Low or absent sexual desire is the most common sexual dysfunction in women, and its prevalence peaks during midlife. Its etiology is complex and may include biologic, psychologic, and social elements. Major risk factors for its development include poor health status, depression, certain medications, dissatisfaction with partner relationship, and history of physical abuse, sexual abuse, or both. Diagnosis is based on criteria set by the Diagnostic and Statistical Manual of Mental Disorders (5th Edition) and requires that a woman experience personal distress. Clinical evaluation should include medical history, sexual history, and, sometimes, a physical examination. Laboratory data are of limited value, except when warranted by history or physical examination. Treatment options include nonpharmacologic interventions such as education, office-based counseling, and psychotherapy. Although there are no U.S. Food and Drug Administration (FDA)–approved treatments for low desire, pharmacologic agents have been used off-label for this purpose. Bupropion is an antidepressant that has been shown to improve desire in some women with and without depression. Systemic estrogen therapy is not recommended in the absence of vasomotor symptoms and is not directly associated with desire. However, vaginal estrogen is useful in patients presenting with concomitant vaginal atrophy and dyspareunia. Ospemifene is a selective estrogen receptor modulator that can be used as an alternative to vaginal estrogen. Exogenous testosterone has demonstrated efficacy in treating loss of desire in postmenopausal women. However, patients should be counseled that it is not FDA-approved for this purpose and there are limited published long-term safety data. Several agents for the treatment of low desire are currently in development. Gynecologists are in a unique position to address concerns about sexual desire in women.

Approximately 40% of women will experience some type of sexual problem over the course of their lifetimes.1,2 A sexual complaint is diagnosed as a dysfunction when the criteria from the American Psychiatric Association’s Diagnostic and Statistical Manual (DSM) for sexual dysfunctions are met and it results in personal distress.3 Although sexual complaints among women are common, the largest and most recent epidemiologic survey places the prevalence of diagnosable sexual disorders at approximately 12%.2 The most prevalent sexual dysfunction in women across all ages is a lack of sexual desire, previously referred to as hypoactive sexual desire disorder in the DSM 4th Edition, Text Revision4 (DSM-IV-TR) and female sexual interest and arousal disorder in the DSM 5th Edition (DSM-5).3 Women with hypoactive sexual desire disorder may report little or no interest in sex, an inability to respond to sexual stimuli, or feeling numbness despite having a good relationship with her partner.

Absent or low sexual desire represents an important problem that has major implications for women’s quality of life, sense of well-being, and interpersonal...
relationships. The Women’s International Study of Health and Sexuality trial, a large national survey of more than 2,000 U.S. women, revealed that those with hypoactive sexual desire disorder had statistically significant decrements in health status, especially in domains that measured aspects of mental health. It has also been shown that postmenopausal women with hypoactive sexual desire disorder experience more health burdens, including more comorbid medical conditions, and are nearly twice as likely to report fatigue, depression, memory problems, back pain, and a lower quality of life. In addition, they are more likely than women with normal desire to agree with statements expressing negative emotional or psychological states, including feelings of frustration, hopelessness, anger, loss of femininity, and decreased self-esteem.

Gynecologists are in a unique position to address these concerns and help women lead the healthy sex lives that they deserve. We review and discuss the diagnosis and treatment of low sexual desire in women with an emphasis on promoting efficient office-based assessment and treatment and referral.

NORMAL SEXUAL FUNCTION AND MODELS OF SEXUAL RESPONSE

“Normal” sexual function is a misleading concept, because there is not an objective measure to define it. “Normal” is often defined by statistical norms, cultural norms, or both. Furthermore, normal function may vary between women and within the same woman over the course of her lifetime. Multiple models have been developed to describe a healthy sexual response. In 1966, Masters and Johnson proposed a linear model of sexual response based on their observations of the physiologic changes that occurred in men and women in a laboratory setting. Their model consisted of four stages: excitement, plateau, orgasm, and resolution (Fig. 1). Subsequently, Kaplan and Leif independently modified this model to include the concept of desire, which reflects the psychological, emotional, and cognitive components of sexual response. This revised linear model encompassed three phases: desire, excitement, and orgasm (Fig. 2). Based on observations that women’s sexual responses often do not follow a linear trajectory, Basson introduced an intimacy-based circular model to help explain the multifactorial nature of women’s sexual response. Her model acknowledges the intricate interplay of emotional intimacy, sexual stimuli, psychological factors, and relationship satisfaction that determine sexual response (Fig. 3). It also introduces the concept of sexual neutrality and responsive desire (the idea that women may not be motivated by spontaneous desire and that desire results from arousal in the context of a loving relationship) and forms the basis for the DSM-5 criteria of Female Sexual Interest and Arousal Disorder.

DISORDERS OF SEXUAL DESIRE: DIAGNOSIS

Definition

According to the DSM-IV-TR, hypoactive sexual desire disorder was defined as “persistently or recurrently deficient (or absent) sexual fantasies and desire for sexual activity that causes marked distress or interpersonal difficulty.” To qualify as a disorder, it should not be better accounted for by another mental disorder, drug, or other medical condition. Diagnosis
should take into account the normal fluctuation seen with relationships over time, age, personal health, and life circumstances.

In the newly released DSM-5,4 hypoactive sexual desire disorder and female sexual arousal disorders have been combined into one disorder, now called “female sexual interest/arousal disorder,” based on data suggesting that sexual response is not always a linear, uniform process and that the distinction between certain phases (particularly desire and arousal) may be artificial (Table 1).9,10 As implied by Basson’s circular model, desire and arousal are difficult to separate and normal desire includes a responsive component.8 To increase objectivity and precision and to avoid overdiagnosis of transient sexual difficulties, diagnosis now requires a minimum duration of approximately 6 months and more precise severity criteria. Also, the DSM-5 requires that women presenting with loss of desire experience personal distress rather than her partner or their relationship.

**Prevalence**

Two of the most recent epidemiologic surveys of low sexual desire include The Prevalence of Female Sexual Problems Associated with Distress and Determinants of Treatment Seeking (PRESIDE) study2 and a survey by West et al.11 The PRESIDE survey included 31,581 U.S. women aged 18 years or older and used validated questionnaires to evaluate sexual function and measure distress.2 In this study, 8.9% of women aged 18–44 years, 12.3% of women aged 45–64 years, and 7.4% of women older than 65 years exhibited low desire and distress, showing that distressing sexual problems peak during middle age. Using similar methods, West et al11 conducted a cross-sectional study of 2,207 U.S. women aged 30–70 years and found that the overall prevalence of hypoactive sexual desire disorder was 8.3%. Other studies have shown similar trends.6,12

**Pathophysiology**

The pathophysiology of low sexual desire is complex and should be considered in the context of the biopsychosocial approach. The biopsychosocial approach emphasizes the importance of understanding human health and illness in their fullest contexts by systematically considering biological, psychological, and social factors and their complex interactions on health and illness.13 Biological factors may contribute to decreased desire by direct or indirect mechanisms. Common medical conditions (such as hypertension and diabetes mellitus)14 and their treatment (including antihypertensives such as calcium channel blockers and angiotensin-converting enzyme inhibitors)15 have been associated with decreased sexual desire. Frequently, sexual problems overlap such as the presence of dyspareunia being an underlying cause of low desire.

Aging can also affect sexual desire. Previous studies have shown that middle-aged women have the highest prevalence of decreased desire with distress.5,12 The intensity of sexual desire a woman experiences may decline as a result of neuroendocrine changes (declining testosterone, changes in neurochemistry, and indirect changes from loss of estrogen). Genital sensation may change, requiring stronger and longer stimulation to achieve arousal. Low estrogen levels may cause vulvovaginal atrophy and dyspareunia, which is associated with decreased desire.16 These factors, along with unique psychosocial factors that
present during this life phase, influence sexual function during the menopausal transition.

Psychological factors play a significant role in sexual desire and may even sometimes override biologic factors. Psychiatric conditions (such as depression and anxiety) and their treatment (medications including selective serotonin reuptake inhibitors and anxiolytics) are associated with decreased

<table>
<thead>
<tr>
<th>Table 1. Classification of Female Sexual Dysfunction: Diagnostic and Statistical Manual of Mental Disorders (4th Edition, Text Revision) Compared With the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DSM-IV-TR</strong></td>
</tr>
<tr>
<td><strong>Sexual desire disorders</strong></td>
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<tr>
<td>Hypoactive sexual desire disorder</td>
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<tr>
<td>Deficiency or absence of sexual fantasies and desire for sexual activity</td>
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<tr>
<td>Sexual aversion disorder</td>
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<tr>
<td>Aversion to and active avoidance of genital sexual contact with a sexual partner</td>
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<tr>
<td><strong>Sexual arousal disorders</strong></td>
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<tr>
<td>Female sexual arousal disorder</td>
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<tr>
<td>Persistent or recurrent inability to attain or to maintain until completion of the sexual activity, an adequate lubrication–swelling response or sexual excitement</td>
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<tr>
<td><strong>Orgasmic disorders</strong></td>
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<tr>
<td>Female orgasmic disorder</td>
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<tr>
<td>Persistent or recurrent delay in, or absence of, orgasm after normal sexual excitement</td>
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<tr>
<td><strong>Sexual pain disorders</strong></td>
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<tr>
<td>Dyspareunia</td>
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<tr>
<td>Genital pain that is associated with sexual intercourse</td>
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<tr>
<td>Vaginismus</td>
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<tr>
<td>Recurrent or persistent involuntary contraction of the perineal muscles surrounding the outer third of the vagina when vaginal penetration with penis, finger, tampon, or speculum is attempted</td>
</tr>
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| **DSM-5†** |
| Female sexual interest or arousal disorder |
| Lack of or significantly reduced sexual interest or arousal as manifested by three of the following: |
| 1. Absent or reduced interest in sexual activity |
| 2. Absent or reduced sexual or erotic thoughts or fantasies |
| 3. No or reduced initiation of sexual activity and unreceptive to partner’s attempts to initiate |
| 4. Absent or reduced sexual excitement or pleasure during sexual activity in almost all or all (75–100%) sexual encounters |
| 5. Absent or reduced sexual interest or arousal in response to any internal or external sexual or erotic cues (written, verbal, or visual) |
| 6. Absent or reduced genital or nongenital sensations during sexual activity in almost all or all (75–100%) sexual encounters |
| Female orgasmic disorder |
| Presence of either of the following on all or almost all (75–100%) occasions of sexual activity: |
| 1. Marked delay in, marked infrequency of, or absence of orgasm |
| 2. Markedly reduced intensity of orgasmic sensations |
| Genitopelvic pain or penetration disorder |
| Persistent or recurrent difficulties with one or more of the following: |
| 1. Vaginal penetration during intercourse |
| 2. Marked vulvovaginal or pelvic pain during intercourse or penetration attempts |
| 3. Marked fear or anxiety about vulvovaginal or pelvic pain in anticipation of, during, or because of vaginal penetration |
| 4. Marked tensing or tightening of pelvic floor muscles during attempted vaginal penetration |

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* Disturbance must cause marked distress or interpersonal difficulty. The sexual dysfunction must not be better accounted for by another disorder and is not attributed to the direct physiologic effects of a substance or medication or general medical conditions.

† Symptoms persist for a minimum of 6 months, are not better explained by a nonsexual mental disorder or a consequence of severe relationship distress or other significant stressors, and are not attributed to the effects of a substance or medication or other medical conditions.
sexual desire. Sexual abuse and trauma in childhood and puberty, perceived stress, distraction, self-focused attention or anxiety, personality disorders, and body image or self-consciousness have all been shown to negatively affect desire.\textsuperscript{18}

The affect of social factors on sexual desire should also be considered. Cultural, social, and religious values and mores can negatively influence women’s sexual desire, especially in women raised in highly restrictive cultures or religions.\textsuperscript{5} Relationship factors such as conflict or a partner’s sexual dysfunction (eg, erectile dysfunction and premature ejaculation in a male partner),\textsuperscript{19} stressors such as financial hardship, career-related pressures, and familial obligations can also contribute to decreased sexual desire.

To gain a better understanding of the etiology of hypoactive sexual desire disorder, the HSDD Registry for Women was designed to characterize a large (1,500 women) cross-section of women with hypoactive sexual desire disorder and to prospectively investigate several biopsychosocial factors associated with the disorder.\textsuperscript{20} Initial findings from the registry confirm the multifactorial nature of hypoactive sexual desire disorder with the majority of premenopausal women identifying multiple factors (such as stress or fatigue, dissatisfaction with physical appearance and other sexual difficulties) that contribute to their decreased desire.\textsuperscript{20}

**Screening**

Sexual concerns should be addressed routinely as part of all comprehensive women’s health visits. Only one-third of women with seriously distressing sexual problems seek help.\textsuperscript{21} Although some women are hesitant to initiate discussions, many still want their health care provider to open the dialogue about sex.\textsuperscript{22} When a health care provider initiates this dialogue, he or she acknowledges and prioritizes the role that sexual health plays in overall well-being. Furthermore, the woman is given the opportunity to discuss issues and concerns that she may otherwise not disclose for fear of embarrassment or perception that it is not important.

Gynecologists are often the first health care provider a woman turns to when seeking help for sexual problems. It is important to provide a safe and nonjudgmental environment that facilitates discussion of these issues. Placing patient-friendly educational materials in waiting and examination rooms and training staff to be knowledgeable and comfortable with sexual topics can create an atmosphere that is conducive to discussing sexual issues. Intake forms can be modified to include questions about sexual health, which provide additional opportunities for patients to disclose their sexual concerns. Women should be reassured that discussions will remain confidential. When women perceive that a health care provider is uncomfortable, disinterested, or reluctant, communication about sexual health can be hindered.\textsuperscript{23,24}

There are a variety of screening instruments that can be used to help identify women who suffer from low desire. In particular, the Decreased Sexual Desire Screener\textsuperscript{25} ([www.obgynalliance.com/files/fsd/DSDS_Pocketcard.pdf](http://www.obgynalliance.com/files/fsd/DSDS_Pocketcard.pdf)) is a validated five-question, self-administered survey that helps practitioners identify generalized acquired hypoactive sexual desire disorder in both premenopausal and postmenopausal women in a timely and practical manner.\textsuperscript{25} This screener is a useful adjunct to the patient history and physical examination in the diagnosis of hypoactive sexual desire disorder.

Because the new DSM-5 diagnostic category of Female Sexual Interest/Arousal Disorder combines the prior DSM-IV-TR disorders of hypoactive sexual desire disorder and Female Sexual Arousal Disorder, screening and assessment should also include inquiry of difficulties with genital and nongenital excitement and arousal.

Although time is limited in the clinical setting, it is important to ask questions that help determine the true nature of problem. When the patient presents with low desire, a detailed description of her problem, including the onset, duration, and severity of her symptoms, should be obtained. Her level of distress should be determined. Open-ended questions allow the patient to provide information essential for accurate diagnosis and the development of an appropriate treatment plan. If there is not enough time to have a complete discussion, a return visit should be scheduled to specifically focus on her sexual concerns.

**History**

A complete medical history can identify conditions that contribute to low sexual desire. Psychiatric conditions should also be identified, because many such as depression and anxiety are associated with low desire. Medications should be reviewed, because some (such as selective serotonin reuptake inhibitors and antihypertensives) are linked to low desire (Box 1). Oral contraceptive use has been associated with low desire.\textsuperscript{26,27} although other studies have not found this association.\textsuperscript{28,29} Although most women will likely not be affected, the possible sexual consequences should be considered with patients during discussions of contraception options.
Gynecologic history can provide additional data about the cause of low desire. The presence of menstrual irregularities can indicate hormonal disorders (such as hyperprolactinemia and hypothyroidism) that interfere with sexual desire. A history of pelvic surgery may point to an anatomical source for sexual problems. Other gynecologic-related issues such as sexually transmitted infections and urinary incontinence can influence a woman’s motivation and desire for sexual activity.

Components of the sexual history should include direct questions about sexual behavior and safe sex practices. Sexual history-taking should always be conducted in a culturally sensitive manner, taking account of the individual’s background and lifestyle and status of the partner relationship.

**Physical**

Although many women with low desire will have normal findings, a physical examination may be warranted in some cases to identify possible contributors to low desire. The gynecologic examination can be particularly informative. The presence of vulvovaginal atrophy may result in dyspareunia, which can negatively affect sexual desire. Other important findings may include genital sensory changes (vulvodynia or neuropathy), pelvic floor muscle contraction (vaginismus), and pelvic floor prolapse, all of which can contribute to sexual dysfunction.

Laboratory evaluation is rarely helpful in the diagnosis of low desire; however, it should be considered as warranted by history and physical examination. Women with physical findings suggestive of hyperprolactinemia or thyroid disease should have prolactin levels and thyroid function tests measured, respectively. Androgen levels alone are not meaningful, because levels have not been shown to correlate with sexual function. Furthermore, the testosterone assays that are currently used are unreliable at the lower levels seen in women.

**TREATMENT CONSIDERATIONS FOR LOW DESIRE**

**Office-Based Counseling for the Obstetrician–Gynecologist**

The complex etiology of low desire often dictates the need for a multifaceted intervention that uses a biopsychosocial approach. Before initiating treatment, it is important to set realistic goals and expectations. Women should be encouraged and empowered to take an active role in their treatment plan.

The value of basic sex education should not be forgotten. Many women demonstrate a lack of knowledge about basic reproductive anatomy and physiology. Having anatomic diagrams and models can help patients gain a better understanding of their bodies and provide them with the vocabulary and knowledge to have effective and meaningful discussions about sex and sexual health. Women should be educated about the heterogeneity of “normal” sexual function. The popular media and society are often sources of misinformation and distorted ideas about sex. Health providers must be ready to identify and dispel myths about sex that can negatively influence sexual behavior.

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**Box 1. Medications Associated With Low Sexual Desire**

**Anticonvulsants**
- Carbamazepine
- Phenytoin
- Primidone

**Cardiovascular and antihypertensive agents**
- Angiotensin-converting enzyme inhibitors
- Amiodarone
- Beta-blockers (atenolol, metoprolol, propranolol)
- Calcium channel blockers
- Clonidine
- Digoxin
- Diuretics (hydrochlorothiazide)
- Lipid-lowering agents

**Hormonal medications**
- Antiandrogens (flutamide, spironolactone)
- Gonadotropin-releasing hormone agonists
- Oral contraceptive pills

**Other**
- Histamine receptor blockers

**Pain relievers**
- Nonsteroidal antiinflammatory drugs
- Opiates

**Psychotropic medications**
- Antipsychotics
- Anxiolytics (alprazolam, diazepam)
- Serotonin norepinephrine reuptake inhibitors
- Serotonin selective receptor inhibitors

**Drugs of abuse**
- Alcohol
- Amphetamines
- Cocaine
- Heroin
- Marijuana
Changes in lifestyle and behavior can help optimize sexual functioning. Gynecologists should not underestimate the effects of providing simple office-based suggestions. Reminding patients that leading a healthy lifestyle through diet, exercise, avoiding tobacco use, and minimizing stress can improve overall well-being and self-esteem, which may make women with low desire more receptive to sexual stimuli or activity. Circumventing boredom and routine by planning romantic encounters or incorporating erotica can foster an environment that optimizes sexual desire. Encourage patients to promote intimacy with one’s partner through shared activities, date nights, and effective communication, which can also help rekindle sexual energy and interest.

The PLISSIT (Permission, Limited Information, Specific Suggestions, Intensive Therapy) model\textsuperscript{37} is an incremental approach to office-based counseling for sexual problems that was designed to assist health care providers who wish to incorporate behavioral and psychological sex therapy techniques into their practice. In this model:

- Women are given permission to discuss their problems and emotions and to explore new solutions (Permission [P]);
- The health care provider gives some basic education specific for sexual function, provides educational resources such as literature, videos, and erotica, or both (Limited information [LI]);
- The health care provider offers specific directives or advice to address the presenting problem (Specific suggestions [SS]); and
- The health care provider gives referral for individual or couples therapy to address hypoactive sexual desire disorder that requires more intensive treatment than the office-based suggestions (Intensive therapy [IT]).

Psychological Interventions

Women who are refractory to office-based counseling should be referred to counselors or therapists with expertise in sexual problems. Psychological interventions include cognitive–behavioral therapy,\textsuperscript{36,37} sex therapy,\textsuperscript{38} and mindfulness training.\textsuperscript{38} Although there is insufficient evidence with regard to controlled trials studying the efficacy of psychological treatment in women with sexual dysfunction, the available evidence suggests significant improvements in sexual function after intervention with traditional sex therapy, cognitive–behavioral therapy,\textsuperscript{39} or both. Psychotherapy is typically favored when the low desire is acquired, situational, or both. In these cases, treatment focuses on modifying precipitating or contributing circumstances or behaviors.

Sex therapy and cognitive–behavioral therapy (individual, couples, or both) are the major treatment approaches represented in the empirical literature. Traditional sex therapy is a behavioral treatment that aims to improve an individual or couple’s erotic experiences while reducing anxiety and self-consciousness about sexual activity. Cognitive–behavioral sex therapy includes traditional behavioral sex therapy components but places a greater emphasis on modifying thought patterns or beliefs that interfere with intimacy and sexual pleasure.\textsuperscript{40} Mindfulness-based cognitive–behavioral treatments have also shown excellent promise for sexual desire problems.\textsuperscript{41} In one of the few empirically tested outcome studies of psychotherapy, Brotto et al\textsuperscript{41} demonstrated that a brief mindfulness-based cognitive–behavioral intervention was successful in improving sexual desire and arousal problems in gynecologic cancer survivors.

Pharmaceutical Interventions

There are no U.S. Food and Drug Administration (FDA)–approved interventions for the treatment of low desire in women. However, some agents are used off-label and several others are currently under clinical development.

Conjugated estrogens and ospemifene are FDA-approved for the treatment of dyspareunia, which can contribute to low or absent desire. Although systemic estrogen has not been shown to improve sexual desire directly, vaginal estrogen significantly improves vaginal atrophy. Ospemifene is a novel selective estrogen receptor modulator with indication for the treatment of vulvovaginal atrophy and dyspareunia in postmenopausal women. A daily dose of 60 mg has been shown to be effective and safe with minimal side effects.\textsuperscript{42,43} Both of these treatments can be useful in the treatment of women who have secondary hypoactive sexual desire disorder as a result of vaginal atrophy and dyspareunia.

Testosterone production is critical for women, both as a major precursor for estradiol production and for its direct actions on androgen receptors throughout the body.\textsuperscript{44} Although it is not FDA-approved for use in women, testosterone is widely prescribed off-label for postmenopausal women throughout the United States.\textsuperscript{45} Substantial evidence suggests that testosterone therapy improves sexual well-being in postmenopausal women with decreased desire.\textsuperscript{46} Improvements have been reported in the number of sexual events reported as satisfactory, sexual desire, pleasure, arousal, and frequency of orgasm as well as a reduction in personal distress. Benefits have been demonstrated in studies of testosterone implants,
oral methyltestosterone, and transdermal testosterone.\textsuperscript{47,48} Data on testosterone treatment in premenopausal women are lacking.

U.S. Food and Drug Administration approval of testosterone use in women has not been achieved as a result of concerns about long-term safety and efficacy. Procter and Gamble submitted an application for a testosterone patch for women (Intrinsa) in 2004, but it was denied by the FDA because of concerns of long-term safety. BioSante Pharmaceuticals Inc.’s testosterone gel for women (LibiGel) failed two large Phase III efficacy studies in 2011.

The potential virilizing effects of exogenous testosterone include development of acne, hirsutism, deepening of the voice, and androgenic alopecia.\textsuperscript{49} However, these effects are dose-related and can be avoided if hormone levels are kept in the female physiologic range. In a 4-year open-label extension safety summary of data of women receiving transdermal testosterone, the most common side effects were application site reactions and unwanted hair growth.\textsuperscript{50,51}

Other important concerns are whether testosterone therapy raises a woman’s risk for cardiovascular disease and breast cancer. So far, there are no studies that have demonstrated a causal role.\textsuperscript{51,52} Transdermal administration avoids first-pass liver effects, thereby avoiding alterations in lipid metabolism.\textsuperscript{44,53} Analysis of data from the Nurses’ Health Study suggested that methyltestosterone users may be at increased risk of breast cancer,\textsuperscript{54} whereas other studies of methyltestosterone use have not shown an increased risk.\textsuperscript{55} A Phase III long-term safety study showed that use of a testosterone transdermal gel did not increase cardiovascular events or breast cancer, even in high-risk women.\textsuperscript{44,55}

Testosterone therapy can be considered in perimenopausal and postmenopausal women for symptoms of decreased desire; however, it remains controversial and caution should be used. Oral formulations are not recommended as a result of its potential negative effects on lipids and liver function tests. The most common formulation used is a transdermal 1% testosterone cream (0.5 g cream = 5 mg testosterone daily) applied to skin of the arms, abdomen, or legs. Testosterone patches and gels formulated for men should be used with caution, because accurate dosing is difficult. Testosterone injections and implants are also available but may be subject to supraphysiologic dosing. Before prescribing testosterone, normal lipid levels and liver function should be documented. Women receiving testosterone therapy should be monitored for potential side effects and lipids and liver function should be reassessed. Free testosterone levels can be assessed to ensure that they remain in the physiologic range for premenopausal women. In all cases, patients must be informed about the lack of long-term published safety data.\textsuperscript{49}

Bupropion is a mild dopamine and norepinephrine reuptake inhibitor and nicotinic acetylcholine receptor antagonist that is used as an antidepressant and smoking cessation aid. In a single-blind study of 51 nondepressed women, 29% responded to treatment with bupropion SR.\textsuperscript{56} A subsequent randomized, double-blind, placebo-controlled study of bupropion (150 mg/day) in 232 premenopausal women without depression also showed a significant increase in desire and decrease in distress in the treated group.\textsuperscript{57} In addition to the treatment of nondepressed women with hypoactive sexual desire disorder, bupropion has been shown to be effective in reversing selective serotonin reuptake inhibitor-induced sexual dysfunction in premenopausal women.\textsuperscript{58}

**Drugs in Development**

Although there are no FDA-approved pharmacologic treatments for hypoactive sexual desire disorder, several are currently in development. Flibanserin is a 5-HT1A receptor agonist and 5-HT2 receptor antagonist that has been studied in more than 11,000 women. Phase III trials have shown 100 mg flibanserin nightly to improve sexual desire, decrease distress, and increased the number of satisfying sexual events. A New Drug Application for treatment for hypoactive sexual desire disorder in premenopausal women was rejected by the FDA in October 2013. A subsequent appeal through a formal dispute resolution has led to additional safety studies currently underway and a resubmission is planned in the Spring of 2015.

Other pharmaceutical agents in development include novel combination drugs that contain sublingual testosterone with a phosphodiesterase inhibitor (Lybriko) or a 5HT1A receptor agonist (Lybridos). Both are proposed to increase sexual motivation through testosterone; however, the addition of the phosphodiesterase inhibitor is thought to increase sexual physiological (vascular) sexual response,\textsuperscript{59} whereas addition of a 5HT1A receptor agonist is thought to act centrally by decreasing sexual inhibition.\textsuperscript{60} Bremelanotide, a melanocortin receptor 4 agonist, is another agent that is being investigated for the treatment of low desire and is also postulated to work through central nervous system mechanisms.\textsuperscript{61}

**Complications of Treatment**

Although gynecologists can diagnose and treat many cases of low desire, there are some that require expert care. The identification of unresolved physical or sexual
trauma, abuse, and the presence of serious psychiatric issues should prompt immediate referral to a specialist. These issues need to be addressed before treating low desire. Women who have lifelong symptoms, psychiatric comorbidities, a partner with sexual dysfunction, or ongoing intrapersonal, interpersonal, and sociocultural issues that affect sexual function can also be particularly challenging and warrant referral to an expert in sexual medicine. Establishing a relationship with a network of health care providers trained in sexual health and medicine is helpful. Organizations such as the International Society for the Study of Women’s Sexual Health (www.ISSWSH.org), the American Association of Sexuality Educators, Counselors and Therapists (www.AASECT.org), and the Society for Sex Therapy and Research (www.SSTARNET.org) have online tools that help people locate health care providers who specialize in sexual health issues.

CONCLUSION
Decreased sexual desire is common among women of all ages and can have negative effects on overall well-being. As frontline providers of women’s health care, gynecologists are in a unique position to effectively diagnose and treat this condition. Sex education, office-based counseling, and medications (including bupropion and testosterone) are viable options in appropriate candidates. Difficult cases warrant referral to specialists in sexual health and medicine. Although there are not any FDA-approved medications for treatment of low sexual desire, several agents are in development.

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