as well as to the vagina and pelvis (58). Small nonblinded studies have shown it may significantly improve arousal, orgasm, and overall satisfaction in patients with sexual arousal disorder (59,60). The treatment provides an alternative for patients who want to avoid use of pharmacologic agents or hormonal therapy.

Orgasmic Disorder

Therapy for orgasmic disorder may be the most challenging for the physician. It is important to document whether the disorder is primary (never had an orgasm) or secondary/situational. Primary anorgasmia is the most difficult to treat and often requires referral for sex therapy. Patients should be encour-

aged to explore self-stimulation if not already done so, with or without a vibrator. Laxity of the pelvic floor muscles may be an etiology for weak or absent orgasms and may improve with pelvic muscle exercises or biofeedback. Hormonal replacement with estrogens or androgens can improve orgasmic dysfunction in patients with deficiency. Patients may also benefit from the Eros Therapy or Zestra (52,58–60).

Sexual Pain Disorders

Psychologic stress and relationship issues often result from pain. There is a cascade of responses from initial pain experience to anticipation of subsequent pain, sexual avoidance, untoward relationship effects, and development of additional sexual dysfunction. The location of the pain, either with entry or deep penetration, provides information of the etiology. Entry pain is associated with vestibulitis, vaginal dryness, or atrophy, whereas deep pain may be secondary to endometriosis, levator spasm, and other causes. Often, a history of sexual trauma may be elucidated.

Cognitive behavioral therapy and couples therapy play a role in treatment. If possible, any etiology for pain should be treated. Pelvic floor physical therapy assists with levator spasm; vaginal dilators are a method of desensitization that may help with vaginismus. Overall, diagnosis and therapy of vulvar and pelvic pain is complex and involves multiple modalities, which are beyond the scope of this discussion.

CONCLUSION

Female sexual dysfunction is multifactorial and highly prevalent disease, affecting a large number of women. Recent media attention to therapies like sildenafil has led to increasing patient awareness and a desire to seek help from their physician. Despite this, many physicians fail to acknowledge FSD as part of the medical history, possibly as a result of lack of time or insufficient training. It is necessary to have a framework for diagnosis and treatment. A collaborative and comprehensive evaluation, patient and partner education, behavior modification, followed by individualized pharmacotherapy in select patients should be the standard management of women with sexual dysfunction. Ultimately, as research in the field progresses, a better understanding of the physiology and pharmacotherapy of FSD will be attained.

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