A 60-Year-Old Woman With Sexual Difficulties

Jennifer E. Potter, MD, Discussant

Dr Burns: Ms B is a 60-year-old woman with diabetes, hypertension, hyperlipidemia, and asthma who has noted sexual difficulties since entering menopause. She wonders whether this is normal or whether anything can be done.

Ms B had menarche at 12 years of age. She has been happily married for 38 years and has had 3 pregnancies and 3 children. She reports a diagnosis of endometriosis when she was younger but had no difficulty conceiving. She had regular menses until age 58, when she underwent simultaneous bladder suspension surgery for incontinence and hysterectomy for uterine fibroids. Several months postoperatively she began noticing vaginal dryness, decreased sexual desire, and more difficulty achieving an orgasm. She was treated with esterified estrogen (0.625 mg) and methyltestosterone (1.25 mg) at the time with resolution of her symptoms. She continued this regimen for a couple of years, after which it was stopped due to concerns about adverse effects. More recently she has been treated with estradiol vaginal tablets and subsequently switched to an estradiol vaginal ring because of its ease of use. Ms B found that both of these helped with the vaginal dryness but not her other symptoms. She was recently seen by a new primary care physician who suggested trying bupropion (100 mg daily). Her last Papanicolaou test was done a couple months ago and her last mammogram was done about a year ago; results of both were normal.

She was recently diagnosed with diabetes and is now treated with metformin (500 mg daily), with a hemoglobin A1c value of 7.6%. She was also recently noted to have hyperlipidemia and was prescribed pravastatin (40 mg daily) for a total cholesterol level of 307 mg/dL (7.95 mmol/L), high-density lipoprotein (HDL) cholesterol level of 57 mg/dL (1.48 mmol/L), and a calculated low-density lipoprotein (LDL) level of 229 mg/dL (5.93 mmol/L). Her blood pressure has been well controlled with lisinopril (20 mg daily). She has allergic asthma that is well controlled with montelukast (10 mg daily). She notes occasional back pain for which she takes cyclobenzaprine (two 10-mg tablets at bedtime) with good relief. She is allergic to ciprofloxacin with development of a rash.

She currently works as a psychologist. She walks 45 minutes daily, has never smoked, and denies any significant alcohol intake.

Ms B: Her View

My perception of it isn’t so much as a dysfunction as an awareness that since menopause, a few years before actual menopause, that it was more of a challenge to really focus on my own sexuality and that upon arousal, when my husband and I would make love, that it takes a little more work now. I just started to feel nowhere near as much desire as I normally did. Things were not as stimulating, and it just became a challenge instead of an adventure.

A growing body of evidence is available to guide care for women with sexual concerns. This article considers the case of a 60-year-old woman who with menopause developed decreased libido, rapidity of sexual arousal, and intensity of orgasm. She requests information about strategies to optimize sexual function. Effects of aging and menopause on female sexual response are reviewed and an evaluation approach presented to help clinicians respond productively to women who request intervention. The effectiveness and safety of different treatment options are discussed, including education, lifestyle changes, counseling, medications, mechanical devices, and pelvic floor exercises; recommendations are made to help postmenopausal women maximize sexual pleasure and satisfaction.

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Within a couple of months after the hysterectomy I noticed real dryness and at that time, I tried Estratest, half-strength. I did that for a couple of years, and it worked very, very well. All of a sudden it just seemed that my response, sexually, was just a great deal—it was almost like turning the volume up. The real change I experienced was that it was not work any longer, to respond sexually.

Then, there was such a concern about getting everyone off of hormones, and I stopped taking them at that time. I began using the cervical ring, I find that it helps the dryness, but my sexual desire is just not the same as when I was younger.

We really have enjoyed our sexual relationship. And I think it’s part of the fusion in our relationship and so it’s very, very hard to give that up. Even though you know you’re getting older and it might be normal, it’s still hard to get rid of the desire to function more fully.

**AT THE CROSSROADS: QUESTIONS FOR DR POTTER**

How does female sexuality change with menopause? How do you distinguish “normal” from dysfunction? What is the pathophysiology of female sexual dysfunction (FSD) in menopausal women? What evaluation is appropriate for the menopausal woman who has a new sexual difficulty? What are the available treatment options and what are the data to support their efficacy? What do you recommend for Ms B? What does the future hold for this area of medicine?

**DR POTTER:** Ms B is a 60-year-old woman who notes changes in sexual function since menopause. She is happily married, and her sexual relationship with her husband is important to her. She is not alone: in a multiethnic sample of 3262 midlife women, 79% had engaged in sexual activity with a partner in the preceding 6 months, and a third considered sex to be very important.\(^1\) However, Ms B misses her younger years, when she felt a higher level of desire, became more quickly aroused, and achieved orgasm more readily.

**Physiology of Normal Female Sexual Function**

Normal sexual function requires intact neural, vascular, and muscular circuitry; complex interactions between multiple neurotransmitter systems; and modulating influences from the endocrine system. Animal and human studies done to date have identified a number of neurotransmitters, bioactive substances, and sex steroids that appear to play a role, including dopamine, norepinephrine, serotonin, acetylcholine, nitric oxide, vasoactive intestinal peptide, prostaglandin \(E_1\), estrogen, testosterone, progesterone, oxytocin, prolactin, and \(\alpha\)-melanocortin–stimulating hormone.\(^2\) The field is young, and details regarding specific sites of action (central, peripheral, or both) and effects on sexual function (excitatory, inhibitory, or neutral) remain to be elucidated.

Clinically, it is useful to consider 3 functional domains of sexual response—desire, arousal, and orgasm—separately. Desire includes 2 components: spontaneous or “innate” sex drive, and cognitive motivation.\(^3\) It is not necessary to have an intact sex drive to enjoy a satisfying sexual life. Diverse cognitive incentives lead women to initiate or participate in sexual activity,\(^4\) including the wish to feel close to a partner, give and/or receive sexual pleasure, relieve tension, or (in reproductive-age women) conceive. No matter what motivates a woman to engage in sexual activity, arousal can proceed in the presence of appropriate erotic stimulation and intact physiological pathways and in the absence of inhibiting influences. Sexual arousal includes both subjective excitement (awareness of, comfort with, and appreciation of erogenous stimulation) as well as objectively measurable signs of physiological (both nongenital and genital) arousal.\(^5\) It is important to make this distinction, as studies show that women often experience measurable physiological arousal in the absence of a subjective sense of excitement or pleasure.\(^6\) Box 1 shows physiological, psychological, relational, and sociocultural variables that affect female sexual response.\(^2\)

**Changes in Female Sexuality With Aging and Menopause**

Most studies suggest a normative and gradual decline in desire with age. In addition, many women describe a decline specifically associated with menopause; this notion is corroborated by some population studies.\(^7,8\) However, a decrement in desire does not occur in all women during the menopausal transition. For example, in a survey of 580 menopausal women, 45% of the respondents reported a decrease in sexual desire after menopause, whereas 37% reported no change, and 10% actually noted an increase.\(^9\) On the other hand, changes in arousal clearly are associated with menopause. Genital perfusion, engorgement, and vaginal lubrication decrease, as do touch perception and vibratory sensation.\(^10\) Orgasmic capacity is maintained as women age, although clitoral stimulation typically needs to be more direct, more intense, and of longer duration for arousal to lead to climax.\(^10\) Decreased muscle tension in the pelvic floor and decreased uterine contractions during climax may diminish the intensity of orgasm and result in more rapid resolution; in addition, uterine contractions sometimes become painful.\(^10\) However, overall perception of satisfaction tends to be preserved.\(^9\)

Modulating effects of estrogen and androgen likely explain many of the changes in sexual function that are associated with both endogenous and exogenous hormone exposure. Low estrogen levels are associated with vulvovaginal changes, including vaginal dryness, pain during vaginal penetration, and dyspareunia.\(^11\) Although supporting data are limited, low androgen levels have been linked to decreased sexual desire, genital sensation, and genital response.\(^12\)

Age, natural menopause, and oophorectomy have differential effects on circulating hormone levels. Estradiol levels decrease sharply across the menopausal transition. In contrast, circulating androgen levels decline most steeply dur-
ing the early reproductive years, do not accelerate as a consequence of natural menopause, and may even increase slightly during later life.\textsuperscript{13} It is unclear what accounts for these changes. Some studies suggest a decline in sex hormone-binding globulin (SHBG) levels across the menopausal transition\textsuperscript{14} or with advancing age,\textsuperscript{15} while others\textsuperscript{13,16} demonstrate higher SHBG levels among older women. Some,\textsuperscript{13,17} but not all,\textsuperscript{18} studies show that the postmenopausal ovary continues to produce preandrogens and testosterone. Bilateral oophorectomy is associated with a decline in both estrogen and androgen levels,\textsuperscript{19,20} which helps explain why women who undergo surgical menopause appear to be more likely to develop sexual problems.\textsuperscript{21} Timing of surgery has differential effects: perimenopausal women who undergo elective oophorectomy are at lower risk than younger women who experience menopausal changes more precipitously.\textsuperscript{22,23}

A number of factors, in addition to aging and menopause, may be contributing to Ms B’s reduced sexual satisfaction. Psychological and relationship factors include unrealistic expectations in the context of being in a long-term relationship and getting older, body image concerns, and the appropriateness of the couple’s sexual techniques to the needs of their changing bodies.\textsuperscript{24} Physiological considerations include damage to pelvic nerves during prior surgeries, neurovascular injury related to atherosclerosis and diabetes mellitus, and adverse effects of medications.

The incidence and severity of sexual problems after hysterectomy depend on preoperative sexual function and psychosocial state, the degree to which the surgery alleviates the symptoms for which it was performed, and the extent of the surgical procedure.\textsuperscript{25} Surgical technique (blood vessel and nerve sparing) is probably a key factor. Detrimental effects of supracervical or total hysterectomy done for benign indications, as in Ms B’s case, are rare.\textsuperscript{26} Surgery for stress incontinence results in improvement in sexual function in many women; however, sexual dissatisfaction due to dyspareunia or orgasmic dysfunction after surgery is also reported.\textsuperscript{27} Animal studies demonstrate that atherosclerosis inhibits vaginal and clitoral engorgement and leads to diffuse vaginal wall and clitoral cavernosal smooth muscle fibrosis.\textsuperscript{28} Experimental hyperglycemia appears to induce similar alterations in vaginal blood flow and structure.\textsuperscript{28}

Sexual adverse effects have been associated with numerous medications. Good-quality evidence implicates antidepressants (especially selective serotonin reuptake inhibitors [SSRIs]) and dopamine receptor blockers in both sexes\textsuperscript{29}, limited data suggest that central nervous system depressants and estrogen-, androgen-, or cholinergic-antagonists also have negative effects.\textsuperscript{30} Several antihypertensive medications (centrally acting sympatholytic agents, \(\beta\)-blockers, diuretics) have sexual adverse effects in men; calcium channel blockers and angiotensin-converting enzyme inhibitors are usually sex neutral.\textsuperscript{31} Very few studies have investigated effects in women specifically.\textsuperscript{32} Medications likely contribute little to Ms B’s sexual problems, since she does not take any of the common culprits on a regular basis.

**Box 1. Factors That Affect Female Sexual Response**

The following physiological, psychological, interpersonal, and sociocultural factors may all contribute to female sexual dysfunction:

**Physiological Factors**
- Aging
- Hormonal changes
- Medical illness
- Injury or disability
- Prescription medications
- Substance use or abuse

**Psychological Factors**
- Lack of self-acceptance (gender identity, sexual orientation)
- Poor body image
- Low self-esteem
- Unrealistic expectations
- Performance anxiety
- Mental health problems
- Prior physical or sexual abuse
- Sexual inexperience
- Stress

**Interpersonal Factors**
- No partner
- Lack of attraction to partner
- Dissatisfaction with nonsexual aspects
- Unresolved conflicts
- Discrepant desire
- Inadequate stimulation or poor technical skill
- Excessive intercourse orientation
- Excessive goal (orgasm) orientation
- Poor communication of needs and preferences
- Sexual problem with partner
- Predictable/boring sexual routine
- Lack of time or privacy

**Sociocultural Factors**
- Inadequate education
- Conflict with religious or family values
- Cultural taboos

*Based on information from Goldstein et al.\textsuperscript{2}
Box 2. The History in Women Who Report Sexual Problems

A. Determine affected functional domains
   - Do you notice a change in your interest in sex?
   - Do you have trouble becoming aroused or sufficiently lubricated?
   - Are you able to reach orgasm?
   - Do you experience discomfort or pain during sex?

B. Ask detailed questions to determine the:
   - Severity of the problem (global vs situational)
   - Chronicity of the problem (primary vs secondary)
   - Context in which the problem has developed

C. Include both members of a couple in the evaluation whenever possible
   - Patient’s level of distress, reasons for seeking help, and response to previous interventions

D. Sample questions for women with low desire:
   - How would you rate your level of desire when it was highest (grade on 0-10 scale)? How about now?
   - When did you notice a change in your level of desire? What do you think is responsible?
   - Can you identify any inhibiting feelings or thoughts that interfere with your level of desire?
   - Are you participating in sexual activities even though your level of desire has changed? If so, what motivates you?

E. Sample questions for women with decreased arousal:
   - When did you notice a change in your level of arousal? What do you think is responsible for the change?
   - Do you experience any pleasurable sensations during sexual stimulation? If yes, can you identify inhibiting feelings or thoughts that interfere with arousal and prevent orgasm?

F. Sample questions for women with difficulty achieving orgasm:
   - Have you ever had an orgasm?

*Based on information from Basson45 and Nusbaum and Hamilton.46

†The questioner must be prepared to respond appropriately when a patient discloses rape or partner violence.
are indicated when sexual difficulties persist over time, cause a satisfying sexual life for one woman may seem woefully which they would like help.37 However, when personal response believe they have a problem or feel distress for to one half of women who report decreased desire or consider themselves to have “dysfunction”: only one third inflated, since not all persons who report “difficulties” in women are sparse. In 3 large population studies that included midlife women, the percentage of participants reporting sexual difficulties ranged widely, from 30% to 71%.34-36 This variation reflects differences in specific questions asked, time intervals studied, demographic of the study populations, and whether individuals without partners were included. The numbers may be inflated, since not all persons who report “difficulties” consider themselves to have “dysfunction”: only one third to one half of women who report decreased desire or response believe they have a problem or feel distress for which they would like help.37 However, when personal distress and the desire for intervention are factored in, revised prevalence estimates (10%-35% of women in the aforementioned studies)34-36 indicate that clinically significant sexual problems are common.

**Appropriate Evaluation for a Menopausal Woman With Sexual Concerns**

Assessment should always begin with a comprehensive history. Several validated questionnaires used predominantly in research can identify affected sexual function domains and measure response to treatment interventions.38-43 These instruments can be useful adjuncts during initial evaluation and follow-up of women with sexual difficulties; however, they do not delve deeply enough into intrapersonal and interpersonal aspects of sexual function to substitute for a thorough medical, sexual, and psychosocial history.44 Productive areas of inquiry have been suggested by several authors45,46; sample questions are outlined in Box 2.

Although few studies have evaluated the reliability and reproducibility of the physical examination to diagnose sexual problems, findings may be discovered that suggest specific etiologies or guide therapy (TABLE 1).44 Very few studies have objectively measured physical effects of either hysterectomy or diabetes on female sexual function; however, clinical observation suggests there is an association. One small study (N = 27) documented reduced vaginal vibratory sensation following hysterectomy47; reduced clitoral blood flow (measured by Doppler ultrasound) has been observed in diabetic compared with euglycemic female rabbits.48 Therefore, a detailed genital examination should be performed and the integrity of pelvic blood vessels and nerves assessed in women like Ms B who present with arousal problems. In addition, both resting pelvic floor muscle tone and the strength of voluntary vaginal/anal sphincter contraction a patient is able to generate during digital vaginal/rectal examination should be noted.49

Measurement of cardiovascular risk factors and hormonal profile have been recommended by expert consensus44; however, few data from randomized controlled trials (RCTs) support this approach. Serum androgens are not useful diagnostically50 because there are no precise definitions of androgen deficiency, the “normal” ranges for serum androgens in women of different ages are poorly characterized, the accuracy of available testosterone assays in women is questionable, and 2 large population studies failed to show a correlation between low serum testosterone level and low sexual desire.51,52 Appropriate laboratory testing is reasonable when hyperprolactinemia, hypothyroidism, or anemia are suspected.

### Distinguishing Normative Changes From Dysfunction

Women vary considerably in how they rate the importance of sex, the specific sexual practices they choose to participate in, the frequency of sexual activity they feel is optimal, and the intensity and duration of stimulation they need to achieve arousal and orgasm.33 Therefore, what might be a satisfying sexual life for one woman may seem woefully inadequate to another. Diagnosis and medical assessment are indicated when sexual difficulties persist over time, cause distress, and when, as with Ms B, the patient requests evaluation and intervention.53

Good quality data that assess the prevalence of sexual difficulties in women are sparse. In 3 large population studies that included midlife women, the percentage of participants reporting sexual difficulties ranged widely, from 30% to 71%.34-36 This variation reflects differences in specific questions asked, time intervals studied, demographics of the study populations, and whether individuals without partners were included. The numbers may be inflated, since not all persons who report “difficulties” consider themselves to have “dysfunction”: only one third to one half of women who report decreased desire or response believe they have a problem or feel distress for which they would like help.37 However, when personal distress and the desire for intervention are factored in, revised prevalence estimates (10%-35% of women in the aforementioned studies)34-36 indicate that clinically significant sexual problems are common.

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### Treatment Options

Investigation of FSD is an evolving area. Methodological challenges include a lack of consensus regarding the definition of FSD, relevant inclusion and exclusion criteria (age, menopause etiology, partnership status, sexual orientation, frequency of sexual activity, concurrent health conditions, disallowed medications), use of outcome measures that are

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**Table 1. The Physical Examination in Women Who Report Sexual Problems**

<table>
<thead>
<tr>
<th>Feature/Examination Maneuver</th>
<th>Anatomic Feature</th>
<th>Possible Source of Sexual Difficulty</th>
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</thead>
<tbody>
<tr>
<td>Blood pressure, peripheral pulses</td>
<td>Atherosclerosis</td>
<td>Nongenital</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Hypothyroidism</td>
<td>Nongenital</td>
</tr>
<tr>
<td>Breasts</td>
<td>Hyperprolactinemia (nipple discharge)</td>
<td>Nongenital</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Osteoarthritis and other conditions that limit comfort and mobility</td>
<td>Nongenital</td>
</tr>
<tr>
<td>Neurological</td>
<td>Neurological impairment</td>
<td>Nongenital</td>
</tr>
<tr>
<td>Vulvar skin inspection</td>
<td>Lesions associated with infection (candida, herpes), dermatitis (eczema, psoriasis, allergic), dermatoses (lichen)</td>
<td>Vulvar</td>
</tr>
<tr>
<td>Labia majora and minora</td>
<td>Atrophy, lesions, adhesions</td>
<td>Vulvar</td>
</tr>
<tr>
<td>Clitoris</td>
<td>Phimosis, adhesions, female genital circumcision</td>
<td>Female genital</td>
</tr>
<tr>
<td>Urethra</td>
<td>Infection, prolapse</td>
<td>Female genital</td>
</tr>
<tr>
<td>Vaginal introitus</td>
<td>Atrophy, lesions, scarring, stricture</td>
<td>Female genital</td>
</tr>
<tr>
<td>Vagina</td>
<td>Intact hymen, atrophy, lesions, discharge</td>
<td>Female genital</td>
</tr>
<tr>
<td>Valsaiva maneuver</td>
<td>Cystocele, rectocele, uterine prolapse, urinary incontinence</td>
<td>Female genital</td>
</tr>
<tr>
<td>Bimanual examination</td>
<td>Masses, pain</td>
<td>Female genital</td>
</tr>
<tr>
<td>Vaginal and rectal muscle contraction</td>
<td>Poor tone</td>
<td>Female genital</td>
</tr>
<tr>
<td>Bulbocavernosus reflex</td>
<td>Pudendal neuropathy</td>
<td>Genital</td>
</tr>
</tbody>
</table>

*Based on information from Hatzichristou et al44 and Basson.45*
both rigorous and clinically meaningful, and adequate duration in which to detect therapeutic and adverse effects. The best studies are appropriately powered, include a clear definition of the study population and appropriate entry criteria, and use end points such as a change in the number of satisfying sexual events recorded in a daily diary or improvement in various sexual function domains as assessed by validated questionnaires.

Available interventions include education and lifestyle changes, counseling, medications, mechanical devices, and pelvic floor exercises, although data from good quality RCTs to support many of these treatment options remain limited. When a woman like Ms B experiences sexual difficulties, there is almost never just one cause; similarly, there is usually no quick fix. To achieve maximal effect, interventions should address each area of distress (psychological, interpersonal, sociocultural, physiological) and attend to each affected functional domain (desire, arousal, orgasm).

**Education and Lifestyle Changes**

Many women have unrealistic expectations about sex and feel that they should be immediately and reliably aroused, despite normal distractions or age-related changes. Education alone can be extremely beneficial. For example, it is important to acknowledge that Ms B’s diminished sex drive represents a loss, but her wish to remain close to her husband should be celebrated, as it provides sufficient impetus to participate in intimate activities. Similarly, it is important to explain that increased intensity and duration of genital stimulation, particularly of the clitoris, are likely to enhance her ability to experience more rapid arousal and stronger orgasms.

Lubricants can be very helpful for women like Ms B who experience vaginal dryness. Unlike vaginal moisturizers, which penetrate and hydrate vaginal cells, lubricants coat the mucosal surface, resulting in decreased friction, trauma, and discomfort during penetrative sex. Available lubricants include water-, oil-, and silicone-based products. Selection should be based on safety, palatability, and glide. Oil-based and silicone lubricants last longest and produce the best glide during penetrative sex. However, oil-based substances degrade latex: only water-based lubricants should be used with latex condoms.

Simple lifestyle measures can enhance sexual interest. Ms B and her husband should be encouraged to maximize opportunities for intimacy by making “dates.” If they are open-minded, the use of versatile sexual techniques, as well as experimentation with different sexual positions, venues, sex toys, fantasy, and erotica, can be suggested as means to add “spice” to their sexual relationship and eliminate routines. Strategies that enhance comfort can also be recommended, including relaxing in a warm bath prior to sex, trying position changes, and strategically dosing mild analgesics prior to sexual activity in patients with arthritis or other musculoskeletal pain.

**Counseling**

Referral for individual, couples, or sex therapy can be helpful when psychological problems or couples issues are present. For Ms B, this might include individual counseling to address body image issues and her feelings about growing older. The purpose of sex therapy is to help women become more aware of and comfortable with sexual feelings, identify thoughts or behaviors that interfere with sexual enjoyment, learn what kind of stimulation is most pleasurable, and enhance communication of sexual needs to their partners.

**Medications**

TABLE 2 and TABLE 3 summarize the best available evidence regarding pharmacological interventions.

**Hormone Therapies.** Ms B previously received an oral preparation of esterified estrogen and methyltestosterone ( Estratest, Solvay Pharmaceuticals, Marietta, Ga) with improvement in sexual function. This improvement she experienced could be due to the estrogen component, the androgen component, or both. Observational data demonstrate an association between endogenous estradiol level and sexual comfort and satisfaction. Few RCTs have examined the effects of systemic estrogen therapy (doses that raise serum levels significantly) on female sexual function specifically. Some of these trials are older, had small sample sizes, or used inadequate outcome measures; however, several conclusions can be drawn. Systemic estrogen reduces vaginal atrophy and improves sexual function in lubrication, comfort, and perhaps orgasm domains, but effects on sexual activity and desire have not been consistently demonstrated. Limited evidence suggests that high doses of conjugated equine estrogen (>0.625 mg/d or the equivalent) are required to achieve central effects. The addition of progestin mutes estrogen’s sexual benefits and is associated with more adverse effects; however, the need for endometrial protection merits this practice in women with an intact uterus. Importantly, use of systemic estrogen with or without progestin is limited by cardiovascular safety considerations, and these therapies are not approved by the US Food and Drug Administration for sexual indications. When short-term systemic estrogen is contemplated for treatment of vasomotor symptoms, choice of therapy is important. Oral estrogens increase SHBG levels and may affect desire negatively; therefore, transdermal estrogens that avoid the hepatic first-pass effect are preferable to oral formulations. Systemic estrogen is contraindicated for Ms B due to its cardiovascular risks.

Vaginal estrogen decreases vaginal dryness and dyspareunia at least as well as systemic estrogen and with fewer systemic adverse effects. Small studies suggest that topical androgen also restores vaginal tissue integrity and increases the genital vasocerestration associated with sexual arousal, but efficacy and safety data from larger randomized trials are needed to confirm these findings. Randomized
<table>
<thead>
<tr>
<th>Source</th>
<th>Design, Purpose</th>
<th>Study Population</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Clinical Response</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dennertstein et al.</td>
<td>12-mo RCT, double-blind placebo crossover comparing effects of estrogen, progesterin, and estrogen + progesterin</td>
<td>N = 49, age 53-53 y, surgically menopausal</td>
<td>3-mo treatment crossover, no washout; 4 medication groups: EE 50 µg/d, levonorgestrel 250 µg/d, combination therapy, placebo</td>
<td>Monthly interviews by 1 investigator; daily subjective assessments</td>
<td>vs placebo, EE increased sexual enjoyment (P &lt; 0.05), vaginal lubrication, and desire (P &lt; 0.01); frequency of orgasm increased in all groups (testosterone &gt; estrogen + progesterone &gt; progesterone &gt; placebo); no effect on colitis frequency</td>
<td>Magnitude of drug effect on orgasm frequency not influenced by including hot flush frequency as a covariate; 13 women withdrew from study; no differences in type of drug taken at time of withdrawal</td>
</tr>
<tr>
<td>Sherwin, et al.</td>
<td>12-mo RCT, double-blind placebo, comparing effects of 2 doses of estrogen with and without progesterin</td>
<td>N = 48, age 47-57 y, naturally menopausal, healthy women, intact uterus</td>
<td>4 study groups: (A) 0.625 mg/d EE (days 1-25)/MPA 5 mg/d (days 15-25); (B) 0.625 mg CEE/placebo; (C) 1.25 mg CEE/MPA 5 mg; (D) 1.25 mg CEE/placebo</td>
<td>Daily Menopause Rating Scale, Menopausal Index</td>
<td>Desire and arousal higher during the first 2 wk than during wk 4 when no hormones administered (P &lt; 0.05)</td>
<td>More withdrawals (excessive bleeding, abdominal bloating) were seen in group C (P &lt; 0.01)</td>
</tr>
<tr>
<td>Nathorst-Boos, et al.</td>
<td>12-wk RCT, double-blind, placebo vs transdermal estradiol</td>
<td>N = 242, age 45-65 y, naturally postmenopausal women requiring hormone therapy for climacteric symptoms</td>
<td>Transdermal estradiol (estradiol 50 µg/24 h), administered twice/wk vs placebo; no progesterin</td>
<td>McCoy Sex Scale Questionnaire, 4 QOL questionnaires</td>
<td>Increased satisfaction with frequency of sexual activity (P = 0.04), sexual fantasies (P = 0.003), degree of enjoyment (P = 0.02), vaginal lubrication (P = 0.006), and decreased pain during intercourse (P = 0.0003); frequency of arousal and orgasm were unaffected</td>
<td>No differences regarding sexual items between groups at baseline; follow-up study using the same data (Wicklund et al. [1993]) found that health-related QOL (P = 0.0003) and well-being (P = 0.003) improved more in the treatment group</td>
</tr>
<tr>
<td>Simun et al.</td>
<td>12-mo RCT, double-blind placebo vs combined estrogen + progesterin</td>
<td>N = 16,608, age 50-79 y, naturally postmenopausal women with intact uterus and moderate-severe postmenopausal symptoms</td>
<td>Oral estrogen (CEE) 0.625 mg/d/MPA 2.5 mg/d vs placebo</td>
<td>Nonvalidated, single-question item with 4-point response scale</td>
<td>No significant effect on sexual satisfaction</td>
<td>Increased risk for myocardial infarction, stroke, venous thromboembolism, breast cancer (described elsewhere)</td>
</tr>
<tr>
<td>Suicking et al.</td>
<td>Cochrane review of 19 randomized trials</td>
<td>Pooled N = 1462 (50-1012), only 4 studies had an N ≥ 200), age 36-85 y; natural or surgical menopause, 3-12 mo</td>
<td>Estrogen-based vaginal creams, slow-release estradiol tablet, estradiol-releasing silicone ring, nonhormonal moisturizing gel</td>
<td>Objective and clinician- and patient-based subjective measures; variable safety and acceptability measures</td>
<td>All forms of vaginal estrogen administration reduced atrophic changes (including dyspareunia) more than placebo; estrogen cream reduced vaginal dryness more than nonhormonal moisturizing gel; serum estradiol level was higher with cream vs tablets</td>
<td>Adherence to treatment, comfort, and ease of use were all significantly higher with the ring and tablets vs creams; adverse effects: endometrial proliferation and hyperplasia; vaginal creams associated with higher incidence of uterine bleeding and breast pain than tablets</td>
</tr>
<tr>
<td>Long et al.</td>
<td>3-mo randomized study comparing effects of oral and vaginal estrogen on vaginal blood flow and sexual function</td>
<td>N = 73, mean age 53.3 y (oral group) vs 54.3 y (vaginal group), postmenopausal women with prior hysterectomy, elevated FSH &gt; 40 IU/L, estradiol level &gt; 20 pg/mL</td>
<td>Oral estrogen (CEE) 0.625 mg/d vs vaginal estrogen cream 0.625 mg/d</td>
<td>Pelvic examination, introtal Doppler ultrasound, personal interviews for sexual symptoms using a validated questionnaire</td>
<td>Decreased prevalence of anorgasmia in both groups; improvement in vaginal dryness and dyspareunia domains significant only in vaginal estrogen group; no change in libido or colital frequency in either group</td>
<td>Adverse effects not stated</td>
</tr>
<tr>
<td>Lobo et al.</td>
<td>16-wk RCT, double-blind placebo vs methyltestosterone</td>
<td>N = 218, age 40-65 y, natural or surgically menopausal women receiving moderate-dose oral estrogen</td>
<td>Oral esterified estrogen (0.625 mg) + methyltestosterone 1.25 mg/d vs estrogen 0.625 mg/d + placebo</td>
<td>Increased sexual interest and desire subscore on SIQ; 2-fold increase in sexual responsiveness score on BISF-W</td>
<td>Baseline levels of total and bioavailable testosterone similar in both groups; increased bioavailable testosterone and SHBG observed in treatment group (P &lt; 0.01); no significant difference in adverse effects except decreased HDL-C in combination therapy group</td>
<td>(continued)</td>
</tr>
<tr>
<td>Source</td>
<td>Design, Purpose</td>
<td>Study Population</td>
<td>Intervention</td>
<td>Outcome Measures</td>
<td>Clinical Response</td>
<td>Comments</td>
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<tr>
<td>Warnock et al., 2005</td>
<td>8-wk RCT, double-blind placebo vs methyltestosterone</td>
<td>N = 102, age 52-62 y, surgically menopausal women receiving high-dose oral estrogen</td>
<td>Oral estrogen (EE 1.25 mg + methyltestosterone 2.5 mg/d vs EE 1.25 mg/d + placebo)</td>
<td>CSFQ-F-C, SES, MSIQ, Improvement in the WHQ, serum hormone concentrations</td>
<td>Treatment with EE + methyltestosterone, but not EE, increased mean concentration of bioavailable EE (<em>P</em> &lt; .001) and free EE (<em>P</em> &lt; .001) testosterone and suppressed levels of SHBG (<em>P</em> &lt; .001); weight gain, nervousness, weight gain, nervousness, vaginitis, acne, and hirsutism; significant decrease in HDL-C (−17.7 ± 9.9 mg/dL, <em>P</em> &lt; .001) was observed in EE + methyltestosterone group</td>
<td>Overall large placebo response; no change in sexual activity was shown according to the daily diary, but there was a high degree of nonadherence in adverse effects</td>
</tr>
<tr>
<td>Shifren et al., 2000</td>
<td>12-wk RCT, double-blind placebo vs testosterone patch</td>
<td>N = 75, age 31-56 y, surgically menopausal women receiving moderate-dose oral estrogen; free testosterone &lt; 3.5 pg/mL or serum testosterone concentration &lt; 30 ng/dL</td>
<td>Oral estrogen (CEE 0.625 mg/d + 150 or 300 µg transdermal testosterone twice weekly or placebo) BISF-W, daily diary (fantasies, desires, sexual activity), serum hormone concentrations</td>
<td>BISF mean composite score increased from 52% ± 27% at baseline to 72% ± 38% placebo, 74% ± 37% during 150 µg of testosterone, and 81% ± 37% with 300 µg of testosterone (<em>P</em> = .05 vs placebo)</td>
<td>Overall large placebo response; no change in sexual activity was shown according to the daily diary, but there was a high degree of nonadherence in adverse effects</td>
<td></td>
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<tr>
<td>Braunstein et al., 2005</td>
<td>24-wk RCT, double-blind placebo vs testosterone patch</td>
<td>N = 447, age 24-70 y, surgically menopausal women receiving oral estrogen</td>
<td>Oral estrogen - either of 3 doses of transdermal testosterone (150, 300, or 450 µg) applied twice weekly, or placebo</td>
<td>SAL, PFSF, PDS, serum hormone levels, lipids, liver function tests, clinical assessment of alopecia, hirsutism, acne</td>
<td>300-µg patch: satisfying sexual episodes per week increased 79% from baseline vs in placebo; no significant differences in the 150-µg or 450-µg dose</td>
<td>Study failed to demonstrate a dose-response effect; no significant difference in adverse effects</td>
</tr>
<tr>
<td>Buster et al., 2005</td>
<td>24 wk RCT, double-blind placebo vs testosterone</td>
<td>N = 533, mean age 48.3 y (testosterone group) vs 49.5 y (placebo group), surgically menopausal women receiving oral or transdermal estrogen</td>
<td>Oral or transdermal estrogen + 300 µg testosterone (EE 300 µg testosterone patch applied twice weekly vs placebo)</td>
<td>SAL, PFSF, PDS, serum hormone levels, lipids, liver function tests, measures of carbohydrate metabolism, clinical assessment of alopecia, hirsutism, acne</td>
<td>Testosterone patch increased satisfying sexual episodes by 1.56 per 4 wk vs 0.73 for placebo (<em>P</em> = .001); total orgasms increased more with testosterone</td>
<td>Testosterone concentrations of total, free, and bioavailable testosterone similar between treatment groups at baseline, and increased in testosterone group at wk 12 and wk 24; changes in all testosterone levels at wk 24 significantly correlated with changes in frequency of satisfying activity, sexual desire, and personal distress; no significant difference in adverse effects</td>
</tr>
<tr>
<td>Simon et al., 2005</td>
<td>24-wk RCT, double-blind placebo vs testosterone patch</td>
<td>N = 562, age 26-70 y, surgically menopausal women receiving oral or transdermal estrogen</td>
<td>Oral or transdermal estrogen + 300 µg testosterone (EE 300 µg testosterone patch applied twice weekly vs placebo)</td>
<td>SAL, PFSF, PDS, serum hormone levels, lipids, liver function tests, measures of carbohydrate metabolism, clinical assessment of alopecia, hirsutism, acne</td>
<td>Testosterone patch increased satisfying sexual episodes 2.10 vs 0.73 (<em>P</em> = .0003) and total orgasms 2.19 vs 0.97 (<em>P</em> = .0002) per 4 wk compared with placebo</td>
<td>Adverse effects similar in each group</td>
</tr>
<tr>
<td>Shifren et al., 2006</td>
<td>24-wk RCT, double-blind placebo vs testosterone patch</td>
<td>N = 549, age 40-70 y, naturally menopausal women receiving oral estrogen = progestin</td>
<td>Oral estrogen + 300 µg testosterone patch applied twice weekly vs placebo; women with intact uterus also received progestin (various forms)</td>
<td>SAL, PFSF, PDS, serum free, total, and bioavailable testosterone, total estradiol, estrone, testosterone, total cholesterol, triacylglycerides, lipids, and plasma testosterone, concentrations with greatest than placebo at 24 wk (<em>P</em> = .0017 and <em>P</em> = .0015, respectively)</td>
<td>Total, free, and bioavailable testosterone increased in the testosterone group at wk 12 and wk 24; statistically significant correlations were observed between efficacy end points of the SAL, PFSF, and PDS and changes in serum testosterone levels at wk 24; adverse effects not significantly different</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BISF-W, Brief Index of Sexual Functioning for Women; CEE, conjugated equine estrogen; CSFQ-F-C, Changes in Sexual Functioning Questionnaire; EE, ethinyl estradiol; FSH, follicle-stimulating hormone; HDL-C, high-density lipoprotein cholesterol; MPA, medroxyprogesterone acetate; MSIQ, Menopausal Sexual Interest Questionnaire; PDS, Personal Distress Scale; PFSF, Profile of Female Sexual Function; QOL, quality of life; RCT, randomized controlled trial; SAL, Sexual Activity Log; SES, Sexual Energy Scale; SHBG, sex hormone-binding globulin; SIQ, Sexual Interest Questionnaire; WHQ, Women’s Health Questionnaire.

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controlled trials comparing the effectiveness, safety, and acceptability of various vaginal estrogens have been reviewed extensively. All forms of vaginal estrogen administration (cream, tablet, ring) are effective. Overall adverse events (vaginal irritation, discharge, bleeding, urinary incontinence, ring expulsion in the setting of previous hysterectomy, breast enlargement, edema, migraine) are infrequent. Long-term, intravaginal use of estrogen cream should be avoided as it results in significant systemic absorption. Both tablets and ring relieve atrophy with minimal systemic absorption and acceptable adherence to treatment, comfort, and ease of use. The addition of progestin to prevent endometrial hyperplasia is generally not advocated; however, evidence for endometrial safety beyond 1 year of use is lacking. Ms B uses the ring with good effect; it is reasonable for her to continue this practice.

The combination of estrogen plus testosterone (intramuscular injection, implanted pellet, oral, or transdermal) improves sexual function in postmenopausal women more than estrogen alone in all studies that have used validated questionnaires. As noted in Table 2, the addition of oral methyltestosterone to systemic estrogen increases sexual responsiveness and desire at the expense of a significant decrease in HDL cholesterol level. Results from 5 more recent, multicenter RCTs that studied the effects of adding transdermal testosterone to systemic estrogen are more encouraging. Four of these trials were performed in surgically menopausal women with hypoactive sexual desire disorder (HSDD) (combined N = 1619). Benefits were modest, with women receiving the 300-µg testosterone patch reporting approximately 2 additional satisfying sexual episodes per month compared with 1 per month in the pla-

### Table 3. Randomized Trials of Nonhormonal Pharmacological Interventions for Sexual Dysfunction in Women

<table>
<thead>
<tr>
<th>Source</th>
<th>Design, Purpose</th>
<th>Study Population</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Clinical Response</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Basson et al.</td>
<td>12-wk RCT, double-blind placebo vs sildenafil</td>
<td>N = 522 estrogenized women (both pre- and postmenopausal age 18-55 y and 204 estrogen-deficient women age 45-70 y)</td>
<td>Estrogenized women: one of 3 doses of sildenafil (10, 50, or 100 mg) vs placebo; estrogen-deficient women: sildenafil 50 mg vs placebo</td>
<td>2 global efficacy questions, 26 questionnaires, SFQ, event log of sexual activity</td>
<td>No significant differences in sexual response were seen</td>
<td>The patient population was heterogeneous, with only 40%-50% having a primary diagnosis of FSAD; no attempt to stratify women with different types of arousal disorder; adverse events: headache, flushing, rhinitis, nausea, visual disturbances, and dyspepsia</td>
</tr>
<tr>
<td>Berman et al.</td>
<td>12-wk RCT, double-blind placebo vs sildenafil</td>
<td>N = 202, age 30-71 y, naturally and surgically menopausal women with primary complaint of FSAD for 6 mo</td>
<td>Sildenafil 50 mg vs placebo, dosed 1 h prior to anticipated sexual activity, and not more than once per day</td>
<td>SFQ, FIEI, sexual event log</td>
<td>Sildenafil improved &quot;satisfaction with sexual desire,&quot; &quot;satisfaction with performance,&quot; and &quot;satisfaction with intercourse&quot; (P = .017) and &quot;satisfaction with sexual desire,&quot; &quot;satisfaction with performance,&quot; and &quot;satisfaction with intercourse&quot; (P = .015) compared with placebo</td>
<td>Adverse effects similar to Basson et al., 2002</td>
</tr>
<tr>
<td>Masand et al.</td>
<td>3-wk RCT, double-blind placebo vs low-dose bupropion SR</td>
<td>N = 31, age, sex, and menopausal status not reported (men and women included), euthymic on SSRIs and sexual dysfunction</td>
<td>Bupropion SR 150 mg/d vs placebo</td>
<td>ASEX</td>
<td>No significant differences in sexual response were noted between treatment groups</td>
<td>1 patient taking bupropion withdrew from study because of insomnia</td>
</tr>
<tr>
<td>DeBattista et al.</td>
<td>6-wk RCT, double-blind placebo vs low-dose bupropion SR</td>
<td>N = 41 (24 women, menopausal status unknown; 17 men), mean age 41 y, euthymic on SSRIs</td>
<td>Bupropion SR 150 mg/d in the morning vs placebo</td>
<td>ASEX, BSF</td>
<td>Few patients from either group showed improvement; no between-group differences were seen</td>
<td>Adverse effects not stated</td>
</tr>
<tr>
<td>Clayton et al.</td>
<td>6-wk RCT, double-blind placebo vs high-dose bupropion SR</td>
<td>N = 55 (48 premenopausal women, 7 men), mean age 38 y, euthymic on SSRIs</td>
<td>Bupropion SR 150 mg/d vs placebo</td>
<td>CSFQ, Desire/frequency</td>
<td>Investigators ratings, CSFQ, SFQ, FIEI</td>
<td>Irritability, dry mouth, and headache with bupropion</td>
</tr>
<tr>
<td>Segraves et al.</td>
<td>112-day RCT, double-blind placebo vs high-dose bupropion SR</td>
<td>N = 75, mean age 38.2 y, nondepressed, premenopausal women with HSDD</td>
<td>Bupropion SR 150 mg/d vs placebo × 7 d, then increased to 300 mg/d</td>
<td>Investigator ratings, CSFQ, BSF-W</td>
<td>Total CSFQ score and subscores for pleasure, arousal, and orgasm significantly higher with bupropion</td>
<td>35 patients withdrew (17 from bupropion group and 18 from placebo group); adverse effects not stated</td>
</tr>
</tbody>
</table>

Abbreviations: ASEX, Arizona Sexual Experience Scale; BSF, Brief Index of Sexual Functioning; BSF-W, Brief Index of Sexual Functioning for Women; CSFQ, Changes in Sexual Functioning Questionnaire; FIEI, Female Intervention Efficacy Index; FSAD, female sexual arousal disorder; HSDD, hypoactive sexual desire disorder; LSC, Life Satisfaction Checklist; RCT, randomized controlled trial; SFQ, Sexual Function Questionnaire; SR, sustained release; SSRI, selective serotonin receptor inhibitor.

*The drugs listed have not approved by the US Food and Drug Administration for labeling for these indications.*
cebo group. A fifth trial showed similar results in 549 naturally menopausal women.71 One study failed to demonstrate a dose-response effect, with use of a 450-µg patch applied twice weekly showing no benefit.70 Short-term adverse events were mild (skin reactions and a nonsignificant increase in acne, alopecia, facial hair, and voice deepening) and no significant adverse effects on lipids were noted. Concerns remain about longer-term adverse effects, as these studies were only 24 weeks in duration. Furthermore, while testosterone appears to influence female sexual function directly, without first requiring aromatization to estradiol,94 it is not known whether coadministration of estrogen is required for testosterone to achieve its beneficial effects, since all studies to date have included systemic estrogen administration. Because of the lack of evidence regarding benefits and risks, particularly in women who are estrogen deficient, prescription of testosterone alone is not recommended for Ms B.

**Bupropion.** Ms B’s internist recommended a trial of bupropion to stimulate desire. Scant data support this suggestion. Three small, placebo-controlled RCTs investigated the efficacy of bupropion as an antidote to SSRI-induced sexual dysfunction in euthymic patients. In the 2 studies (N=31 patients, N=41 patients77) that used 150 mg/d of bupropion sustained release (SR), no change in sexual function was observed after 3 or 6 weeks, respectively. The third study (n=42), in which a higher dose of bupropion SR (300 mg/d) was used for 4 weeks, demonstrated an increase in sexual desire and frequency of sexual activity in treated patients, as measured by the Changes in Sexual Functioning Questionnaire (CSFQ).78

Whether bupropion is useful as a sexual stimulant in women who are not taking SSRIs is unclear. Segraves et al compared the effect of bupropion SR (300 mg/d for 112 days) vs placebo in nondepressed, premenopausal women (N=75) with HSDD.79 Outcome was measured using the CSFQ; significant increases were seen in sexual arousal, orgasm completion, and sexual satisfaction, but not desire. Larger trials are needed to further investigate these findings, determine the optimal bupropion preparation and treatment dose, and ascertain which specific sexual function domains are affected. Use of bupropion requires careful assessment for possible medication interactions, as well as precautions regarding seizures, particularly among women with eating disorders.95

**Phosphodiesterase Inhibitors.** Phosphodiesterase inhibitors increase genital perfusion in women, as in men.96 A large multicenter placebo-controlled trial examined the efficacy and safety of sildenafil (10-100 mg), taken 1 hour prior to sexual activity, in 2 groups of women (estrogen-replete, n=577; estrogen-deficient, n=204) with female sexual arousal disorder (FSAD). No increase in sexual arousal was seen in either group at any treatment dose.74 There was a substantial (30%-40%) placebo response: adverse events included headache, flushing, rhinitis, nausea, visual disturbance, and dyspepsia. The patient population was heterogeneous, with only 40% to 50% of women having a primary diagnosis of FSAD. In another study of sildenafil vs placebo in postmenopausal women with FSAD, in a subgroup analysis of women without concomitant HSDD, significant improvements were seen in vaginal lubrication, genital sensation, ability to achieve orgasm, and overall satisfaction.75

Limited data suggest that phosphodiesterase inhibitors may be useful in selected women in whom genital arousal difficulty predominates. One placebo-controlled study examined the effect of sildenafil (50 mg) in 34 postmenopausal women with FSAD who were stratified according to degree of genital vasocongestion using vaginal photoplethysmography97; sildenafil increased perception of genital arousal and reduced the latency to orgasm in women with a low vaginal pulse amplitude response. In a second placebo-controlled pilot study, sildenafil (100 mg) improved measures of both subjective and objective arousal in 36 women with type 1 diabetes and FSAD.98 Larger trials of phosphodiesterase inhibitors in women with arousal problems and documented vascular disease would be of interest. Caution is advised in women with recent myocardial infarction or stroke, active coronary ischemia, or episodes of heart failure, and these medications are contraindicated in patients taking nitrates.99

Several other agents increase genital blood flow in response to erotic stimuli, including ephedrine,100 phenolamine,101,102 topical alprostadil,103-105 and a combination of yohimbine and L-arginine (a nitric oxide precursor).106 As with sildenafil, changes in genital blood flow are not accompanied by improvements in subjective arousal in most of these studies. However, a recent phase II, placebo-controlled, double-blind study of 3 doses of topical alprostadil cream in 400 women with FSAD demonstrated significant improvement in arousal scores in the highest dose (900 µg) group.107 Further studies of prostaglandin E1 agonists are needed.

**Mechanical Devices**

Mechanical devices can also be used to overcome the effects of vascular or neurological compromise. These devices work either through vibratory stimulation or by causing clitoral vascular engorgement using a vacuum system.108 Vibrators supply stimulation that is high in intensity, can be delivered directly to the genital sites that have greatest sensitivity, and have the advantage that, unlike a human partner, they do not fatigue with prolonged duration of use. While there are no comparison studies, these characteristics support the use of vibrators by women who require high-intensity, direct clitoral stimulation for prolonged periods of time to achieve arousal. The ErosClitoral Therapy Device (UroMetrics Inc, St Paul, Minn) is a small, handheld, battery-powered vacuum pump that can be used to increase blood flow to and around the clitoris during foreplay and self-stimulation. The device received Food and Drug Administration approval on the basis of a small (N=19) study that demonstrated significant improvement.
in sensation, vaginal lubrication, ability to orgasm, and greater overall sexual satisfaction in women with and without FSAD.\textsuperscript{100}

**Pelvic Floor Exercises**

Limited data suggest that the use of pelvic floor exercises to increase pelvic floor muscle tension enhances sexual arousal and orgasmic pleasure in some women, including women who experience sexual incontinence.\textsuperscript{110} While existing studies are small, lack appropriate controls, and include inconsistent outcome measures, pelvic floor exercises are easily taught, pose little potential for harm, and cost to learn is little or nothing. Effectiveness can be augmented using biofeedback techniques or vaginal weights.\textsuperscript{111}

**RECOMMENDATIONS FOR MS B**

Ms B and her husband should optimize opportunities for intimacy, maximize comfort during sexual activity, and use effective sexual techniques. Lubricants and continued use of topical estrogen are likely to be helpful, as well as increasing the intensity and duration of clitoral stimulation using mechanical devices such as a vibrator or a clitoral pump. Pelvic floor exercises are recommended to improve tone and enhance orgasm.

General health benefits of cardiovascular risk factor modification should be emphasized. In addition, a recent study of 187 obese women and men showed that weight loss was associated with improvement in several measures of sexual quality of life.\textsuperscript{112} In another study that examined the effects of psychosocial variables and free testosterone on sexual function across the menopausal transition, exercise was the sole variable significantly associated with sexual satisfaction.\textsuperscript{113}

**WHAT DOES THE FUTURE HOLD?**

Exciting developments continue in the field of human sexuality. Current studies focus on the efficacy and safety of androgens (patch, gel, spray, vaginal ring), the dopaminergic agonist apomorphine (sublingual, intranasal), and \( \alpha \)-melanocortin–stimulating hormone (intranasal) for desire, as well as selected vascular smooth muscle relaxants for genital arousal, including nitric oxide pathway agents such as arginine and prostaglandins such as topical alprostadil cream.\textsuperscript{114,115} In addition to biological interventions, the importance of educating both clinicians and patients about sexual anatomy, function, and technique cannot be overemphasized.\textsuperscript{99} As the high placebo rate in many trials indicates, and as Ms B herself notes (“Everything you ask doesn’t need a solution”), sometimes it just helps to talk.

**QUESTIONS AND COMMENT**

A **PHYSICIAN:** Can you comment on the existence of the “G-spot?”

**DR POTTER:** The “G-spot” (Grafenberg spot) is described in popular literature as a highly erogenous area located along the lower third of the anterior vaginal wall. Although few studies provide objective evidence supporting its existence,\textsuperscript{116} stimulation of this area is said to result in a kidney bean–sized area of swelling, a high level of arousal, and powerful orgasms. The existence of female ejaculation is also postulated, based on the observation that fluid is released during orgasm in some women. Whether this fluid is urine or represents emission of secretions from female paraurethral glands (analogous to the male prostate) is unclear.\textsuperscript{116} A trial of pyridium (which turns urine orange) may serve to distinguish between the two.

A **PHYSICIAN:** What is the data on the use of dehydroepiandrosterone (DHEA)?

**DR POTTER:** Studies of DHEA, available as an unregulated, over-the-counter, oral dietary supplement, are sparse. One small (\( N=24 \)) double-blind, placebo-controlled, randomized crossover trial in women with adrenal insufficiency showed that 4 months of DHEA at a dose of 50 mg per day significantly increased sexual interest and the level of satisfaction with sex, as well as overall well-being and mood.\textsuperscript{117} A second study, in which 140 women aged 60 to 79 were randomized to DHEA (50 mg/d) vs placebo for 12 months, demonstrated a significant increase in sexual satisfaction and a trend toward an increase in sexual interest and activity in older (70-79) but not younger (60-69) women.\textsuperscript{118} Questions about sexual function were “prepared by one of the researchers”; no standardized, validated questionnaire was used. Negligible data address adverse effects and long-term safety of DHEA use.

A **PHYSICIAN:** Is there any benefit from the use of herbal products?

**DR POTTER:** Various plant-derived remedies are purported to treat sexual problems.\textsuperscript{119} Of these, both ginseng and ginkgo biloba increase genital blood flow; however, neither of these individual compounds has yet been shown to benefit women with sexual arousal disorders. However, a pilot study of ArginMax [Daily Wellness Co, Honolulu, Hawaii], a nutritional supplement containing ginseng, ginkgo, L-arginine, damiana, vitamins, and minerals, demonstrated improvements in sexual desire, vaginal dryness, clitoral sensation, and frequency of sexual activity in normal female volunteers.\textsuperscript{120}

A **PHYSICIAN:** How should I bill for a sexual health consultation in order to be reimbursed?

**DR POTTER:** Clinicians can utilize diagnoses listed in the American Psychiatric Association’s Diagnostic and Statistical Manual (DSM-IV-TR)\textsuperscript{121} or the International Statistical Classification of Diseases and Related Health Problems (ICD-10).\textsuperscript{122} Examples of reimbursable ICD-10 diagnoses include: lack or loss of sexual desire (F52.0), failure of genital response (F52.2), menopausal and female climacteric states (N95.1), postmenopausal atrophic vaginitis (N95.2), dyspareunia (N94.1), and orgasmic dysfunction (F52.3).
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Role of the Sponsor: The funding organization did not participate in the collection, analysis, or interpretation of the data; or in the preparation, review, or approval of the manuscript.

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There is a paradox in rereading. You read the first time for rediscovery: an encounter with the confirming emotions. But you reread for discovery: you go to the known to figure out the workings of the unknown, the why of the familiar how.
—Cynthia Ozick (1928- )