Female Sexual Dysfunction

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KEYWORDS
- Female sexual dysfunction
- Hypoactive sexual desire disorder
- Testosterone therapy
- SSRI-induced sexual dysfunction
- Atrophic vaginitis

KEY POINTS
- Ask patients about their sexual health and explore their concerns: broad categories of female sexual dysfunction include decreased desire, difficulty with arousal, delayed or absent orgasm, and pain with intercourse.
- Evidence supports the use of topical testosterone to treat hypoactive sexual desire disorder; although the magnitude of the benefit was small, there is a lack of long-term safety data, the studied testosterone replacement preparations are not available in the United States, and it is not approved by the Food and Drug Administration.
- Selective serotonin reuptake inhibitor–induced female sexual dysfunction can be treated with addition of bupropion or use of sildenafil.
- Topical estrogen is the most effective treatment for atrophic vaginitis, which is a common cause of pain with intercourse.

INTRODUCTION
The topic of female sexual health and dysfunction is a challenging one for health care providers. Discomfort with the topic, inadequate training, and insufficient clinical time with patients to discuss in-depth sexual histories and limited treatment options hinder providers’ desire to address this issue. Academically, before the 1950s, this topic was rarely discussed. In the 1950s, Kinsey\textsuperscript{1} introduced landmark literature addressing the sexual lives of women and their sexual practices in the United States. In the 1960s, Masters and Johnson\textsuperscript{2} introduced a model of the female sexual response cycle, defined as the linear progression of 4 distinct physiologic phases, including excitement, plateau, orgasm, and resolution (Fig. 1). In the late 1970s, Kaplan\textsuperscript{3} modified...
this to a 3-phase model, including desire, arousal, and orgasm. In both of these genitally focused models, orgasm was considered essential for sexual fulfillment and the importance of intimacy and the emotional aspects of sexuality were not addressed. Basson\(^4\) significantly modified this linear model of female sexual response. She proposed a cyclical model incorporating intimacy, relationship satisfaction, and sexual stimuli. In Basson’s model,\(^4\) the stages of female sexual functioning occur in a nonlinear fashion and orgasm is not essential for sexual fulfillment (Fig. 2).

It is important to realize that the Diagnostic and Statistical Manual of Mental Disorders-IV-text revision (DSM-IV-TR) criteria for female sexual dysfunction is based on the traditional linear model, which we have learned may not represent the most accurate pattern of sexual functioning for most women.\(^5\) However, many women still believe normal sexual functioning to be the traditional desire-arousal-orgasm process. As a provider, some brief education about alternative theories and the importance of intimacy and emotionality and not just orgasm can go far in decreasing women’s distress about their sexual health.

Not surprisingly, numerous biopsychosocial factors impact sexual function. Multiple medical and mental health conditions and medications can impact sexual health.

Fig. 1. Traditional sexual response cycle. (From Basson R. Female sexual response: the role of drugs in the management of sexual dysfunction. Obstet Gynecol 2001;98(2):351; with permission.)

Fig. 2. Cyclical sexual response cycle. (From Basson R. Female sexual response: the role of drugs in the management of sexual dysfunction. Obstet Gynecol 2001;98(2):351; with permission.)
Family and cultural beliefs, early sexual experiences, partner relationship, and external stressors also play a strong role. Exploring these issues with patients may reveal modifiable obstacles to sexual fulfillment through better disease management, medication changes, mental health treatment, and discussion around personal and cultural beliefs or counseling.

As providers, we should bring up the topic of sexual health because only approximately 18% of women with sexual concerns will spontaneously volunteer information about sexual dysfunction to their doctor. Simple screening questions could include the following: “Sexuality is such an important part of our overall health. I would like to ask you some questions about that now. Is that okay with you?” “Are you currently sexually active?” “With men, women, or both?” “Do you have any concerns about your sexual health?” Based on her responses, clinicians should further tailor their questioning around areas of concern. In 2000, the Female Sexual Function Index (FSFI) was developed for use in research. It is a brief, 19-item, multidimensional self-report instrument that assesses key dimensions of desire, arousal, lubrication, orgasm, satisfaction, and pain. Although it is validated for use in research, it is not yet used in clinical practice. However, the questions are quite useful and may be helpful to clinicians in obtaining a more comprehensive sexual history. How to interpret FSFI scores in the clinical setting has yet to be determined, but the individual responses to each question may be very informative when evaluating a sexual complaint.

To meet criteria for a diagnosis of female sexual dysfunction, symptoms must be recurrent or persistent and they must cause significant personal distress. Sexual complaints are common and occur in approximately 40% of US women with 12% to 22% of those reporting personal distress related to their sexual issue. The next step is determining whether it is a primary or lifelong issue, or a secondarily acquired problem. Understanding whether their problem is more generalized or situational is also important.

The classification of female sexual dysfunction (FSD), based on the DSM-IV-TR criteria, falls under the 4 categories of desire, arousal, orgasm, and pain. The most common disorders are related to desire. Desire disorders include hypoactive sexual desire disorder (HSDD) and sexual aversion disorder. HSDD, which is described as decreased libido, is by far the most common issue for women, whereas sexual aversion disorder is quite rare. The prevalence rates for arousal, orgasm, and pain complaints are similar. Based on a 2006 review of published literature on prevalence studies of FSD, in women with sexual complaints, the average prevalence of women who experienced desire difficulties was 64%, arousal difficulties 31%, orgasm difficulties 35%, and sexual pain 26%.

As mentioned before, there are new theories about the female sexual response cycle that are moving away from the linear model with distinct phases of arousal. The DSM-5, published in May 2013, aimed to incorporate these new philosophies and made some subtle changes to their diagnostic criteria. In the new criteria, female hypoactive desire disorder and female arousal dysfunction were merged into a single syndrome called sexual interest/arousal disorder. The diagnosis of sexual aversion disorder was deleted from the DSM-5 based on the fact that the diagnosis had limited empirical support and shared more similarities with phobias and anxiety disorders rather than sexual disorders. Also, the previously separate categories of dyspareunia and vaginismus are now called genito-pelvic pain/penetration disorder. Female orgasmic disorder remains in place. Different from the DSM-IV criteria, diagnosis of sexual dysfunction requires a minimum duration of 6 months of symptoms and symptoms must occur 75% to 100% of the time for all diagnoses except substance-induced and medication-induced sexual dysfunction. Also, the disorder must cause “clinically
significant distress in the individual” and not just “interpersonal difficulty.”\textsuperscript{11,12} A number of other subtle changes were added that can be reviewed in the DSM-5 handbook or cited articles.\textsuperscript{5,11,12} Please refer to Table 1 for summary.

For the purpose of this article, we focus on the 4 categories of desire, arousal, orgasm, and pain so as to help delineate history taking and treatment options for each component. As one can imagine, despite having criteria that defines sexual dysfunctions in relation to the phases of the sexual response cycle, in clinical practice it is uncommon to see a disorder that is limited to a single phase.\textsuperscript{5} Although there are many controversies around these diagnostic criteria and whether sexual difficulties are being overclassified as true “disorders,” it is still at least helpful to have a generalized approach to history taking, diagnosis, and treatment. This approach will help women with these issues regardless of whether they should be defined as disorders or not.

Case:

A 34-year-old female, Mrs Jones, presents to your clinic for several issues. She is 6 months post-partum and she reports fatigue, difficulty with losing the weight she gained with pregnancy, and notes that her husband thinks they are not having sex very often. She has a history of depression and insomnia. Her medications include norethindrone 0.35 mg daily, citalopram 20 mg daily, and diphenhydramine 25 mg at bedtime as needed for insomnia.

### DESIRE DISORDERS

In the DSM-IV, the desire disorders consist of HSDD and sexual aversion disorder. The patient’s history for both these conditions will be very similar, apart from one major difference. The patient with HSDD will not report anxiety or aversion to sex, whereas the patient with sexual aversion disorder will report severe anxiety or aversion to sex. They will be similar in their reports of having absent or diminished interest in sex, infrequent sexual activity, decreased receptivity to sex, and infrequent or absent initiation of sexual activity.

Case:

Additional patient history: Mrs Jones feels that she is not currently interested in sex, she attributes this to feeling tired and unattractive, but the lack of interest bothers her: she previously had a good sexual relationship with her husband and she would like to again.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Categories for female sexual dysfunction</th>
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<td><strong>DSM-IV Categories</strong></td>
<td><strong>DSM-5 Categories</strong></td>
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<tr>
<td>Desire disorders</td>
<td>Desire/arousal disorders</td>
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<tr>
<td>• Hypoactive sexual desire disorder</td>
<td>• Merged desire and arousal into one category</td>
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<tr>
<td>• Sexual aversion disorder</td>
<td>• Deleted sexual aversion disorder</td>
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<tr>
<td>Arousal disorders</td>
<td></td>
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<tr>
<td>Orgasm disorder</td>
<td>Female orgasm disorder</td>
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<tr>
<td>Pain</td>
<td>Genito-pelvic pain/penetration disorder</td>
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<tr>
<td>• Dyspareunia: Pelvic pain with intercourse</td>
<td>• Merged dyspareunia and vaginismus</td>
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<td>• Vaginismus: Pelvic floor muscle spasm leading to pain with penetration</td>
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Abbreviation: DSM, Diagnostic and Statistical Manual of Mental Disorders.
Potential causes for the desire disorders are similar; however, a history of sexual abuse or trauma is more common in women with sexual aversion disorder compared with those with HSDD. Relationship issues and religious or cultural beliefs can certainly influence libido. Sleep deprivation, stress, depression, or treatments with antidepressants or antipsychotics are common contributors. Pregnancy, breast-feeding, or a postmenopausal state can be associated with decreased libido. Any number of chronic medical conditions, including hypothyroidism, may contribute as well.

Many women will ask whether their form of contraception may be contributing. The data on this are conflicting. Most of the available data are on combined oral contraceptives (COCs), and most often they are libido neutral. A comprehensive review article on the subject was published in 2012. In some cases, libido may be decreased from COCs due to antiandrogenic effects and a decrease in lubrication. In other studies, libido may increase due to decreased fear of pregnancy and improvement in certain gynecologic conditions, such as dysmenorrhea, menorrhagia, or endometriosis. The data for the NuvaRing (etonogestrel/ethinyl estradiol vaginal ring), the combined contraceptive patch (norelgestromin/ethinyl estradiol patch), and Depo-Provera (medroxyprogesterone acetate injection) appear similar. There are minimal data on the progesterone-only “mini pill” (norethindrone). One study of the Mirena (levonorgestrel) intrauterine device showed an increase in desire, whereas Implanon (etonogestrel) subdermal implant showed a decrease in libido in 2.5% of patients.

Laboratory evaluation for FSD is rarely indicated unless there is a suspicion for a specific medical condition contributing to the patient’s complaint. There are no data to support checking testosterone levels for FSD unless you are concerned about a hyperandrogenic medical condition. Endogenous serum androgen levels do not appear to be an independent predictor of sexual function in women.

Simple interventions that may help your patient include discussions about stress reduction and education about average frequency of sex. Unfortunately, the media has given us an unrealistic view of typical sexual practices. Helping your patients understand that there are a wide variety of practices and frequency of sexual activity may help alleviate concern. Based on the results of a survey performed in the United States in 2009, you can provide the patient with information regarding the average frequency of sexual activity in women: for women older than 25 years, the most common frequency of vaginal intercourse reported was “a few times per month to weekly”; overall, in women in their 40s, 30.5% reported intercourse a few times a month to weekly, 17.5% reported intercourse 2 to 3 times a week, and 3.5% reported intercourse 4 or more times a week. Overall, the frequency of intercourse decreased with age and intercourse is more frequent in partnered women than single women.

Case:

Mrs Jones feels better knowing that it is not uncommon for her to feel diminished libido considering the multiple issues affecting her on a daily basis. However, she still asks about testosterone therapy. She heard about it from a friend of hers.

Many women will ask their providers about whether testosterone therapy is an option. The benefit of testosterone therapy in postmenopausal women with HSDD is supported by several randomized controlled trials. See Table 2 for a summary of important trials, including the patient population studies, testosterone preparation, and risks and benefits.

Review of the literature is of benefit for several reasons. There is a good evidence base regarding a benefit of testosterone therapy in the treatment of HSDD, but the
<table>
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<tr>
<th>Study</th>
<th>Patient Population</th>
<th>Testosterone Preparation</th>
<th>Results</th>
<th>Testosterone Side Effects</th>
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<tbody>
<tr>
<td>Davis SR, Moreau M, Kroll R, et al. Testosterone for low libido in postmenopausal women not taking estrogen.</td>
<td>814 postmenopausal women not on hormone replacement therapy</td>
<td>Transdermal testosterone patches, 150 μg/d or 300 μg/d</td>
<td>300-μg/d patch resulted in an increase of 2.1 satisfying sexual episodes/4 wk; the placebo group had increase of 0.7 episodes/4 wk. No significant increase with the 150-μg/d dose of testosterone.</td>
<td>Hair growth, but very few women withdrew from the study because of this. More frequent vaginal bleeding, attributed to endometrial atrophy. No significant increase in acne, alopecia, or voice deepening. Three cases of breast cancer, all in the testosterone-treatment group.</td>
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<tr>
<td>Panay N, Al-Azzawi F, Bouchard C, et al. Testosterone treatment of HSDD in naturally menopausal women: the ADORE study.</td>
<td>272 postmenopausal women with nonsurgical menopause, many of whom were also being treated with estrogen replacement</td>
<td>Transdermal testosterone patches, 300-μg/d</td>
<td>Testosterone therapy resulted in an increase of 1.69 satisfying sexual episodes/4 wk, compared with an increase of 0.53 episodes/4 wk in the placebo group.</td>
<td>Hair growth and acne, neither severe enough to lead to withdrawal from the trial. No major adverse effects were noted.</td>
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<tr>
<td>Study</td>
<td>Participants</td>
<td>Treatment</td>
<td>Dose</td>
<td>Outcomes</td>
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<td>Braunstein GD, Sundwall DA, Katz M, et al. Safety and efficacy of a</td>
<td>447 postmenopausal women who underwent surgical menopause, all on oral</td>
<td>Transdermal testosterone patch, 150 μg/d,</td>
<td>300 μg/d patch resulted in an increase of 0.58 satisfying sexual episodes a week.</td>
<td>No major adverse effects.</td>
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<tr>
<td>testosterone patch for the treatment of hypoactive sexual desire</td>
<td>estrogen replacement</td>
<td>300 μg/d or 450 μg/d</td>
<td>No significant increase on 150 μg/d or 450 μg/d dose of testosterone.</td>
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<td>disorder in surgically menopausal women: a randomized, placebo-</td>
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<td>controlled trial.20</td>
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<tr>
<td>Davis S, Papalia MA, Norman RJ, et al. Safety and efficacy of a</td>
<td>261 premenopausal women with low circulating testosterone levels</td>
<td>Transdermal testosterone spray, 56 μL, 90 μL or 180 μL</td>
<td>90 μL/d dose resulted in an increase of 2.48 satisfying sexual episodes/ 4 wk compared with an increase of 0.8 episodes/ 4 wk on placebo.</td>
<td>Increased hair growth, primarily at the application site, and an increase in severity of acne. No other significant adverse events.</td>
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<td>testosterone metered-dose transdermal spray for treating decreased</td>
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<td>sexual satisfaction in premenopausal women: a randomized trial.21</td>
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Data from Refs.18–21
magnitude of this benefit is small. It is thought that an increase of $\geq 1$ satisfying sexual episodes per 4 weeks is meaningful to patients, but when weighed against potential risks, this needs to be carefully considered.\textsuperscript{22} It also should be noted that long-term safety data are nonexistent. Finally, availability of the studied testosterone replacement preparations is limited. In the United States, there are no testosterone preparations approved for use in women. There is no 300-µg per day transdermal testosterone patch available; the patches designed for men are much higher doses than those studied for use in women. There are ongoing trials of a low-dose testosterone gel, brand name LibiGel, designed for use in women. The trial under way is being completed to assess long-term safety data in response to requests by the Food and Drug Administration (FDA) for cardiovascular and breast cancer safety data before potential approval of testosterone therapy for treatment of postmenopausal women with HSDD.\textsuperscript{23} It also should be noted that efficacy of this preparation has not yet been demonstrated in the literature.

Use of products designed for use in men would clearly be off-label and should be done with caution. As noted, the concentration of testosterone in these preparations is much higher, and therefore the dose would need to be carefully adjusted. Transdermal patches designed for men cannot be cut; therefore, options primarily include injections and gels.

**Case:**

Mrs Jones is on an antidepressant. Is there anything to help with HSDD in this population?

Selective serotonin reuptake inhibitors (SSRIs) can negatively affect any component of the sexual response cycle, including desire, arousal, and/or orgasm, with estimates of 30% to 70% of patients on SSRIs reporting some degree of sexual dysfunction.\textsuperscript{24} Delay of orgasm and lack of orgasm are the most commonly reported side effects. Sexual dysfunction is a potential side effect for all drugs within the SSRI class of antidepressants. In addition, sexual side effects are frequently reported with venlafaxine, a serotonin-norepinephrine reuptake inhibitor (SNRI). Evidence regarding the severity of sexual side effects with mirtazapine is mixed, in some studies comparable to SNRIs, in others much less severe.\textsuperscript{25,26} Notably, bupropion, an antidepressant that is thought to primarily act on the dopamine and noradrenergic receptors, is not commonly associated with high rates of sexual side effects.

There are several potential strategies to manage sexual dysfunction in the setting of antidepressant use; see Box 1 for a concise summary. First, it is important to investigate the onset of a patient’s sexual dysfunction. Depression itself may lead to sexual dysfunction, and treatment with an SSRI may actually be helpful, although this may take weeks of therapy. It is also possible that the symptom will resolve spontaneously;

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<th>Box 1</th>
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<td>Strategies for managing FSD in the setting of depression and SSRI therapy</td>
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<tr>
<td>- Continue SSRI, add bupropion sustained release 150 mg twice a day</td>
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<tr>
<td>- Continue SSRI, prescribe sildenafil 50–100 mg as needed before sexual activity</td>
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<tr>
<td>- Reduce dose of SSRI if possible</td>
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<td>- Switch antidepressant classes from SSRI to bupropion</td>
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*Abbreviations: FSD, female sexual dysfunction; SSRI, selective serotonin reuptake inhibitor.*
similar to other common SSRI side effects, such as nausea, it has been estimated that 10% of the time sexual side effects will resolve as the body adapts to the medication.\textsuperscript{25} Several studies have found a reduction in SSRI-related sexual side effects with the addition of bupropion. In a Cochrane Database Systematic Review, Taylor and colleagues\textsuperscript{27} performed a review of management of SSRI-induced sexual dysfunction. They identified 5 high-quality randomized trials, including a total of 579 participants, regarding addition of bupropion to an SSRI for management of sexual side effects. One of these studies was exclusively of women; the other studies included predominantly women. They found improvement in sexual rating scores with use of bupropion sustained release 150 mg twice daily, but no statistically significant improvement with bupropion sustained release 150 mg once daily. Based on the limited data available in the studies, there was no evidence of a worsening of control of patients’ underlying mental illness with augmentation.

The use of sildenafil for management of SSRI-induced FSD may be considered as well. In a randomized, double-blinded, placebo-controlled trial of 49 premenopausal women with SSRI-induced sexual dysfunction, patients treated with sildenafil 50 to 100 mg as needed before sexual activity had an improved global sexual function score, the study’s primary outcome measure.\textsuperscript{28} Improvement in sexual function based on other scales, used as secondary outcome measures, was not consistently seen with sildenafil compared with placebo.

Other strategies can be considered, although they are less evidence-based. One option is a reduction in dose of a patient’s SSRI or SNRI, in hopes of reducing sexual side effects. A switch in antidepressants could be made, from an SSRI to bupropion. Or a “drug holiday” could be considered. There is one small observational study in which 30 patients were instructed to hold their SSRI antidepressant, fluoxetine, sertraline, or paroxetine, on Friday and Saturday for a month.\textsuperscript{29} There was a reported improvement in sexual function for the patients taking a “holiday” from sertraline and paroxetine; there was no improvement in patients on fluoxetine. There was no worsening in depression scores. These strategies would all carry the risk of worsening control of a patient’s depression and should be undertaken with caution if the patient’s symptoms are well controlled on their current drug regimen.

There is some evidence to support the use of bupropion for treatment of HSDD even in the absence of depression or SSRI therapy. There have been 2 studies completed regarding this question.\textsuperscript{30,31} Studies were of premenopausal women with HSDD who did not have depression. Different doses were used in each study, bupropion sustained release 150 mg daily and 300 to 400 mg daily; both studies found benefit compared with placebo. Bupropion improved all domains of sexual function. In the study by Safarinejad and colleagues,\textsuperscript{31} common side effects of bupropion included headache, insomnia, dry mouth, and nausea, although overall these symptoms were well tolerated, only leading to withdrawal of 3 of the 112 participants in the study group.

\textbf{Case:}

\textit{Mrs Jones returns to your clinic a month later. She is concerned that when she and her husband have been sexually active over the past several weeks it has been uncomfortable, noting that she has poor vaginal lubrication.}

\section*{AROUSAL DISORDERS}

Arousal disorder is defined as the recurrent inability to attain or maintain sufficient sexual arousal despite adequate stimulation. Once again, numerous psychosocial
issues and mental health conditions can influence arousal, as can medications, such as SSRIs, tricyclic antidepressants, antihistamines, anticholinergics, certain antihypertensives (alpha-blockers, beta-blockers, calcium channel blockers, diuretics), and illicit substances. Pelvic neurogenic or vascular impairments due to local nerve damage from pelvic surgeries or spinal cord injuries, peripheral nerve disorders from conditions such as diabetes and multiple sclerosis, and vascular impairment from diabetes, hypertension, hyperlipidemia, and smoking can affect arousal.

Educating patients on the importance of adequate stimulation and the use of lubricants and vaginal moisturizers can be helpful. There are a variety of lubricant products on the market available without a prescription. Broad categories include water-based, silicon-based, and oil-based lubricants. The water-based formulations are most commonly used; examples include Astroglide, K-Y Jelly, and Slippery Stuff. They are unlikely to cause skin irritation or stain bedding but may dry up more quickly than the silicone-based products. Silicone-based products are more expensive and more likely to stain bedding; examples include Pjur and ID Millenium. Many women will report using oil-based lubricants, such as baby oil, which can irritate the vaginal tissues and should not be used with latex condoms as they can reduce the effectiveness of the contraception and the prevention of sexually transmitted illnesses. Natural oils, including olive oil or avocado oil, are less irritating, although still should be avoided if the patient is using condoms with her partner.

Teaching patients about self-stimulation with vibrators or medical devices such as the Eros Clitoral Therapy device can be effective. The Eros Clitoral Therapy device is an FDA-approved hand-held vacuum used to increase blood flow to the clitoris and surrounding vaginal tissues. Whereas vibrators do not require a prescription and come in a variety of prices, the Eros Therapy device does require a prescription and costs approximately $179 as listed on the Eros Therapy Web site, eros-therapy.com.

Zestra is a natural oil-based topical therapy marketed as an “arousal oil.” It contains a combination of natural oils, including borage seed and evening primrose oils, and extracts and vitamins. In a randomized controlled study comparing efficacy of Zestra to placebo, a soybean oil–based product, in 178 patients with FSD, including arousal, desire and orgasmic disorders, there was a significant improvement in arousal and desire with the Zestra product, with a nonstatistically significant improvement in global satisfaction as well.32 This product was associated with mild-to-moderate genital burning in approximately 15% of subjects in the study.

**Case:**

*Her husband is using Viagra. She wonders if that will help her too.*

As reviewed previously, there have been encouraging data regarding the use of sildenafil in the treatment of SSRI-induced FSD.28 However, the evidence supporting the use of sildenafil in women who have female sexual arousal disorder has not been consistent. A study performed in premenopausal and postmenopausal women found no benefit with sildenafil doses ranging from 10 to 100 mg, although other, smaller studies have found some benefit.33–35 At this time, sildenafil would not be a recommended therapy.

**Case:**

*Mrs Jones returns to clinic again, several months later. Several issues have improved; she feels that her interest in sexual activity has returned to a level she*
is happy with, and with adequate stimulation she has normal vaginal lubrication. Today she is concerned about a decrease in the frequency of orgasms; she feels that she more frequently had orgasms before her pregnancy.

**ORGASM DISORDERS**

Female orgasmic disorder can be primary or secondary. A patient who has never had an orgasm would be described as having primary orgasmic disorder. There may be a history of sexual abuse, and if so, psychotherapy may be useful in treatment. But in some cases it is idiopathic, in which case there are no recommended treatments. Patients with secondary orgasmic disorder have achieved orgasm in the past but have a distressing change in their ability to achieve orgasm at the time of presentation. There are many possible etiologies, including psychosocial causes such as relationship conflict, religion or cultural beliefs, and body image issues. Neurologic and vascular disease can lead to orgasm disorders; examples include spinal cord injury, diabetes, and multiple sclerosis. A class of medications frequently associated with anorgasmia and delayed orgasm is SSRIs. Management of secondary female orgasm disorder involves normalizing the patient’s experience, educating the patient on possible ways to achieve orgasm, consideration of counseling, and possible change of antidepressant if the patient is taking an SSRI, as described previously.

A model of assessment and treatment that could be used by the primary care provider is the PLISSIT model. PLISSIT stands for Permission, Limited Information, Specific Suggestions, Intensive Therapy. Permission stands for the discussion with the patient around normalization of sexual behaviors. Limited Information could include information about behaviors that may increase arousal, including foreplay and a discussion of medical conditions or medications that could be contributing to the problem. Specific Suggestions could include use of lubricants, vaginal estrogen, and position changes. Intensive Therapy would be referral to a specialist, such as a sex therapist or couples counselor, if appropriate. “Sex therapy” is psychotherapy aimed at treating sexual dysfunction. The organization American Association of Sexuality Educators, Counselors, and Therapists offers certification. The focus of sex therapy can be variable based on the patient’s needs. It frequently focuses on reducing anxiety in sexual situations, based on the assumption that anticipation and performance anxiety often contribute to sexual dysfunction, in addition to discussion of sexual skills. Sexual exercises are frequently assigned; these may include sensate focus, in which the focus of intimate physical interactions is on sensations and not orgasm. This therapy has not been well studied, and there is great heterogeneity in both specific treatments and results.36

**Case:**

Mrs Jones returns to clinic 2 years later. She had her second child 4 months ago. Despite reviewing all the recommendations you made to her previously she is again having pain with intercourse. Even with adequate stimulation she feels that she doesn’t have adequate vaginal lubrication and is having significant pain with insertion. She is currently breast-feeding and is back on the norethindrone “mini pill.”

**PAIN DISORDERS**

In the DSM-5 criteria, the categories of dyspareunia and vaginismus were merged under a new category called genito-pelvic pain/penetration disorder (GPPD). The
primary reason for this change was because these 2 disorders could not be reliably differentiated. The presence of “vaginal muscle spasm,” which is part of the diagnostic criteria for vaginismus, has not been supported by empirical evidence and the fear of pain or the fear of penetration is common in the clinical descriptions of vaginismus. Because there is tremendous overlap between dyspareunia and vaginismus, the term “genito-pelvic pain/penetration disorder” is all encompassing. For the diagnosis of GPPD, one of the following should occur persistently or recurrently: difficulty in vaginal penetration, marked vulvovaginal or pelvic pain during penetration or attempt at penetration, fear or anxiety about pain in anticipation of, during, or after penetration, and tightening of pelvic floor muscles during attempted penetration. Sexual pain may be localized to the vulva, vestibule, vagina, pelvis, or at multiple sites simultaneously. Currently research in pelvic pain syndromes is lacking in women for whom insertive vaginal intercourse may not be part of their typical sexual practices. Future revisions to the DSM criteria will hopefully incorporate more information about nonpenetrative sexual activities and women without partners.

To diagnose GPPD, other causes of pelvic pain must be ruled out. Etiologies for genitoo-pelvic pain are numerous. From the perspective of a health care provider, it may be easier to think of broader categories such as “irritative,” “anatomic,” and “infectious” causes; see Table 3. Regarding infectious causes, evaluate for sexually transmitted illnesses, candidiasis, and pelvic inflammatory disease when appropriate. Under the category of “anatomic,” one might elicit a history or physical examination finding of previous pelvic surgery, episiotomy, fibroids, uterine or bladder prolapse, gynecologic malignancy, or endometriosis, to name a few. In this article, we focus on “irritative” causes, which include diminished lubrication, atrophic vaginitis, vulvar dermatoses, and vulvodynia.

Atrophic vaginitis is most common in menopausal women. Hypoestrogenic states also can occur in the postpartum period, during lactation, and in premenopausal women with the administration of antiestrogenic drugs, such as tamoxifen, aromatase inhibitors, and medroxyprogesterone that may cause vaginal atrophy. Typical physical examination findings for vaginal atrophy include loss of labial or vulvar fullness, minimal vaginal moisture, pallor of urethra or vagina, narrow introitus, and loss of vaginal rugae (Fig. 3). Placing a piece of pH paper on the vaginal wall until it is moistened can test vaginal pH. The pH of an estrogenized vagina ranges from 3.5 to 5.0. A vaginal pH of 4.5 or greater in the absence of infection or recent semen in the vaginal vault can be an indicator of vaginal atrophy due to estrogen deficiency.

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<th>Categories</th>
<th>Examples</th>
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<td>Irritative</td>
<td>Vaginal dryness</td>
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<td>Atrophic vaginitis</td>
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<td>Scarring related to previous pelvic surgery, episiotomy</td>
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<td>Gynecologic malignancy</td>
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<td>Infectious</td>
<td>Sexually transmitted infections (gonorrhea, chlamydia)</td>
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<td>Vulvovaginal candidiasis</td>
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<td>Pelvic inflammatory disease</td>
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Women with atrophic vaginitis should be encouraged to use vaginal moisturizers and lubricants. The different lubricant products available are outlined previously in the section on arousal disorders. Over-the-counter vaginal moisturizers used on a regular basis with intercourse rather than as needed can help manage symptoms of atrophic vaginitis. Replens is an example of a vaginal moisturizer, with results of 2 small studies showing equal efficacy as topical estrogen, although the authors’ clinical experience would suggest it is less effective. Vaginal estrogen is also an option for many women. Unless there is clinical indication for systemic estrogen therapy, the recommendation is to use low-dose vaginal estrogen for atrophic vaginitis, as it appears more effective with less risk of side effects. This is based on a meta-analysis of 58 studies demonstrating higher patient satisfaction with vaginal versus oral estrogen therapy for the relief of urogenital atrophy symptoms. Low-dose vaginal estrogen options include estradiol (Vagifem) 10-μg tablets, estradiol ring (Estring), conjugated estrogen cream (Premarin) 0.625 mg/g (low dose ≤0.3 mg), or estradiol cream (Estrace) 100 μg/g (low dose ≤50 μg). Remember that the high-dose estradiol ring of 50 to 100 μg/d (Femring) is not a low-dose option and is equal to systemic estrogen therapy. For the tablets and creams, treatment is usually initiated nightly for 2 weeks, then twice weekly for maintenance. The low-dose estradiol ring is placed intravaginally for 3 months and then replaced with a new ring. Symptoms may improve within the first few weeks of starting therapy but it may take up to 4 to 6 weeks for complete restoration of the urogenital tissue. See Table 4 for summary of therapies for atrophic vaginitis.

There is minimal systemic absorption with these vaginal preparations, but the highest absorption may occur with the creams. Circulating estradiol levels measured in women treated with the low-dose vaginal estradiol tablet and estradiol ring are similar to normal levels in menopausal women. There are fewer data available on estradiol levels in women treated with the vaginal creams. Well-designed, long-term studies evaluating potential risks of low-dose vaginal estrogen are lacking. Therefore, it is still controversial whether these preparations are safe in the setting of a previous history of breast cancer, particularly hormone-receptor-positive breast cancer, or venous thromboembolism and whether progesterone therapy should be used in the setting of an intact uterus. We recommend conferring with a woman’s oncologist before

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Fig. 3. Atrophic vulva. Slightly enlarged clitoris owing to loss of estrogen, with a pale, thin vulvar vestibule. (From Apgar BS, Brotzman GL, Spitzer M. Colposcopy, principles and practice, an integrated textbook and atlas. Philadelphia: WB Saunders; 2002; with permission.)
initiating treatment with vaginal estrogen in patients with breast cancer. Based on limited data, it appears that use of vaginal estrogen in women on tamoxifen is safe.\textsuperscript{40} Data are lacking about the effects of low-dose vaginal estrogen on endocrine therapy for breast cancer. At this point, we would recommend against use of vaginal estrogen in women taking aromatase inhibitors for treatment of breast cancer. The goal of aromatase inhibitor therapy is to maximally reduce systemic estrogen levels. There is a very small study demonstrating that the use of low-dose vaginal estrogen

<table>
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<th>Categories</th>
<th>Examples</th>
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<tr>
<td>Over-the-counter vaginal lubricants</td>
<td>Water-based: Astroglide, K-Y Jelly, Slippery Stuff Silicon-based: Pjur, ID Millenium Oil-based: synthetic (baby oil) or natural oils (olive, avocado)</td>
<td>As needed with intercourse</td>
<td>Dry up more quickly than other products More expensive than other products Potential to stain bedding Reduce effectiveness of condoms Synthetics: Vaginal irritation</td>
</tr>
<tr>
<td>Over-the-counter vaginal moisturizers</td>
<td>Replens</td>
<td>Every 3 d</td>
<td>Endometrial safety: Use of an opposing progestin unnecessary when using low-dose vaginal tablets and rings, less clear with the creams Patients with an h/o breast cancer: Risk likely very low, confer with a woman’s oncologist before initiating treatment with vaginal estrogen</td>
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<td>Prescription topical estrogen therapy</td>
<td>Estradiol (Vagifem) 10-μg tablets Estradiol ring (Estring) Conjugated estrogen cream (Premarin) 0.625 mg/g (low dose ≤0.3 mg) Estradiol cream (Estrace) 100 μg/gram (low dose ≤50 μg)</td>
<td>Tablets and creams: treatment typically initiated nightly for 2 wk then twice weekly for maintenance The low-dose estradiol ring is placed intravaginally every 3 mo</td>
<td>Endometrial safety: Use of an opposing progestin unnecessary when using low-dose vaginal tablets and rings, less clear with the creams Patients with an h/o breast cancer: Risk likely very low, confer with a woman’s oncologist before initiating treatment with vaginal estrogen</td>
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<td>Prescription oral medications</td>
<td>Ospemifene (Osphena), a selective estrogen receptor modulator that acts as an estrogen agonist in the vagina</td>
<td>60 mg daily</td>
<td>FDA recommends use of opposing progestin. Potential risk of venous thromboembolism. Yet to be determined if safe in women with history of breast cancer and if protective in women at high risk for breast malignancy.</td>
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Abbreviations: FDA, Food and Drug Administration; h/o, history of.
reversed the suppression of serum estradiol levels achieved by aromatase inhibitor therapy.41

Regarding endometrial safety, low-dose vaginal estrogen used for the treatment of atrophic vaginitis does not appear to cause proliferation of the endometrial epithelium regardless of vaginal preparation used.39,42 The use of an opposing progestin is likely unnecessary when using low-dose vaginal tablets and rings, but it is less clear with the use of the creams. The conservative approach would be to use opposing progestin in women treated with vaginal estrogen creams. Progestin can be taken either daily or for 10 to 12 consecutive days per month. Typical progestin formulations include medroxypregesterone 10 mg, norethindrone acetate 5 to 10 mg, or micronized progesterone 200 mg. Regardless of the type of vaginal estrogen used, any menopausal woman who develops vaginal bleeding should be evaluated for endometrial hyperplasia or cancer.

Ospemifene (Osphena) 60 mg/day is a newly FDA-approved oral tablet for the treatment of moderate to severe menopausal dyspareunia. This is a selective estrogen receptor modulator (SERM) that acts as an estrogen agonist in the vagina. Two randomized trials have shown that ospemifene 60 mg per day is more effective than placebo in the treatment of menopausal dyspareunia and vaginal dryness at 12 weeks.43,44 To date, there are no studies comparing ospemifene to vaginal estrogen. Other SERMs on the market (tamoxifen and raloxifene) have not shown the same improvements in atrophic vaginitis symptoms. The most common side effect of ospemifene is hot flashes. Whether opposing progestin should be used in women with an intact uterus is still unclear. In a 1-year, long-term safety extension study of ospemifene for the treatment of atrophic vaginitis, neither ospemifene 30 mg or 60 mg daily resulted in significant endometrial changes.45 Currently, the FDA recommends the use of opposing progestin; however, studies evaluating the protective effects of progestin are lacking. There is also a potential risk of venous thromboembolism; however, further data are needed. Additional studies also are needed to determine if ospemifene is safe in women with history of breast cancer and whether it has protective effects for women at high risk for breast malignancy.

Is it important to evaluate for evidence of vulvar dermatoses when women complain of dyspareunia. Lichen sclerosis is a chronic, progressive inflammatory skin condition of unknown etiology. It most commonly affects the labia minora and/or labia major, but can extend to the perineum and around the anus. Women will complain of pruritus and/or pain. Dyspareunia is often a late symptom due to introital stenosis, fissuring, or labial agglutination. Classic findings include white atrophic papules that may coalesce into ivory or pink plaques. Lichen sclerosis can also be hemorrhagic, purpuric, hyperkeratotic, bullous, eroded, or ulcerated. Fissuring perianally, around the clitoris and in the intralabial folds is common (Figs. 4 and 5). As the condition progresses, labial scarring may occur, which can lead to the loss of the vulvar architecture and narrowing of the introitus. Women with lichen sclerosis are at higher risk of developing squamous cell cancer of the vulva. Treatment usually involves the use of superpotent topical steroids to improve symptoms and prevent progression of the disease. It is not known whether topical steroids prevent the development of squamous cell cancer. Typical treatment includes the application of a thin film of clobetasol or halobetasol propionate 0.05% ointment nightly to the affected areas for 6 to 12 weeks and then 1 to 3 times per week for maintenance.

Another vulvar dermatosis that can lead to dyspareunia is vulvar lichen planus. This is a chronic, desquamative, erosive dermatitis that can result in severe destruction of the vulvar tissues and stenosis of the vaginal opening. Symptoms most often develop in women age 50 to 60 years and include severe pruritus or vulvar pain, soreness, or burning. Vulvar lichen planus can involve the labia minor and vestibule. The anus is
Lesions can be isolated or diffuse. Vulvar lichen planus is described as glassy, brightly erythematous erosions with white striae or a serpentine white border along the margin (Wickham striae) (Figs. 6–8). A violaceous border is occasionally seen. Data regarding efficacy of treatments for vulvar lichen planus are limited; however, treatment often involves the use of super-potent topical steroids with daily

Fig. 4. (A) Vulvar lichen sclerosus. Pallor, atrophy (wrinkled aspect on the perineum) and perineal fissures. (B) Early changes in lichen sclerosus. White thickened areas of vulva caused by lichen sclerosus. (From Moyal-Barracco M, Wendling J. Vulvar dermatosis. Best Pract Res Clin Obstet Gynaecol 2014;28:949; with permission.)

treatment followed by maintenance therapy. Evaluation and management by a dermatologist is recommended.

Vulvar pain disorders also can include localized or generalized vulvodynia. Once other causes for pain are excluded, localized vulvodynia can be diagnosed using the Q-tip test, in which pain is “provoked” in the vestibule, interlabial sulci, introitus, or around the clitoris with light touch from a moistened Q-tip (Fig. 9). Pain may be prevented or reduced with the use of topical lidocaine 5% ointment or EMLA (lidocaine-prilocaine) cream applied to the painful areas 10 minutes before intercourse.

Generalized vulvodynia is defined as “unprovoked” stinging, burning, irritation, rawness, or pain anywhere on the vulva that is not explained by another condition. In generalized vulvodynia, physical examination is often normal or there may be areas of tenderness, hyperesthesia, or hypesthesia. The use of topical anesthetics before intercourse can be tried, otherwise numerous oral medications used for the treatment of chronic pain can be considered. Working closely with a gynecologist and possibly a pelvic floor physical therapist is recommended.

Once other conditions have been excluded, the treatment of GPPD is often multifactorial. Referral to a psychiatrist or psychotherapist may be necessary to deal with any potential psychological factors contributing to the pain. Pelvic floor physical therapists are able to instruct women in desensitization techniques, such as Kegel exercises and

Fig. 7. Wickham striae. The most classic and only pathognomonic findings of vulvar lichen planus are the white, reticulate, lacy papules. Even these papules are most often accompanied by vulvar or vaginal erosions. (From Mirowski GW, Goddard A. Treatment of vulvovaginal lichen planus. Derm Clinics 2010;28(4):720; with permission.)

Fig. 8. Vulvar lichen planus. Most often manifested by vestibular erosions, loss of vulvar architecture caused by scarring, and surrounding white epithelium; patients experience both itching and pain. (From Stewart KM. Clinical care of vulvar pruritus, with emphasis on one common cause, lichen simplex chronicus. Derm Clinics 2010;28(4):673; with permission.)
vaginal dilator therapy with the goal of giving the woman control over her pelvic floor tonicity and relaxation. Numerous other treatments have been tried but lack well-designed studies. Working with a gynecologist or other women’s health provider versed in the treatment of this condition is important.

**SUMMARY**

FSD is a term applied to a heterogeneous group of disorders. Providers and patients are frequently uncomfortable discussing sexual health, leading to neglect of this important issue in patients’ well-being. When a patient has sexual concerns, these should be explored and if distressing to the patient, may represent an FSD “disorder.” There are several broad categories of FSD to consider, including desire, arousal, orgasm, and pain disorders, although it should be acknowledged that frequently one patient may have symptoms of several of these types of sexual dysfunction. We hope to have offered the reader guidance in how to evaluate a patient with sexual concerns, how the history can lead to diagnosis and in turn treatment strategies for the patient. In the setting of HSDD, there is evidence to support the use of topical testosterone therapy, although the magnitude of the benefit was small, there is a lack of long-term safety data and the studied testosterone replacement preparations are not available in the United States. At this time, use of testosterone for HSDD in women is not FDA approved. For patients with SSRI-induced FSD, addition of bupropion or use of sildenafil may be helpful. Patient education regarding adequate stimulation and use of lubricants is likely one of the most effective means of treating arousal disorders. In the absence of SSRI therapy, treatment of secondary female orgasmic disorder also involves patient education and potentially more intensive “sex therapy.” Pain with intercourse is common, especially in postmenopausal women. Treatment of atrophic vaginitis is most effectively accomplished with topical estrogen treatment. In the absence of other painful vaginal conditions, GPPD can be diagnosed. Treatments are not well studied, but may include pelvic floor physical therapy for desensitization exercises.
REFERENCES


