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Female Sexual Dysfunction—Medical and Psychological Treatments, Committee 14

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ABSTRACT

Introduction: Since the millennium we have witnessed significant strides in the science and treatment of female sexual dysfunction (FSD). This forward progress has included (i) the development of new theoretical models to describe healthy and dysfunctional sexual responses in women; (ii) alternative classification strategies of female sexual disorders; (iii) major advances in brain, hormonal, psychological, and interpersonal research focusing on etiologic factors and treatment approaches; (iv) strong and effective public advocacy for FSD; and (v) greater educational awareness of the impact of FSD on the woman and her partner.

Aims: To review the literature and describe the best practices for assessing and treating women with hypoactive sexual desire disorder, female sexual arousal disorder, and female orgasmic disorders.

Methods: The committee undertook a comprehensive review of the literature and discussion among themselves to determine the best assessment and treatment methods.

Results: Using a biopsychosocial lens, the committee presents recommendations (with levels of evidence) for assessment and treatment of hypoactive sexual desire disorder, female sexual arousal disorder, and female orgasmic disorders.

Conclusion: The numerous significant strides in FSD that have occurred since the previous International Consultation of Sexual Medicine publications are reviewed in this article. Although evidence supports an integrated biopsychosocial approach to assessment and treatment of these disorders, the biological and psychological factors are artificially separated for review purposes. We recognize that best outcomes are achieved when all relevant factors are identified and addressed by the clinician and patient working together in concert (the sum is greater than the whole of its parts). **Kingsberg SA, Althof S, Simon JA, et al. Female Sexual Dysfunction—Medical and Psychological Treatments, Committee 14. J Sex Med 2017;14:1463–1491.**

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INTRODUCTION

Since the millennium we have witnessed significant strides in the science and treatment of female sexual dysfunction (FSD). This forward progress has included (i) the development of new theoretical models specifically for FSD[1]; (ii) alternative classification strategies of female sexual disorders[2,3]; (iii) major advances in brain, hormonal, psychological, and interpersonal research[4–6]; (iv) strong and effective public advocacy for FSD; and (v) greater educational awareness of the impact of FSD on the woman and her partner.[6,7] This report focuses on the distressing complaints of hypoactive sexual desire, impaired arousal, and orgasmic problems. The pain dysfunctions renamed in the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* (DSM-5) as *genito-pelvic pain/penetration disorders* are reviewed in a separate publication.

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FSD is best viewed through the lens of the biopsychosocial model.[8] This is an integrative and ever-changing model reflecting fluctuations in a woman's health status, neurochemical balance, psychological issues, interpersonal concerns, and sociocultural factors. In writing this report, we chose to artificially disentangle what is the more appropriately integrated biopsychosocial approach to treatment by presenting the biological, psychological, interpersonal, and sociocultural aspects of each dysfunction separately.

In addition, the committee chose to use the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision* (DSM-IV-TR)[9] classifications of female sexual disorders instead of those from the *DSM-5*.[10] This is consistent with the recommendations of the International Consultation of Sexual Medicine (ICSM) Committee on Definitions[11] and a recent article on nomenclature by the International Society for the Study of Women's Sexual Health.[2] By separating desire and arousal, it is easier to characterize the assessment and treatment of each dysfunction, rather than combining them as seen in the new and controversial diagnosis of female sexual interest/arousal disorder (FSIAD).[10] We acknowledge that there is often significant overlap and comorbidity among all DSM-IV-TR diagnoses. However, treatment is typically focused on the primary disorder identified by the woman. For example, if she presents with hypoactive sexual desire disorder (HSDD) and reports difficulty reaching orgasm, the clinician and patient would determine whether the low desire is causing the anorgasmia or whether the anorgasmia is caused by the low desire.

As sexual medicine evolves, no trend is clearer than that toward a more unified understanding of the pathophysiology and treatment effects from various forms and approaches to therapy. The unification of the biological and the psychosocial should be the essential goal. The innate ability to change brain functions and associated anatomy, whether cognitive and/or behavioral, could be uniquely human. Even among primates, humans stand out in their extraordinary neuroplasticity such that the development of neural circuits that underlie behavior can be shaped by the environmental, social, and cultural context more intensively in humans, thus providing an anatomic basis for behavioral and cognitive evolution.[12,13] Examples demonstrate that psychological (eg, mindfulness[14]) and pharmacologic approaches[4,15] confer benefits as seen in non-invasive neuroimaging as a correlate of neuroplasticity. Further, such imaging can actually predict response to therapy.[13]

After carefully reviewing peer-reviewed publications on the psychological and pharmacologic treatments for HSDD, female sexual arousal disorder (FSAD), and female orgasmic disorder (FOD), the committee crafted Table 1, which presents a summary of levels of evidence for major treatment interventions. We hope this will guide the clinician to choose appropriate treatments for the patient. Some treatment interventions could not be given a level of evidence because the studies used small cohorts and/or there was insufficient or conflicting evidence.

Table 1. Evaluation of treatment interventions for HSDD, FSAD, and FOD

Type of intervention	Level of evidence
Psychological interventions for HSDD	
Sex therapy (sensate focus)	2*
CBT	2*
Mindfulness + CBT	2*
Pharmacologic interventions for HSDD	
Flibanserin	1
Bremelanotide	1
Testosterone therapy	1
Bupropion	2
Buspirone	2
Lybrido/Lybridos	2
Psychological interventions for FSAD	
Mindfulness + CBT	2*
Pharmacologic interventions for FSAD	
Tibolone	2
Bupropion	2†
Testosterone therapy	1
PDE5i in well-established medical conditions interfering with genital neurovascular substrates	2
Psychological interventions for FOD	
Directed masturbation	2*

CBT = cognitive behavioral therapy; FOD = female orgasmic disorder; FSAD = female sexual arousal disorder; HSDD = hypoactive sexual desire disorder; PDE5i = phosphodiesterase type 5 inhibitor.
*It is unclear whether the same criteria for levels of evidence should be applied to psychological and pharmacological studies.
†Unable to confer levels of evidence because of small cohorts, inconsistent and weak evidence for bibliotherapy alone, L-arginine plus yohimbine, alprostadil, phentolamine, apomorphine, Zestra, and the coital alignment technique.

In addition, we recognize that it is somewhat problematic and controversial to use the same rating system to grade psychological and pharmacologic studies given issues of sample size, randomization of treatments, treatment manuals, placebo control, and duration of follow-up, but this issue is best left for future discussion.[16] Based on specific criteria, effective psychological treatments meeting these criteria were deemed established treatments or probably efficacious treatments.[17]

HYPOACTIVE SEXUAL DESIRE DISORDER—PSYCHOSOCIAL APPROACHES

Overview of Assessment

The assessment of women's sexual function, including loss of sexual desire, should include a comprehensive clinical interview, the objectives of which are to identify the etiology of the woman's complaints and dysfunction, determine the predisposing, precipitating, and maintaining factors, determine her level of distress, and ascertain a clinical diagnosis. Although there is often

an overlap among the predisposing, precipitating, and maintaining factors of women's low sexual desire, determining these contributing factors is important because they inform the health care professional (HCP) as to what treatment options would best suit an individual patient.[18]

Because women's sexual desire is multifactorial, within a biopsychosocial model of female sexual response,[19] the clinician should attempt to clarify factors contributing to the sexual complaint across biological (eg, neurotransmitter imbalance, hormonal factors, medications, poor sleep), psychological (eg, depression, stress), interpersonal (eg, relationship problems, partner sexual dysfunction), and cultural (eg, cultural messages) dimensions. Although all these dimensions are important to assess, women's psychological and relationship health have been found to be particularly strong predictors of women's sexual desire.[20,21] For instance, psychological factors could include psychiatric diagnoses (eg, anxiety, depression, personality disorders), poor body image, a history of trauma or abuse, distraction, or life stress.[8] Moreover, according to Basson's model of women's sexual response, women's low desire could result from an unsatisfying sexual relationship or other sexual problems such as pain during sex or the inability to achieve orgasm.[22,23] Given the overlap or comorbidity of female sexual disorders, it is important to understand the patient's sexual response across all components of her sexual life and how her motivation for sex is related to other aspects of sexual response. Because of the significance of the intimate relationship in the etiology of HSDD,[18] it can sometimes be helpful to include the patient's partner in the clinical assessment. In addition to assessing the symptoms of FSD and their potential etiologies, it is important to determine the woman's degree of distress. In so doing the clinician attempts to identify the woman's personal distress and distress experienced from partner complaints or interpersonal conflicts.

Contextual factors also should be assessed. These could include changes in the patient's life, such as in her health or medications or psychological functioning or in her social situation or intimate relationship. Recent life events such as onset of a medical condition, unemployment, infertility, childbirth, or partner infidelity, as examples, are important to identify.[24,25] Although these can cause a woman to lose her desire, they are considered factors that typically exclude her from the diagnosis of HSDD; nonetheless, they warrant clinical attention. It is important to determine the factors that have led her to seek treatment at a particular time ("why now?"). Understanding the woman's motivation for seeking treatment is relevant because this motivation can influence prognosis and guide the selection of treatment approaches. For instance, the treatment focus is likely to differ for a woman who seeks help for low desire because she misses having intimate time with her partner compared with a woman who seeks help because she thinks that she and her partner "should be having more sex" or because of her partner's wishes (or more commonly, veiled threats of leaving the relationship). Women's motivation to engage in sexual activity also can be multifactorial and is not always precipitated by sexual desire but for other reasons such as a desire to feel close to her partner.[26] Further, these motivators might differ for women by menopausal status.[27]

Self-Report Measures

Despite the importance of thorough clinical assessment of women's sexual function, there is evidence that HCPs avoid asking women about their sexual lives, even for women undergoing medical treatments known to affect their genital function and ability to engage in sexual activity (eg, treatment of gynecologic cancer).[28] In a recent observational study, 819 patients with cancer were surveyed about their experiences of patient-provider communication about sex. Having a greater interest in sexual activity was associated with having asked an oncology professional about sexual problems. Overall, however, only 29% of respondents had ever asked.[29] It is likely that a brief screener to assess multiple domains of sexual function could be helpful in facilitating this discussion and focusing a clinical conversation.

Multidimensional patient-reported outcome measures designed for research also can be used in clinical practice. Examples include the Female Sexual Function Index[30] (FSFI; 19 items; 6 domains include desire, arousal, lubrication, pain, orgasm, and satisfaction), the Sexual Function Questionnaire[31] (34 items; 7 domains include desire, arousal-sensation, arousal-lubrication, orgasm, enjoyment, pain, and partner), and the PROMIS Sexual Function and Satisfaction Brief Profile measure[32] (13 items; 8 domains include interest in sexual activity, lubrication, vaginal discomfort vulvar discomfort-labial, vulvar discomfort-clitoral, orgasm ability, orgasm pleasure, and satisfaction with sex life). In addition to using one of these measures, the HCP must assess the woman's distress to qualify for a diagnosis of sexual dysfunction. The advantages of these measures are that they cover a range of domains of sexual response, often have clinically meaningful cutoff scores, and have demonstrated psychometric validity.

Even HCPs who are relatively unfamiliar with HSDD can easily use the Decreased Sexual Desire Screener (DSDS)[33] as a screening measure. The DSDS is designed to help HCPs diagnose acquired HSDD and identify the subset of patients with HSDD who might benefit from a pharmacologic treatment. Alternatively, a single-item screener that captures common sexual problems and concerns might be less burdensome and more useful in clinical practice settings. One such screener was recently tested in a large representative sample of US adults and differentiated individuals who had higher vs lower function as measured by the PROMIS Sexual Function and Satisfaction measure.[34] The investigators used the following single-item measure:

In the past 12 months, has there ever been a period of at least 3 months when you had any of the following problems or concerns? Check all that apply.

___You wanted to feel more interest in sexual activity
___Your vagina felt too dry
___You had pain during or after sexual activity
___You had difficulty having an orgasm
___You felt anxious about sexual activity
___You did not enjoy sexual activity
___Some other sexual problem or concern
___No sexual problems or concerns

Suggested Interview Questions

Below is a list of interview questions that assess women's sexual desire (and other sexual complaints).[35,36] In addition to determining etiology and distress associated with low desire, it is recommended that questions assessing arousal also be included (eg, absent or decreased genital or non-genital sensations during sexual activity). If the partner is present, the partner's perspective could prove helpful in the evaluation process and in determining her motivation for therapy (eg, does her partner lack respect for her and interrupt her frequently, does she seem to lack emotional connection with her partner). For diagnostic purposes, the interviewer should assess the presence of other psychological disorders (eg, depression, substance use disorders) or medical conditions (eg, cancer, diabetes). The following questions can help elucidate the etiology and contributing factors to HSDD.

- How long has this been a problem for you? (This question distinguishes those with acquired vs lifelong HSDD or FSIAD.)
- What was happening in your life when this became a problem?
- How often do you have sexual or erotic thoughts or fantasies? How, if at all, has this changed?
- How often do you initiate sexual activity with your partner? When your partner initiates sexual activity, how much of the time are you responsive to these advances (ie, do you willingly and positively go along with sexual activity)? Has this changed for you?
- Do you find that you are uninterested in sex in some circumstances, but interested in others (eg, with a partner)? Is there anything at all that triggers sexual interest or excitement (eg, movies with sex scenes, reading sexy books, or seeing someone you find sexually attractive)?
- How often do you engage in sexual activity alone and with a partner?
- During sex, how much mental excitement and pleasure do you experience?
- Do you have any pain with sexual activity and, if so, please describe where and the kind of pain (eg, sharp, throbbing)?
- How often (what percentage of the time) do you experience orgasm and how pleasurable is orgasm for you? Has the latency or intensity changed?
- How much of a problem is your low sexual desire? (To what extent are you bothered by it?)
- Additional questions that can help clarify the etiology of the sexual desire complaint and guide treatment options include:
- How happy are you with your relationship overall?
- Does your partner have any sexual problems or concerns?
- How is your body image? (Follow-up with clarifying whether low desire affects body image or vice versa.)
- What is your explanation for your low sexual desire?
- How would you rate your level of interest in sex from 0 to 10, where 0 is lowest and 10 is highest possible sexual desire? Where would you like to be on this rating scale? What is the best score you ever had in your lifetime? What do you think it would it take for you to get there?
- What are you hoping to achieve from treatment?
- If I could snap my fingers and our work were successful, what would be different in your sex life?
- How would you know you're better off than when you started?

Stepped Care Approach

A model that can be used to guide the provision of stepped sexual counseling to women with low sexual desire is the well-described PLISSIT model (Figure 1).[37] Although this model is not new, it continues to be relevant as a guide to provision of sexual counseling, often because clinicians have various levels of training in sexual counseling and this model emphasizes identification of concerns and referrals for resources when necessary. *Permission* refers to raising and discussing the subject (eg, asking about sexual function or letting the patient know she can raise the issue later). *Limited Information* includes information about the sexual problems or about resources (eg, information about the role of physiology in sexual response). *Specific Suggestions* refers to advice regarding aids, self-help books, or techniques the patient can try (eg, using vaginal lubricants). *Intensive Therapy* would be provided by a trained therapist, which can involve referrals to specialists with experience in sex therapy.[21] A clinician can provide care at the various levels in this model with which he or she feels comfortable and should identify appropriate referral sources to provide additional care when appropriate.

Overview of Psychosocial Treatments

Treatments with evidence for improving low sexual desire in women include exogenous hormone therapies, central nervous system (CNS) medications, and psychological therapy.[38] In this section we provide a stepped care approach to clinical management, an overview of psychosocial approaches to treating women's sexual desire, and a review of relevant intervention studies published within the past 10 years. There is some controversy as to what constitutes a well-designed psychotherapy trial. Pyke and Clayton[39,40] recommended that psychotherapy trials use the same standards as drug trials (eg, a hierarchy of end points with a planned primary end point, sufficient information on the intervention to reproduce it, randomization, adequate control, accepted measures of benefits and harms, compliance data, and/or outcomes of clinical relevance). McCabe[41] argued that a "robust study design for psychological interventions should adhere to these same requirements. Some aspects will be shared,

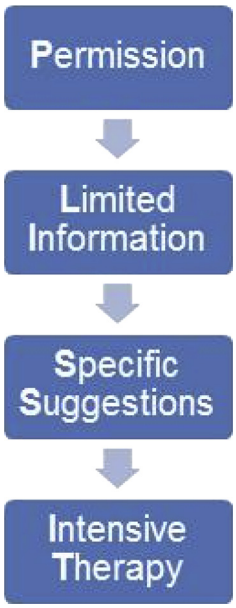

Figure 1. PLISSIT model. Figure 1 is available in color at www.jsm.jsexmed.org.

but others will be different (finding an appropriate active control group for HSDD studies)."

A 2013 meta-analysis evaluating psychological treatments for sexual dysfunctions found a large effect size of 0.91 for these treatments on the outcome of symptom severity in women with HSDD.[42] This was obtained from 4 randomized controlled trials (RCTs) evaluating psychological treatments[43–46]; the effect size for sexual satisfaction in this population was 0.51. All 4 studies were conducted more than 10 years ago and had samples smaller than75. It is notable that this meta-analysis found that, overall, the effects of psychological interventions were much more substantial for patients with HSDD compared with other sexual dysfunctions; effects also were notable on FOD. Perhaps the nature of women's sexual desire lends itself particularly well to the format or content of psychological treatments.

Treatment Considerations

In evaluating the appropriate sequence of treatment goals, some important considerations include assessing the relative contribution of relationship vs individual factors. Recent research has suggested that for women with low relationship satisfaction, improving sexual function alone might not be sufficient to alleviate their sexual distress.[46] Therefore, focusing on improving the intimate relationship would be a necessary and, in rare cases, sufficient component of treatment for a partnered woman with low sexual desire and concomitant low relationship quality; this could be accomplished using couple or marital therapy. Alternatively, couple or marital therapy alone, without adjunct sex therapy, might not be sufficient to improve women's sexual desire.[47] Specifically, the aforementioned meta-analysis found that marital therapy yielded an effect size of 0.63 on symptom severity for female HSDD but only 0.02 on sexual satisfaction.[42] This was based on only 1 comparison from 1 study.[45] Addressing a woman's poor body image or low self-esteem should be a part of the treatment plan in cases in which this is an etiologic factor in maintaining her low sexual desire. Body image is a strong correlate of women's sexual desire[48] and poor body image can hinder progress. However, body image could improve through increasing self-knowledge and providing positive sexual experiences through therapy. Further, because sexual desire and arousal are so intertwined, techniques that can improve a woman's arousal and enjoyment also might increase her motivation for sex. Decreasing pain or discomfort with sexual activity is a first step for women experiencing pain or discomfort as a factor that is lessening their desire.[22]

Sex Therapy

Sex therapy is a specialized form of counseling or psychotherapy that is designed to help individuals and couples with sexual problems.[49] It uses specific techniques to address problems of sexual desire, arousal, orgasm, and pain. In general, sex therapy is a short-term (approximately 3 months) treatment conducted in an individual, couples, or group setting. The decision of which modality is appropriate is based on the particulars of any patient's presenting problem. Sex therapy generally consists of psychoeducation, couple exercises including sensate focus, and counseling. When considered as an amalgam of sensate focus exercises and counseling, it has been demonstrated to be moderately effective at improving sexual desire especially when compliance with the recommended exercises is high.[47]

A core component of sex therapy is sensate focus therapy, which involves a graded series of non-demand sensual touching exercises.[50] In a couple-based approach, the objectives of sensate focus therapy are to decrease avoidance of sensual touching or sexual activity and related anxiety, improve sexual communication between partners, and improve intimacy by reintroducing sexual activity in a gradual way. Exercises might begin with nongenital touching and, assuming successful achievement of each successive series of exercises, move to genital touching and ultimately intercourse (or other genital sexual activity that is not so heterosexually limited).

A 2013 meta-analysis found an effect size of 1.03 on the outcome of symptom severity and an effect size of 0.86 for sexual satisfaction based on 2 comparisons involving sexual skills training (which included sensate focus) for women with HSDD,[42] thus suggesting a high level of efficacy (Level of Evidence = 2). Throughout the exercises, the focus is on moment-to-moment sensations rather than on achieving arousal or orgasm. Thus, the overlap with mindfulness-based approaches to treating women's sexual dysfunction is evident.[51–53] Sensate focus therapy also has been applied more recently to women in an individual model to improve their sexual self-knowledge and sexual function including their orgasmic ability through self-stimulation.[54] Moving forward, sensate focus exercises could continue to be included as a key behavioral exercise in interventions using more modern approaches, as we discuss below.

Cognitive-Behavioral Therapy

Contemporary psychosocial approaches have melded sex therapy techniques within a broader framework such as cognitive-behavioral therapy (CBT).[47] CBT focuses on identifying and altering behaviors (eg, avoidance of sexual activity) and cognitions (eg, unrealistic expectations) that contribute to low sexual desire and function for women. Education also is an important component of CBT and can help the woman or couple understand how adequate erotic stimulation and physical stimulation contribute to women's sexual desire and arousal.[55] The aforementioned meta-analysis supported the benefits of CBT (Level of Evidence = 2). More recent therapeutic studies have often combined elements of CBT with mindfulness-based therapy and sex therapy techniques to optimize outcomes (Level of Evidence = 2).

Mindfulness-Based Studies

The concept of mindfulness, that is, acceptance or being present without judgment, comes from Buddhist meditation and has been adapted into mindfulness-based interventions. After some encouraging small studies in women with gynecologic cancer[52,53] and those who did not have history of cancer,[5,56] a larger controlled study of a brief (4-session) group mindfulness-based cognitive sex therapy intervention was shown to significantly improve sexual desire (and multiple other domains of sexual function) in 95 women seeking treatment for low sexual desire and/or arousal.[5] The intervention, called mindfulness-based cognitive behavioral sex therapy, included psychoeducation about sexual response, cognitive therapy, and mindfulness training delivered in a group format. Home practice exercises included skills practice (eg, mindfulness practice, non-masturbatory genital self-stimulation, body scans) and completion of worksheets. This was a 2-group comparison of scores before and after intervention on the Sexual Interest and Desire Inventory (Level of Evidence = 2).[57] There also is evidence that mindfulness might be particularly beneficial for women with sexual difficulties characterized by a disconnect between genital and subjective arousal (eg, low subjective arousal even in the context of adequate genital engorgement). In a small study of 20 partnered women with a history of childhood sexual abuse and experiencing sexual difficulties and distress,[56] women in a mindfulness-based therapy group and a CBT group experienced significant decreases in sexual distress but those in the mindfulness-based therapy showed greater improvements in the concordance between subjective and genital arousal. Therefore, mindfulness-based therapy could be helpful for women with arousal problems that are, at least in part, due to a lack of attention and/or focus on their bodily sensations.

Self-Help Educational Materials

Self-help education can be an accessible, low-cost approach to treating low sexual desire in women with "subclinical" low desire. Two recent small studies have suggested that written self-help education ("bibliotherapy") can improve self-reported sexual desire scores compared with waitlist controls. In the first study, Mintz et al[58] randomly assigned partnered heterosexual women who self-identified as having low sexual desire secondary to "stress and exhaustion." Women in the intervention arm were assigned to read a book that included self-help education and treatment based on the cognitive-behavioral model. Of 45 women who completed the pretest and 6-week post-test questionnaires, the effect size for the intervention was large (Cohen d = 0.50). 7 weeks after that, 9 women who completed an additional questionnaire had maintained their gains in sexual desire.

A second study following the same assessment schedule randomized women to 1 of 3 groups: women in the first 2 groups read different self-help books and the third group was a waitlist control group.[59] 45 married heterosexual women completed the pre- and post-test assessments, and women in the intervention arms were found to have large increases in self-reported sexual desire, on average, compared with women in the waitlist control group, a finding that was maintained 6 weeks after the post-test. Self-help education has appeal in treating low sexual desire for women because it is widely available, has low cost, and has no side effects. These materials could be of particular use for patients lacking resources for therapy or medications (because insurance might not cover treatment of low sexual desire). One limitation of these studies is that they were conducted in non-clinical and narrow populations; as such, whether these materials would be effective for women with clinical levels of low sexual desire and arousal needs to be investigated.

A recent study compared the effectiveness of skill-based bibliotherapy with a placebo pill intervention.[60] Compared with the placebo pill group, the bibliotherapy group made statistically greater gains from pretest to follow-up in sexual desire and satisfaction.

Conclusion

We have provided an overview of psychosocial approaches to treating women's low sexual desire, including a stepped care approach to clinical management and a review of relevant intervention studies published within the past 10 years. Overall, the most promising psychological approaches to treating women's sexual desire appear to incorporate elements from sex therapy, CBT, and mindfulness-based interventions. A 2013 meta-analysis showed medium to large positive effects of psychosocial treatments on symptom severity and sexual satisfaction for women with low sexual desire; CBT and sexual skills training (eg, sensate focus) were particularly strong compared with marital therapy alone. Given changes in the conceptualization of women's sexual desire in the past 15 years, it will be important to supplement available evidence with newer trials that take into account this evolution. These approaches have the benefits of demonstrating positive effects on multiple domains of women's sexual function, not just desire. Limitations of these interventions are that they need to be given by trained

professionals, a scarce and expensive resource in some communities. Bibliotherapy is less costly and widely available, but untested in a clinical population. In conclusion, there is Level 2 Evidence supporting several psychological treatments for low sexual desire in women.

HYPOACTIVE SEXUAL DESIRE DISORDER—BIOLOGICAL APPROACHES

The neuroendocrine milieu is the major determinant of women's sexual functioning as evidenced by major reproductive milestones (menarche, pregnancy, menopause) and endocrine manipulations (eg, hormonal contraception, hormonal chemotherapies, other hormonal therapies), which are associated with significant variations of sexual response at multiple levels (CNS, urogenital organs).[61,62] There are many central hormonal and non-hormonal targets for FSD and its treatment because the neuroendocrine contribution regulating excitatory and inhibitory neurochemicals is crucial to sexual desire and arousal and orgasm and satisfaction.[63] Sexual inhibition involves neurochemicals such as serotonin (5-HT), endocannabinoids and opiates, whereas sexual excitation involves other neurochemicals such as oxytocin (OXT), norepinephrine, dopamine, and the melanocortin system.

Sex steroids (estrogens, progestogens, and androgens) exert organizational and activational effects and prime the brain to be selectively responsive to sexual incentives. With proper functioning, this creates a neurochemical state more likely to induce sexual excitation than sexual inhibition.[64] Sex steroids exert a trophic effect within the genitals and modulate the threshold of tissue response to external and internal stimuli throughout a vast array of molecules (eg, vasoactive intestinal peptide, neuropeptide Y, nitric oxide, cytokines, etc), with vasoactive, neuroactive, and immunoactive properties that have been considered suitable targets for potential treatments to improve genital arousal and orgasm.[65–67] However, sexual motivation and performance capability are not totally controlled by sex steroids in humans and difficulties in identifying a link between circulating hormonal levels and sexual function constantly challenge researchers.[68] Over the years, we have learned a great deal about individual variability at the level of endogenous sex steroid biosynthesis and intra-crinology, receptor binding, absorption rate, bioavailability, elimination, and so on, which likely explains the difficulty in accurately measuring peripheral sex steroids to clearly document the "hormonal factor" and to balance benefits and risks of potential hormonal treatments. Even non-hormonal treatments targeting other molecules, for example, neurotransmitters, can display a similar individual variability. Future research will shed light on the genetic and epigenetic factors influencing human sexuality to develop effective and safe therapeutic strategies to manage FSD.[69]

Menopause is the most studied condition in the context of FSD, and sex hormones specifically designed to treat climacteric symptoms associated with endocrine deficiency also have been used to treat sexual symptoms,[70] whereas data on hormonal pharmacotherapy in premenopausal women are scant and poorly controlled. The significant decrease of circulating estrogen levels with natural menopause, the decrease of androgen with age, and the rapid decrease with surgical menopause contribute to FSD in some women. Sex steroid deprivation has multisystemic implications for women's health and specifically for sex hormone–dependent tissues (ie, vulva, vagina, etc). In their absence, conditions associated with menopause become easily evident and clinically assessable, without the need to measure serum sex steroid concentrations to make or confirm a diagnosis, unless indicated by the clinical history.[71] The most important practical issue seems to be the early recognition of endocrine-related sexual concerns such as genito-urinary syndrome of menopause, an objective, chronic, age-dependent condition, resulting from estrogen deficiency, associated with symptoms such as dryness, itching, irritation, burning, dyspareunia.[72] Indeed, after menopause, HSDD can be associated with sexual pain disorders[3,73] or primarily induced by the "androgen insufficiency syndrome," a clinical diagnostic entity more frequently occurring as a consequence of iatrogenic premature menopause. Additional information on the treatment of FSD using hormonal therapy, particularly androgens, can be found in articles by Davis et al,[74] Santoro et al,[75] and Worsley et al[76] based on the ICSM meeting (Level of Evidence = 1).

Non-Hormonal Treatments

The potential use of CNS medications to treat FSD arises from laboratory and clinical studies suggesting the role of some neurotransmitters in the activation and/or deactivation of brain areas affecting sexual response.[64,67,77] Specific patterns of CNS functioning have been documented by functional magnetic resonance imaging in women with HSDD compared with women with no history of HSDD.[4] Brain activity also has been investigated to unravel the mechanisms of orgasm and reward,[78] whereas dynamic genital magnetic resonance imaging studies have enabled the visualization of the physiologic arousal response to develop possible neuroactive and/or vascular treatments for FSAD.[79]

Flibanserin is a novel non-hormonal therapy, initially developed as an antidepressant medication and subsequently studied in premenopausal and postmenopausal women with HSDD.[80,81] Flibanserin is a 5-HT_{1A} agonist and 5-HT_{2A} antagonist and binds with moderate affinity to 5-HT_{2B}, 5-HT_{2C}, and dopamine D_4 receptors. Flibanserin shows a mixed mechanism of action facilitating the normalization of CNS neurotransmitter levels to enhance sexual desire. It inhibits serotoninergic "anti-sexual" effects and promotes "pro-sexual" dopaminergic effects. In addition, by decreasing 5-HT levels, flibanserin increases norepinephrine, another "pro-sexual" neurotransmitter.[82] Starting from the hypothesis that HSDD is the result of an imbalance between excitatory and inhibitory neurochemicals,[64] extensive clinical research[83–86] demonstrated statistically and clinically significant improvement in the number of satisfying sexual

events, level of sexual desire, and decrease of distress compared with placebo after 24 weeks and up to 52 weeks in open-label extensions (Level of Evidence = 1). European studies have reported data similar to phase III North American trials, but with more variability among various countries.[87,88] No withdrawal reactions were evident after discontinuation and the rate of serious adverse events with flibanserin was less than 1% and not related to treatment dose or duration. Frequency of common adverse events, such as nausea, dizziness, fatigue and somnolence, was approximately 10%.[89]

In 2015, flibanserin received US Food and Drug Administration (FDA) approval for a 100-mg night-time dose for premenopausal women under the brand name Addyi (Valeant, Laval, QC, Canada).[6] Because of safety concerns, the approval was coupled with a Risk Evaluation and Mitigation Strategy (REMS) with Elements To Assure Safe Use (ETASU) program to ensure the benefits of flibanserin would outweigh the increased risk of hypotension and syncope from an interaction with alcohol. The interaction with alcohol was not seen in the phase III clinical trials but was reported in a separate alcohol interaction study.

The antidepressant bupropion, a compound with dopamine and norepinephrine reuptake inhibition and no direct serotoninergic effect, has shown a mild to moderate pro-sexual effect vs placebo in small randomized clinical trials (Level of Evidence = 2).[90] It could be considered a possible off-label treatment option in women with HSDD. In addition, trazodone, an antidepressant belonging to the class of 5-HT receptor antagonists and reuptake inhibitors, has a similar sparing and pro-sexual effect on sexual function. Buspirone, an anxiolytic drug that is a partial agonist for 5-H_{1A} receptors,[91] likewise has been shown to have pro-sexual effects (Level of Evidence = 2). Daily use of a combination of bupropion and trazodone and the on-demand use of buspirone combined with testosterone are currently under investigation with the aim of balancing the neuroendocrine substrates of the sexual response in women.[92] Another centrally acting compound, apomorphine, a non-selective dopaminergic receptor agonist, was tested in premenopausal women with HSDD and FSAD and found to have mildly positive results.[93]

A novel pharmacologic approach for the treatment of HSDD and FSAD involves melanocortins, a class of neuropeptides produced by many tissues including the CNS the modulate sexual behavior at the level of the hypothalamus in women and men.[94] Bremelanotide is a synthetic melanocortin analog of α-melanocyte—stimulating hormone that acts as an agonist at the melanocortin 3 and 4 receptors, an effect that might confer benefits on desire and arousal, facilitating the ability to translate sexual cues in genital response.[95] Administered subcutaneously, bremelanotide has demonstrated efficacy and safety in a phase IIB program and is currently in phase III trials. In phase IIB, statistical significance on every clinical outcome (desire, arousal, orgasm, satisfying sexual events, and sexually related distress) was found to be improved over placebo when premenopausal women with HSDD self-injected on demand the 1.75-mg dose vs placebo after 12 weeks of treatment. Different dose-dependent separations from placebo also were found according to the clinical end points in women with HSDD and/or FSAD (Level of Evidence = 1).[96–98]

Phosphodiesterase type 5 inhibitors (PDE5is) are discussed in the section under arousal disorders; they have not been found to be efficacious for HSDD. There is a growing interest in the neuropeptide OXT as a facilitatory agent of arousal and orgasm. Well-designed studies in women with FSD need to be conducted to support the observation that acute intranasal OXT administration exerts specific effects on parameters of sexual function and partner interactions.[99] However, the crucial role played by OXT in sex, reproduction, and emotional bonding paves the way to multidimensional biopsychosocial research examining sexual and relationship problems.

Combined Pharmacotherapy on Demand: New Hope for FSD?

It has been hypothesized that women with HSDD fall into 2 distinct subgroups: those women whose HSDD symptoms are due to relatively insensitive brain systems for sexual cues and those women whose HSDD might be due to enhanced sexual inhibitory mechanisms. This distinction in etiologic state prompted the use of sublingual testosterone (0.5 mg) in combination with a PDE5i (sildenafil 50 mg) to enhance sexual responsiveness in women with low sensitivity to sexual cues.[100] Conversely, for women with an overly active sexual inhibition mechanism, buspirone (10 mg), a 5-HT_{1A} receptor partial agonist in combination with sublingual testosterone (0.5 mg), was theorized to increase sexual motivation.[101] Physiologic and subjective measures of sexual functioning significantly improved in the 2 groups of women as a result of the 2 drug combinations (Level of Evidence = 2). This combination therapy also might hold promise for women with FSD induced by selective serotonin reuptake inhibitors (SSRIs).[102,103] In addition, on-demand vardenafil (10 mg) has been tested in combination with sublingual testosterone to reinforce the importance of acting at multiple levels with hormonal and vasoactive strategies to improve genital response in women with low attention to sexual cues.[104]

FEMALE SEXUAL AROUSAL DISORDER

Subjective vs Objective Arousal: A Challenging Construct

Female sexual arousal has been a target of experimental assessment since the 1970s. This construct has been persistently challenging because of the lack of concordance between subjective sexual arousal and genital arousal. Subjective sexual arousal refers to a woman's perception about her genital responses, whereas genital arousal refers to the physiologic activation such as vaginal lubrication and vasocongestion. Lack of concordance reflects the weak relation between subjective and physiologic sexual responses. The preparation hypothesis states that women's genital response occurs automatically to diverse sexual stimuli

(including those rated as non-preferred stimuli) as a means to prevent genital injury such as the rupture of the perineal area that often occurs in rape scenarios.[105] The lack of concordance between subjective and physiologic responses, which has been traditionally regarded as a proxy of dysfunction or impairment (eg, Gannon and Haynes[106]), in fact might represent an adaptive mechanism.

Several psychophysiologic studies have focused on the relation between subjective and genital sexual responses in women. Most of these studies have used vaginal photoplethysmography, the current gold standard method to assess female genital arousal. This technique consists of a perceptible red or orange light-emitting diode and a photodiode placed inside an epoxy glass device (shaped like a tampon) that measures the blood volume in the tissue surrounding the probe. Prause et al[107] conducted a study in which women were asked to rate their level of genital blood flow while being exposed to a sexual stimulus (thus increasing the level of awareness to genital phenomena). Even with this directed focus, the level of concordance was low. The instruction to rate vaginal blood flow increased the experience of subjective sexual arousal and genital arousal but not the concordance. Other studies have shown that the low concordance in women is not related to their (low) interoception ability (ie, awareness of physiologic cues).[108,109] These findings suggest that although cognitive strategies can be used to direct attention to sexual sensations and thereby increase the physiologic and subjective components of arousal, they might fail to increase the concordance between subjective and genital arousal. In a meta-analysis, Chivers et al[110] corroborated the general tendency for female low concordance. More recently, a study using pupil dilatation as a measure of sexual arousal also corroborated the lack of concordance in women.[111] Carvalho et al[112] reported low concordance in 2 experimental conditions in which women were exposed to an uncommitted and a committed relational context. This is in line with the work of Chivers et al[110] showing that women-centered erotica did not improve subjective and genital concordance. It is worth noting that sexually healthy women present increased genital responses to explicit and non-explicit or romantic stimuli, although subjective responses are higher to the latter.[113,114] This makes subjective sexual arousal more likely to be associated with the emotional valence attributed to a stimulus, whereas genital arousal seems to be independent of such assessment. It is likely that subjective and physiologic sexual responses are affected by distinct structures at different levels of awareness.[115]

Despite this body of evidence demonstrating low concordance between subjective and genital arousal in women, some have challenged this notion. Rellini et al[116] offered evidence that the lack of concordance between subjective and genital arousal in women was a methodologic byproduct or statistical artifact rather than a real psychophysiologic phenomenon. Other psychophysiologic studies using thermography, rather than vaginal photoplethysmography, have shown concordance between subjective and physiologic sexual responses.[117,118] Also, in a study using laser Doppler imaging (a method that targets the external genitalia), subjective sexual arousal significantly predicted genital arousal in women.[119] It appears that external genital arousal is more concordant with women's subjective appraisals of sexual arousal than internal (vaginal) arousal. It might follow that women rely on their external genital sensations as feedback for monitoring sexual arousal. These results also call into question what is really being measured. If the output from the external genitalia correlates with the subjective responses (whereas the outputs from internal genitalia do not), then distinct components of genital arousal have been measured under the same label. To what extent these components (internal vs external) contribute to the phenomenon of female sexual arousal is still unknown. Thus, if psychophysiologic measures focusing on the external genitalia correlate more with subjective sexual arousal, then future studies would be expected to test the utility of such measures in genital biofeedback.

More recently, a study on the lack of concordance focused on the central processing of sexual stimuli rather than on the peripheral activation. Surprisingly, a concordance between subjective and physiologic sexual activation was stronger for women than for men.[120] Using vaginal photoplethysmography, Laan et al[121] found no differences in genital responses from women with and without sexual arousal disorder. Similarly, women with combined genital and subjective arousal disorder presented increased vaginal pulse amplitude (ie, more genital arousal) compared with healthy controls.[122] Also, Rellini and Meston[123] found that the FSFI was more accurate than the genital measurement (using vaginal photoplethysmography) in assessing treatment efficacy in women with sexual arousal disorder. These data add to the controversy regarding the role of vaginal vasocongestion in sexual arousal. However, it is worth noting that women with sexual arousal disorder evidenced lower concordance (compared with healthy controls and women with orgasm disorder), which offers preliminary evidence for the utility of considering subjective and genital concordance in the assessment of sexual arousal difficulties in women.[122]

In all, it is uncertain how the subjective appraisal of sexual phenomena mirrors psychophysiologic processes in women. Future studies, using new techniques or simply moving the focus to other areas such as the CNS or the external genitalia, are expected to provide better evidence on this apparent dyssynchrony, its sources, and function. Unfortunately, an additional limitation of this area of research is its almost exclusive focus on Western cultures.

Recommendations

The low concordance between subjective and genital arousal in women has long been recognized when assessed by vaginal photoplethysmography. More recently, new methods focusing on the external genitalia (and, to a lesser extent, on the central processing of sex stimuli) have suggested higher concordance between subjective and genital female sexual arousal. These

findings suggest that the various components comprising female sexual arousal might be processed differently in women's appraisal of sexual arousal. Understanding the processes under which these components shape female sexual arousal would be of great importance for the design of new clinical tools.

Psychosocial Approaches—Clinical Presentation of Female Arousal Disorder

FSAD has a controversial history in diagnostic criteria. In the DSM-IV-TR,[9] FSAD was a single, distinct disorder. In the DSM-5,[10] FSAD was merged with HSDD. This new disorder is known as *female sexual interest/arousal disorder*.[124]

Neither version of the DSM categories and their criteria appears to fully correspond with women's subjective experience. In 1 survey using phone interviews, 75% of women who had sexual problems did not qualify for any DSM-IV-TR diagnosis and 92% did not qualify for a DSM-5 diagnosis.[125] The prerequisite that symptoms persist for 4 to 6 months further lowered the rate of women qualifying for a DSM diagnosis. A survey by Sarin et al[125] and a set of detailed interviews by Mitchell et al[126] support the newer FSIAD concept in which problems with desire and arousal are closely linked.

Nevertheless, experts in the field have not reached a consensus on FSIAD. Balon and Clayton[127] contended that the change in nomenclature was not based on field trials, contradicts recent evidence about the heritability of FSD, and fails to take genital sensation or lubrication into account, making it possible for some women to qualify for a diagnosis even if they only have a desire disorder. As Giraldi et al[128] noted, the DSM-IV-TR ignored subjective excitement and pleasure in defining FSAD. Those supporting the FSIAD diagnosis[129] cite literature reviews showing that women typically cannot distinguish between desire and subjective arousal, so that having 2 separate disorders is not justifiable. The committee also judged that problems with lubrication were often associated with menopausal changes or could easily be remedied by the use of over-the-counter lubricants and thus were not important as diagnostic criteria for FSIAD. The committee agreed that field trials were needed but pointed out the difficulties in funding them.

Interview Assessment of Sexual Arousal

In identifying a problem with sexual arousal, the most crucial element is to understand a woman's subjective experience. A semistructured interview could be the best tool for such an assessment. It might be helpful to define for the patient the concepts of sexual arousal, including erotic mental images, emotions of sexual excitement, pleasurable genital sensations, and noticing physical changes such as vaginal lubrication. Table 2 presents examples of questions that could be helpful.

Most questionnaires developed to assess FSAD are long and of limited value in a clinical assessment. The FSFI has a specific sexual arousal subscale, but the overall score for all 19 items is probably clinically more useful in screening for sexual dysfunction than arousal specifically.[130] Outside a research protocol, a clinician might find it more practical to gather information in a brief assessment interview, rather than by giving patients relatively long questionnaires.

Psychosocial Factors Contributing to a Women's Problems Getting Sexual Aroused

Understanding the factors that might have led to a woman's difficulty experiencing sexual arousal is crucial before developing a treatment plan. Interventions for a woman who is continuously stressed because of an overwhelming work and home life will differ from those for a survivor of severe sexual trauma, a woman who believes that women of her age should not be interested in sex, or a woman who does not feel sexually attracted to her current partner.

Culture, Sex Guilt, and Ability to Enjoy Sex

As Laumann et al's[131] Global Survey of Sexual Satisfaction in middle-aged and older adults noted, women in gender-egalitarian Western nations have the highest levels of sexual satisfaction and consider sexuality moderately important. Women in Middle Eastern societies have less satisfaction but consider sex extremely important. Women in East Asian countries tend to have low sexual satisfaction and rate sex as relatively unimportant. Studies that specifically measure guilt about feeling sexual demonstrate a close link with sexual desire and presumably arousal,[132] even when religiosity is taken into account.[133] In a sample of Iranian American women, sex guilt and negative perceptions of themselves as sexual people, rather than acculturation, predicted lower overall life satisfaction.[134] In the United States, older African American women might be particularly likely to have had traumatic experiences because of institutionalized racism and sexual exploitation, making it difficult for them to discuss sexual concerns with health professionals.[135] Sexual satisfaction is important, not only in itself but also because it is related to general well-being, although of course cause and effect are unclear.[136]

Quality of the Dyadic Relationship

A number of studies have found that women who feel satisfied with the quality of their overall intimate relationships[137] or rate the emotional intimacy in their relationship as higher[138] are less likely to have problems with sexual desire and arousal. Sociobiologists have hypothesized that women who find their partners more sexually attractive rate their relationship as more satisfying during ovulation, whereas women who are as not attracted to their partners get more critical of his faults at ovulation, perhaps leading to extramarital sex to secure the genes of a more desirable man. The ability to get aroused easily through self-stimulation or with a particular partner but not with another suggests that lack of sexual attraction plays a major role for women in arousal disorders. Even in a study of monozygotic twins discordant for sexual dysfunction, relationship quality was the strongest predictor of sexual problems.[139]

Table 2. Assessment of subjective sexual arousal

How often do you notice yourself feeling sexually excited?
What situations help you feel excited (ie, seeing an attractive person, engaging in sexual caressing, viewing erotic images, or reading an erotic story)? It might be useful to note that Ogi Ogas and Sari Gadam analyzed internet usage of men and women. In their book, *A Billion Wicked Thoughts: What the Internet Tells Us About Sexual Relationships* (New York: Dutton, Penguin Group; 2011), they described a gender difference. Women are more easily aroused by narrative stories, whereas men look for visual images.
Do you sometimes have sexual fantasies?
Is there a particular type of scenario in a fantasy or story that arouses you?
How easy is it to get aroused with your current sexual partner? (Partner-specific problems can signal relationship issues rather than a generalized sexual problem.)
What sensations do you notice in your genital area when you feel excited (ie, warmth, tingling, pleasure, increased wetness)?
Do you ever have erotic dreams?
Do you believe that your sexual excitement is healthy? (Guilt about sex can inhibit arousal. Some women, raised in a culture with a strong double standard restricting female sexuality, might rarely or never have felt sexually aroused.[114] Women who had a sexually traumatic experience in childhood also might have difficulty feeling sexual excitement.[305])
If you used to get aroused more easily, what do you think is interfering now?

Attentional Factors

Like other emotional states, sexual arousal is higher to novel stimuli and can habituate over time to the previously novel stimuli. Focusing on the "hot" emotional aspects of an erotic film by following instructions to try to experience it through the personal and emotional experiences of the actor produces higher arousal than the instructional set of being asked to watch the film as an observer.[140] Distracting, non-erotic thoughts during sex have been implicated as a cause of women getting or maintaining sexual arousal.[141] The correlation between distracting thoughts and low arousal has been observed in clinical populations and community samples.[55,141,142] Common distracting thoughts or concerns include feeling unattractive[143] or perceiving the partner's disapproval of the woman's body,[138] feeling pressure about "performing" sexually for the partner, or worrying about becoming pregnant or contracting a sexually transmitted infection. Women report more sexual arousal if they feel comfortable accessing erotic images on the internet,[144] welcome allow arousal while viewing an erotic video,[145] or feel entitled to sexual pleasure during activities such as oral sex,[146] suggesting that positive attitudes about sexuality are correlated with self-efficacy for enjoying sexual activity.

Chronic and Acute Stress

Although cognitive distraction is ubiquitous in life, some women experience high levels of stress in their external environment during an acute period of difficulty or on a continuous basis (eg, due to poverty or living in a violent neighborhood). Even for more affluent women, juggling work outside the home, household duties, and parenting (particularly of young children) can leave little interest in sexual activity.[147] Several recent studies have found that women under continuous high stress report less sexual arousal while watching erotic films. In addition, high levels of continuous stress weaken sexual desire and arousal, perhaps more severely than even severe acute stressors that could cause post-traumatic stress symptoms.[147–149]

Attachment and Mood Disorders

Although daily life issues can be enough to trigger sexual problems in many women, psychopathology also has been implicated in sexual arousal disorders. In humans, sex is a complex, learned behavior that can be influenced by a negative childhood environment, particularly the trauma of being sexually abused.[150] However, an insecure attachment to parents[151] and difficulty maintaining clear boundaries for the self[152] also can cause persistent difficulties getting sexual aroused. Of college students, those who had less intimacy in their relationship and more anxiety about attachment had poorer self-reported sexual function.[153] In young women not identified as clinical patients, anhedonic depression also appeared to be associated with sexual dysfunction.[154] A study of sexual function, distress about sexual problems, and sensitivity to anxiety in female monozygotic vs dizygotic twin pairs suggested a large inherited component that led to elevated sensitivity to anxiety and to sexual dysfunction, with less, but still substantial, influence on whether women were distressed about their sexual problems.[155] Thus, environmental and biological factors link a tendency to negative emotion with difficulties with sexual desire or arousal.

Aging and Menopause

In many societies, it is expected that women will lose desire for sex and have trouble getting aroused with aging. What is striking is that although the prevalence of problems with sexual desire and arousal increase with age in women, distress about sexual dysfunction decreases concomitantly.[156–158] As women age, from their 40s through their 80s, fewer and fewer have a sexual partner because of attrition through divorce or death. Because men tend to have relationships with younger women and have shorter average lifespans than women, the pool of available male partners shrinks drastically over time.[159] Furthermore, men's problems with erections increase with age, often leading to discontinuation of sex[157] or poor-quality sex for the female partner.[160] In the National Social Life Health and Aging Project,

a population-based study in the United States of people 57 to 85 years old, women who reported rarely engaging in sexual touching had more trouble with sexual arousal and reaching orgasm.[161] Thus, demographic factors and attitudes about aging and sexuality can contribute significantly to the prevalence of sexual dysfunction in women older than 40 years.

Potential Treatments for the Psychosocial Aspects of Female Sexual Arousal Disorder

Creating a treatment plan for a woman with difficulty getting or staying subjectively aroused during sexual situations requires a careful assessment to see whether at least 1 of the factors identified below might be causing the problem:

- Are cultural or religious factors causing sex guilt and inhibition?
- Is the problem with arousal specific to the partner and associated with problems in a dyadic relationship?
- Does the woman have many distracting cognitions during sex, and what kinds of thoughts interfere (insecurity about attractiveness or ability to please the partner sexually, memories of past sexual trauma, or other issues)?
- Is the woman under high levels of stress and/or does she have poor stress management skills?
- Does she have a tendency to focus on negative affect that might be related to her genetic disposition or her developmental attachment issues?
- If she is older than 40 years, does she lack a sexual partner or have a partner whose ill health or erectile dysfunction limits sexual activity and pleasure?

Overcoming Cultural or Religious Concerns

No publications have described an evidence-based treatment designed to lessen women's guilt and negative views of sexuality. However, innovative work is being done using online role-playing games to lessen shame in ethnic minority men who engage in sex with other men, with some evidence that decreasing shame leads to a decrease in unsafe sexual activity.[162] A similar approach could be applied to the issue of sex guilt in women. However, the ethical issue arises that many women might not wish to change their cultural or religious beliefs about sexuality, even if they lead to negative affect that interferes with arousal and pleasure. Within religious or cultural communities, a member of the clergy or local community leader who has a moderate stance on sexual pleasure might be more effective in decreasing guilt than a mental health professional from outside the community. Peer counseling with similar women who are sexually functional could be another option. Research is certainly needed in this area.

Improving Attentional Focus During Sex

Undoubtedly the most promising recent approach to improving women's sexual arousal is to incorporate mindfulness techniques into more traditional sex CBT treatment.[5,51,163] Brotto et al[5,51] created and evaluated a group treatment for women with sexual desire or arousal disorders. This was described in the section on HSDD. In a pilot randomized trial, 19 of 26 women in the intervention provided pre- and post-treatment self-report questionnaires and data from physiologic recordings while viewing an erotic film.[51] Measures of self-reported sexual arousal and positive emotions increased significantly from before to after treatment. Questionnaire measures of sexual function (FSFI) and distress (Female Sexual Distress Scale [FSDS]) also improved. Women who had a history of sexual abuse were more likely to make gains, suggesting that mindfulness helped them stop judging themselves negatively and allowed them to focus on pleasure while in sexual situations. In a randomized clinical trial, 117 women were assigned to immediate or delayed mindfulness sex therapy groups.[5] Treatment resulted in significant improvements on the FSFI on sexual desire, arousal, lubrication, and satisfaction, but scores on sexual distress improved over time in the treatment and waitlist groups. Gains were maintained at 6-month follow-up.

Incorporating mindfulness training into sex CBT approaches could help women learn to focus on pleasurable sensations while becoming less likely to be distracted by negative thoughts and feelings during sex. Indeed the sensate focus exercises[164] could be viewed as training mindfulness by asking each partner to focus on his or her own bodily sensations while noticing any negative thoughts but refocusing attention on physical feelings. Brotto et al expanded the amount of training and focus on mindfulness in their group treatment (Level of Evidence = 2).

Stress Management Approaches

Mindfulness meditation can help women manage acute and long-term stress, which appear to interfere with sexual arousability. The potential for mind-body training to improve sexual function has rarely been assessed. Two small randomized trials suggested that this approach has promise, especially for women whose sexual dysfunction is associated with a chronic illness. In women with irritable bowel syndrome, a nurse delivered a disease management program including education, diet, relaxation, and cognitive-behavioral homework that improved sexual function compared with usual care.[165] A 12-week yoga exercise group improved sexual arousal and lubrication in women with metabolic syndrome compared with those in a waitlist control group.[166] Programs that focus on weight loss and improving health through better nutrition and exercise also can have a positive influence on women's sexual function, not only because of enhanced well-being but also because of increased feelings of attractiveness and decreased distraction from negative thoughts about body image during sex. An intensive lifestyle intervention for women with type 2 diabetes resulted in not only significant weight loss after a year but also higher rates of being sexually active and improved FSFI scores.[167] Bariatric surgery also has been reported to improve sexual function in women,[168] although reproductive hormones also normalized in this sample; it is

unclear whether ancillary education and exercise programs play a role in addition to the weight loss.

Treating Attachment and Mood Disorders

Studies that use evidence-based techniques to treat attachment and mood disorders have not reported sexual dysfunction outcomes. Depression or anxiety disorders have often been regarded as poor prognostic factors for sex therapy,[169] and women with these diagnoses typically have been excluded from randomized trials of sex therapy or drug treatments[86] for FSD. Although psychotropic drugs can be effective for depression or anxiety, they have side effects that can decrease sexual arousal and pleasure.[170] Thus, psychological treatments for depression or anxiety would be preferable. One interesting study assigned 5 30-minute expressive writing sessions to women who had a history of childhood sexual abuse.[171] Women were randomized to write about the trauma or about their sexual schema (self-view as a sexual person). Those who wrote about their sexual schema had more improved sexual function, although at 6-month follow-up, the 2 groups improved on measures of depression and post-traumatic stress disorder.

Hormonal Pharmacotherapy for FSAD

Testosterone

There are high-quality RCTs previously discussed in the section on HSDD that demonstrated that transdermal testosterone patch therapy can improve not only sexual desire but also arousal (Level of Evidence = 1).[172] In a placebo-controlled study in hypogonadotropic hypogonadal women, treatment with testosterone undecanoate (40 mg/day orally during an 8-week period) enhanced genital arousal as measured by vaginal photoplethysmography. Because women swallowed the capsules each morning and the measurements were performed in the afternoon, it was assumed that this effect on genital sexual responding could be caused by a time-dependent effect of testosterone. To test this hypothesis, eugonadal and sexually functional women were administered a single dose of testosterone sublingually (0.5 mg). Such pulsed testosterone delivery produced supraphysiologic testosterone levels 15 minutes after treatment, with levels returning to normal within 1.5 hours.[173] A 4-hour delay effect of testosterone at vaginal photoplethysmography was demonstrated.[173,174] This finding was replicated in another laboratory.[175]

Testosterone could have a direct effect on the vagina and genital structures independent of the effects of estrogen.[176] An RCT comparing the use of vaginally administered compounded testosterone cream alone or in combination with a vaginal estrogen cream demonstrated improvements in the sexual function of the 80 postmenopausal women studied.[177] In addition, the daily use of vaginal testosterone might attenuate dyspareunia in women with breast cancer who are on aromatase inhibitors.[178]

Selective Tissue Estrogenic Activity Regulator

Tibolone, a 19-nortestosterone derivative, is metabolized into 3 main metabolites: the 3α-hydroxy and 3β-hydroxy isomers, which are estrogenic, and the δ-4 isomer, which has progestogenic and androgenic properties. Tibolone is classified as a selective tissue estrogenic activity regulator. It has the potential to act differently in multiple organs because of the dissimilar steroid properties of its metabolites.[179] For example, in postmenopausal women, it acts as an estrogen on the brain, vagina, and bone but not on the endometrium and breast. It has been used outside the United States to treat postmenopausal symptoms and was found to enhance mood and libido.[180,181] A randomized, double-blinded, crossover study was conducted in 38 postmenopausal women who received tibolone 2.5 mg/day and placebo. Vaginal blood flow during erotic stimulation was measured using vaginal photoplethysmography and subjects completed sexual function questionnaires and daily diaries. Women receiving tibolone showed a significant increase in vaginal photoplethysmographically measured arousal in response to erotic fantasy, but not during erotic film stimulation. Tibolone was associated with significant increases in sexual desire and the frequency of arousability and of sexual fantasies compared with those with placebo (Level of Evidence = 2). Vaginal lubrication was significantly improved on tibolone.[182]

In another study, 72 women were randomized to treatment with tibolone or continuous combined conjugated equine estrogens 0.625 mg/day and medroxyprogesterone acetate 5 mg/day. After 6 months of treatment, the 2 groups demonstrated significant self-reported improvements in sexual function, but women receiving tibolone had significantly higher sexual desire, sexual excitement, intercourse frequency, and vaginal dryness scores.[183] In an RCT comparing tibolone to transdermal estradiol with norethisterone acetate, tibolone showed a greater effect in postmenopausal women with FSD through increased responsiveness to partner-initiated sexual activity.[184]

Non-Hormonal Pharmacotherapy for FSAD

Phosphodiesterase Type 5 Inhibitors

The use of vasoactive drugs such as PDE5is in women is based on the notion that an increase in blood flow to the clitoris and vagina might improve sexual function like that seen in men with erectile dysfunction.[185] The data for PDE5is from clinical RCTs for FSAD have been reviewed and found to be contradictory and ultimately lacking in efficacy.[179,185] This is likely because there is discordance between the genital and subjective measures of the female sexual response.[179,185] Specifically, sildenafil was the first pharmacologic treatment investigated in controlled studies including women. In the very first laboratory study, which was done in sexually healthy women, sildenafil 50 mg produced an increase in physiologic but not in subjective arousal.[186] In a large study of diagnostically heterogeneous women, sildenafil 10 to 100 mg similarly showed no benefit in subjective sexual response.[187] In general, the literature has conflicting findings, with some studies showing a benefit[187–190] and others failing to find a significant benefit over placebo, and 1 study showing that

the benefit depended on psychophysiologic-measured impairments in sexual arousal.[189]

Sildenafil has been the most studied of the PDE5is in large-scale RCTs with a broad population of women with FSAD.[185] The evidence that in specific populations of premenopausal women with clear medical conditions, such as type 1 diabetes, spinal cord injury, multiple sclerosis and FSAD secondary to SSRI use, acute or even long-term PDE5i administration can result in significant improvements in subjective aspects and objective parameters of sexual response.[191−194] The data suggest a potential therapeutic role for these vasoactive agents in well-established medical conditions interfering with genital neurovascular substrates (Level of Evidence = 2).[195]

In 2004 Pfizer (New York, NY, USA) ended its program of testing sildenafil in women, perhaps resulting from the conflicting findings in medically healthy women.[196] It became important to investigate which factors might have been responsible for these inconsistent findings. Possible candidates were inadequate sexual stimulation (sildenafil will not be effective without sexual stimulation that is useful); inadequate outcome measures; improper patient selection (eg, women with sexual problems unrelated to genital responsiveness); and estrogen depletion.

L-Arginine

The nitric oxide precursor L-arginine was investigated in a double-blinded, placebo-controlled study combined with yohimbine, an adrenergic antagonist, in women with FSAD.[197] The combination significantly increased physiologic measures of sexual arousal (vaginal photoplethysmography) but had no effect on subjective measures of arousal or affect. A nutritional supplement, ArginMax (Daily Wellness Co, Honolulu, HI, USA), a proprietary blend of components L-arginine, ginseng, ginkgo and damiana, B-complex vitamins, vitamins A, C, and E, and minerals iron, calcium, and zinc, was studied in a double-blinded, placebo-controlled study of women older than 21 years who wanted to improve their sexual function.[198] In this study, the treatment group experienced an increase in lubrication, clitoral sensitivity, frequency of orgasm, and desire without any significant side effects.

Prostaglandins

During sexual arousal dilation of the vessels along the vaginal epithelium occurs. Topical alprostadil (prostaglandin E_1) is a vasodilatory agent as a result of its action of smooth muscle relaxation. Prostaglandins also enhance the activity of sensory afferent nerves, which improves sensation. One placebo-controlled, single-blinded, dose-response study of 0.1% alprostadil found a significant increase in self-reported lubrication and transudate volume, but no significant benefit over placebo by physiologic measurement (vaginal photoplethysmography).[199] Another small trial in postmenopausal women found a significant benefit on genital sensation, subjective sexual arousal, and sexual satisfaction.[200] A review from 2006 could not identify consistent or reproducible results of beneficial effects.[201] A phase III multicenter, randomized, double-blinded, placebo-controlled trial examined the use of 0.4% alprostadil cream with a skin penetration enhancer, an ester of N,N dimethyl alanine and dodecanol, and found that the 900-μg dose resulted in significant improvement in arousal and pain.[202]

Phentolamine

Two controlled studies investigated the effect of the α_1- and α_2-adrenergic receptor antagonist phentolamine based on the hypothesis that, as in men, the smooth muscle surrounding the vaginal arterial vascular bed is mainly α-adrenergically innervated. In a small study of 6 postmenopausal women with FSAD, it showed a positive effect on subjective and genital sexual arousal (vaginal photoplethysmography).[203] In the second, study a placebo-controlled administration of oral and vaginal applications in 41 estrogenized and non-estrogenized postmenopausal women found a benefit to genital response and subjective sexual arousal but only in the estrogenized women.[204]

Dopamine Agonists

Dopaminergic drugs have a direct effect on the brain and therefore could have a positive influence on sexual arousal and desire. Apomorphine is a non-selective dopamine agonist that acts on D_1 and D_2 receptors. In female rats, apomorphine has been shown to increase hormone-dependent genital vasocongestion and behavioral sexual response,[205] and in rabbits it has been shown to increase genital engorgement.[206] In an open-label, dose-escalating study in which an as-needed administration of sublingual apomorphine was given, there was significant improvement of sexual function in this group of premenopausal women with HSDD and FSAD. Side effects were mainly nausea, vomiting, and dizziness.[93] Another study assessing the effects of apomorphine was a small randomized, double-blinded, crossover, prospective study looking at the use of apomorphine before and after vibrator use with placebo. It demonstrated significant improvement in arousal and lubrication, but not in orgasm.[207]

Bupropion

Bupropion is an antidepressant with dopamine and norepinephrine reuptake inhibition. It has no serotonergic effect and has been shown to have to mild pro-sexual effects with improvement in all domains of sexual dysfunction compared with placebo.[78,90] In a Cochrane Database Systematic Review of management of SSRI-induced sexual dysfunction, 5 high-quality randomized trials, including 579 participants, found improvement in sexual rating scores with the use of bupropion 150 mg twice daily.[208] Bupropion was used in 1 uncontrolled study to counteract the sexual side effects of SSRIs. Keeping in mind that no adequate control was used, the investigators concluded that the results point to the relief of sexual complaints (Level of Evidence = 2).[209]

Oxytocin

OXT is a neuropeptide mostly known for its role in parturition and lactation, but has gained interest for a potential role as

an agent of arousal and orgasm. Behavioral studies have demonstrated that it might be responsible for prosocial behaviors in humans such as positive physical contact and communication methods with a partner.[210] Most studies with humans have used an intranasal approach. In a double-blinded, placebo-controlled, crossover design study, sexual arousal and orgasm were induced by sexual intercourse in 29 healthy heterosexual couples who were grouped according to their contraceptive method. Intranasal oxytocin 24 IU or placebo was administered and then sexual activity took place based on a standardized format during which physiologic parameters were measured and then followed by completion of questionnaires. In this study, OXT appeared to increase the intensity of orgasm and contentment after sexual intercourse.[99] More study is required to understand the potential pro-sexual and pro-relationship effects.

Zestra

Zestra (Innovus Pharmaceuticals, San Diego, CA, USA) is an over-the-counter massage oil of a blend of -borage seed oil, angelica extract, evening primrose oil, coleus extract, and vitamins C and E and was designed to increase blood flow to the clitoris, labia, and vaginal opening.[211] Borage and evening primrose oils contain large amounts of γ-linolenic acid, which is metabolized to prostaglandin E_1; angelica root contains osthole, which increases cyclic guanosine monophosphate and cyclic adenosine monophosphate; and the components of coleus extract are adenylate cyclase stimulants.[211] In a small, randomized, double-blinded placebo-controlled, 2-way crossover study of 10 women with FSAD and 10 women without FSAD, this topical application demonstrated an increase in levels of arousal, desire, ability to have orgasm, sexual pleasure, and satisfaction in women with and without FSAD compared with placebo. Women with FSAD showed greater response than women without and women using SSRIs had the same improvement as women not using antidepressants.[211]

ORGASMIC DISORDER

Psychosocial Approaches—Diagnostic Criteria and Clinical Presentation

FOD refers to absence of orgasm, difficulty experiencing orgasm, or decreased intensity of orgasm during all or most occasions of sexual activity. The symptoms can be lifelong or acquired. Difficulty reaching orgasm might be isolated to specific sexual activities, situations, or partners. Symptoms must be distressing to the individual.

A few subtle but important differences distinguish the diagnostic criteria for FOD in the *DSM-IV-TR* and *DSM-5*. A significant change in the *DSM-5* was the removal of the criterion requiring that difficulty with orgasm occur despite "a normal excitement phase." This potentially confusing criterion was construed at times to mean that FOD could not be diagnosed concurrently with FSAD,[212] an issue that the current criteria have clarified. Another change is that the criteria refer not only to frequency and/or latency of orgasm but also to intensity; a problem with any one of these aspects of orgasm is diagnosable as FOD.

FOD is often diagnosed concurrently with at least 1 other sexual dysfunction. However, the diagnosis is ruled out when symptoms are better explained by a non-sexual mental disorder, severe interpersonal distress, a medical treatment, or a medical condition.[10] The clearest example is when the onset of symptoms follows the introduction of certain known medical risk factors. For instance, delayed, weakened, or absent orgasm is a well-known side effect of SSRIs and other psychotropic medications.[213] From a psychologic standpoint, the onset of a major life stressor or a negative change in relationship adjustment could hypothetically interfere with orgasm,[214] although in practice the effects of these changes are unpredictable and not necessarily abrupt.

The psychological treatment outcome literature for FOD focuses predominantly on 2 broad types of presentations. The first is lifelong, generalized FOD, commonly termed *primary anorgasmia.* Although this subtype is less common than acquired or situational FOD, the early sex therapy literature covered primary anorgasmia extensively.[215–218] The second group consists of women with situational FOD that is specific to partnered sexual activity, especially vaginal intercourse. Studies of this population have often defined treatment "success" in terms of orgasm frequency during partnered activity.[43,219–222] Although women also can experience acquired, generalized orgasmic disorder, this pattern appears to be more typical when the etiology is medical or iatrogenic.

Even among women without sexual dysfunctions, subjective experiences of orgasm vary considerably,[78,223] and female orgasm has been a difficult concept to operationalize.[223–225] Hence, the diagnostic criteria for FOD are broad and rule out more than they rule in. One important consideration explicitly mentioned in the *DSM-5* is how to interpret a lack of orgasm through vaginal intercourse alone (ie, without external stimulation of the clitoris). The distinction between "clitoral orgasm" and "vaginal orgasm," which emerged in the early psychoanalytic literature,[226] continues to be of interest to the lay public and among clinicians. With few exceptions,[227] orgasm triggered by clitoral stimulation has been de-pathologized and viewed as a normal variation in sexual response.[50,228–230] Accordingly, the *DSM-5* states that "a woman's experiencing orgasm through clitoral stimulation but not during intercourse does not meet criteria for a clinical diagnosis of FOD."[10] This is significant for the large proportion of women (at least 1 third) who report that they are reliably unable to experience orgasm during vaginal intercourse,[231] a trait that appears to have a substantial heritable component.[232–234] Furthermore, although most women can reach orgasm through masturbation, orgasm during partnered sexual activity of any sort is less frequent and consistent.[235,236] Although lack of orgasm with a partner might be attributable to FOD, the clinician must always be sensitive to the possibility that situational factors or the

partner's skill and behavior are contributory. It is notable that self-identified lesbians appear more likely to reach orgasm during sexual activity with a partner than heterosexual or bisexual women,[235] although rates of self-reported orgasm problems appear to be roughly comparable between heterosexual and non-heterosexual women.[237]

Interview Assessment of Female Orgasmic Disorder

The clinical interview is the primary method of assessment for FOD. After establishing the nature, onset, and chronicity of difficulties with orgasm, it is useful to evaluate other aspects of sexual response. Infrequent or delayed orgasm often accompanies complaints of low sexual desire and/or difficulty becoming sexually aroused. Although some women might complain of rarely sensing an impending orgasm, others might report that they experience feelings of increasing arousal or tension but without a peak or climax that resolves these feelings.

Women who present with symptoms of lifelong generalized anorgasmia have never experienced orgasm in any context. They tend to be younger and have less experience with sexual activity, including masturbation. Although reports of lifelong anorgasmia are usually accurate, it is nevertheless advisable to confirm this through a detailed history to ensure the problem does not stem from unclear or unrealistic expectations. In women with acquired or situational anorgasmia, it is important to establish the conditions or parameters under which orgasm has occurred in the past because this can help to rule out inadequate stimulation, contextual factors, or physiologic factors as a cause of current problems with orgasm.

Assessing the degree of bother or distress caused by problems with orgasm is the other key facet of diagnosis. Most women indicate that the ability to experience orgasm is important,[238] and multiple studies have indicated that frequency of orgasm during partnered sexual activity predicts overall sexual satisfaction.[239–241] Conversely, sexual satisfaction also is influenced by emotional intimacy and other relational factors,[239,240] perhaps to a greater extent than sexual function.[153] Although the woman's partner might be distressed by her infrequent or absent orgasm, this alone is not sufficient to warrant a diagnosis of FOD.

Through interview or record review, the clinician can assess certain risk factors that have been associated with orgasmic dysfunction in population- and community-based samples. Women with lower socioeconomic status, poorer physical health status, and poorer mental health (especially those with anxiety disorders or severe anxiety symptoms[242–247]) are at increased risk for problems with orgasm.[20,214,248,249] Conversely, age appears to have a negligible influence on orgasmic dysfunction.[214,244,250–252] Relationship adjustment is a reliable predictor of orgasmic function in the general population. In 2 large samples, problems with orgasm were significantly related to relationship dissatisfaction or concerns about the viability of the intimate relationship.[214,250] Restrictive attitudes and beliefs about sexual activity also are a risk factor for anorgasmia.[253] Further, there is some evidence that anorgasmic women are less likely to have had sex education during childhood or adolescence,[244] although it is unclear to what extent this effect is mediated by internalized negative beliefs vs lack of sexual experience.

Despite the variety of factors that can inhibit orgasm, the ability to experience orgasm should never be ruled out pre-emptively. The literature describes women who can experience orgasm during sleep,[254,255] through non-genital stimulation, through fantasy alone,[256] and through cervical stimulation.[257] Reports of women who retain the ability to reach orgasm after spinal cord injury[258] and clitoridectomy[259,260] illustrate how resilient this function can be even in the face of substantial physiologic or anatomic changes. These examples, although not necessarily typical, attest to the importance of physiologic and behavioral factors in the maintenance of orgasmic capacity.

Assessment of Orgasmic Function by Validated Questionnaires

Many measures of sexual function in women have at least 1 item pertaining to the frequency or intensity of orgasm during sexual activity. For instance, the FSFI[30] includes a 3-item orgasm subscale that inquires about frequency, difficulty, and satisfaction with orgasm during sexual activity. The FSFI total score and the orgasm subscale score have been found to differ significantly between women with FOD and women without sexual dysfunctions.[261] Similarly, other sexual function measures, such as the Changes in Sexual Functioning Questionnaire[262,263] and the Brief Index of Sexual Function for Women,[264] include orgasm-specific items. None of these measures provide sufficient information to establish the presence of FOD. However, in clinical practice they can be useful to track treatment progress empirically or benchmark against known populations. The FSDS[265] is a helpful adjunct that measures the degree of a woman's distress or bother related to sexual concerns and distinguishes women with from women without sexual dysfunctions.

Psychosocial Intervention Strategies

Most published clinical trials on FOD involve treatments that can be loosely classified as behavioral or cognitive and behavioral. Psychoanalytic and systemic conceptualizations and treatments also are used in FOD but have received little empirical evaluation. A notable feature of the treatment outcome literature is that most trials specific to FOD were published more than 30 years ago.

Psychoeducation

Education is the cornerstone of all evidence-based psychological interventions for FOD. In general, women are receptive to accurate information about sexual anatomy and physiology, variations in sexual response, and common forms of stimulation used to reach orgasm. This process can be therapeutic in itself.[266] Educating the patient (and her partner) also is useful to the clinician because it can offer clues about misinformation, attitudes, or beliefs that contribute to the woman's sexual

difficulties. Psychoeducation can provide a clear rationale and justification for therapeutic techniques that might be anxiety-provoking to some patients.

Directed Masturbation

Of the psychological and behavioral treatments for FOD, directed masturbation,[218,267] also known as *masturbation training,* has received the most study and empirical support. Directed masturbation has been evaluated in multiple RCTs including 1 head-to-head comparative intervention trial[268] and trials comparing different delivery formats (Level of Evidence = 2).[216,269] Directed masturbation consists of a series of self-awareness and exploration exercises that are intended to help the woman become more familiar and comfortable with her genitals and other areas of the body that are experienced as erotic. In a progressive fashion, the woman is asked to complete a series of exercises between therapy sessions to explore her body and genitals, become more aware of sexually arousing stimuli, and eventually use her self-knowledge to masturbate to orgasm.[54] A partner can be incorporated into later phases of treatment as the woman applies her knowledge and skills to partnered sexual activity.

Sensate Focus

Sensate focus was discussed in the sections on HSDD and FSAD.[50] As with directed masturbation, home exercises are central to sensate focus approaches.

Coital Alignment Technique

The coital alignment technique is a strategy that has been taught to male partners seeking greater frequency of the woman achieving orgasm during vaginal intercourse. The technique allows for greater clitoral stimulation during vaginal intercourse.[43,222] A variant of treatment, termed *orgasm consistency training,* combines education about coital alignment technique with directed masturbation and sensate focus exercises.[43]

Summary and Treatment Recommendations

Several psychosocial treatment strategies for FOD have been evaluated in clinical trials, although there is little recent evidence that meaningfully extends earlier findings that established treatment efficacy. Previous reviews of the literature have concluded that skill-enhancing interventions, particularly directed masturbation and sensate focus, are effective treatments for FOD.[229,270] Since the last ICSM, a recent meta-analysis reaffirmed these findings.[42] Other therapeutic approaches, including anxiety management techniques and cognitive therapy, might be of benefit especially where distraction is an issue.

Therapeutic Issues: Use of Vibrators, Erotica, and Other Sexual Enhancement Products in Treatment

Often, treatment of FOD involves modifying the type or intensity of sexual stimulation that a woman receives. Vibrators and sexually explicit/erotic media are effective ways to enhance physical and psychological sexual stimulation, respectively. Vibrators and erotica have long been recommended to facilitate self-pleasuring exercises in directed masturbation programs. Vibrators have been widely available in many countries for nearly a century. In some countries vibrators are readily available through drugstores, internet sales, novelty retailers, and specialty erotica shops.

A common concern about the use of vibrators is that the woman will learn to "depend" on this source of stimulation to reach orgasm, to the exclusion of other sexual activities.[54,271] However, the data on vibrator use and sexual function tell a different story. Positive attitudes toward vibrator use and actual frequency of vibrator use predict higher scores on measures of sexual function.[272,273] Vibrator use during partnered sexual activity also is relatively common.[272] Therefore, patients and their partners should be offered reassurance and counseling about how to incorporate vibrator use into lovemaking, if mutually desired.

"Faking" Orgasm and the Role of the Partner

Several recent studies have sought to better understand the phenomenon of "faking" orgasm during partnered sexual activity. Most women with sexual experience have reported feigning orgasm in the past, most often during vaginal intercourse.[232,274] Although believed to be very common, the clinical implications of this behavior have received little study. Recent work has identified several reasons why women feign orgasm, chief among them the desire to reassure, satisfy, or prevent negative feelings in a partner.[275,276] Other motives for feigning orgasm include to avoid feeling ashamed or dysfunctional, to escape sexual activity that is unwanted, to move on to a another activity such as watching television or doing chores, and even to enhance one's own excitement or arousal.[275] Although this behavior can be innocuous in many cases, it also can point to beliefs or attitudes that stand in the way of more direct and adaptive sexual communication. Unfortunately, there is no empirical evidence on whether or how a history of feigning orgasm influences treatment engagement or outcomes for FOD.

Conclusion

Although desire and arousal concerns have been the primary focus of recent psychological treatment development efforts, problems with orgasm remain relatively prevalent and distressing. Although psychological treatments are efficacious for treatment of FOD, no new evidence has added to our knowledge of treatment outcomes since the 3rd ICSM. Further research should leverage the considerable body of evidence from previous research to develop efficient, flexible treatment programs that can be readily disseminated.

ORGASMIC DISORDER—BIOLOGICAL APPROACHES

Medical therapy is based on the understanding of the physiology of the orgasmic response.[64,67,78,79] Orgasm can be

understood as a complex summation reflex that is regulated by the somatic and autonomic nervous systems linked to CNS processing regions.

Medical Treatment of Orgasmic Disorders

With respect to the medical treatment of orgasmic disorder, 2 types of clinical situations can be distinguished. They are the treatment of orgasmic disorder in the context of desire and arousal disorders and the treatment of orgasmic disorder in women without desire or arousal disorder.

Medical Treatment of Orgasmic Disorders in the Context of Desire and Arousal Disorders

Most drugs have been studied in the context of desire and arousal disorders. As a secondary outcome, orgasmic function is assessed, and when there is improvement in desire and arousal, there is generally an increase in orgasmic capacity, frequency, or intensity.

These compounds enhance the afferent part of the spinal orgasmic reflex by improving the intensity of the sexual stimulus and/or increasing the receptivity to the stimulus (structural integrity of vulva and vagina, blood flow to the vulva and the vagina). Other drugs enhance the efferent pathway by noradrenergic and cholinergic activation and/or enzymatic action on the guanosine monophosphate system.

Phosphodiesterase Type 5 Inhibitors

These drugs increase vaginal blood flow through the guanosine monophosphate system. A randomized crossover study with sildenafil showed improvement in arousal and orgasmic function.[189] Studies using self-reported measures of sexual functioning have shown mixed results, whereas studies examining physiologic effects of PDE5 on genital vasocongestion consistently report significant effects on genital sexual response.[185]

Systemic Estrogen and Testosterone Therapy

Systemic testosterone and combined estrogen and testosterone therapy decrease arousal dysfunction, increase desire, and improve orgasmic function in premenopausal and postmenopausal women and in women after unilateral or bilateral oophorectomy. These effects are due to the receptive central nervous effects, the positive effects on vulvovaginal structure of estrogens, and the activating and excitatory effect of testosterone on the limbic system.[172,277–289]

Tibolone

Tibolone was previously discussed in the section on medical FSAD. It combines estrogenic, progestogenic, and androgenic actions, thus increasing desire, arousal, and orgasm.[180–182,184]

Conclusion

Effective medical treatment of desire and arousal disorder increases the chances of orgasmic response in the individual woman.

Medical Treatment of Orgasmic Disorder in Women With Subjectively Sufficient Arousal

There are very few studies including women with the primary complaint of not being able to experience or attain orgasm despite experiencing desire and subjective excitement. The underlying pathophysiology can be described as a stop or decrease in the increasing intensity of arousal toward the development of the orgasmic response beyond what was described as a plateau phase. The goal of any medical treatment of this group would be to intensify the arousal stimulation in strength, frequency, and greater stimulation.

Mechanical and vibratory devices were reviewed in the previous section on the use of vibrators, erotica, and other sexual enhancement products in treatment. Although many vibratory stimulating devices are available, only 1 FDA—cleared-to-market device is available by prescription to treat FSD (Eros therapy device; UroMetrics, Inc, St Paul, MN, USA). The Eros device is a small battery-powered appliance used to gently apply a direct vacuum over the clitoris, causing the clitoral erectile chambers and labia to fill with blood. The vibration from the suction pump also can aid in stimulation. In addition, the Fiera Arouser for Her, known as Fiera (Nuelle, Inc, Mountain View, CA, USA) is the first wearable "intimacy enhancer." The device consists of a small, rechargeable, battery-operated vibrating device that "adheres" to a woman's clitoris by gentle suction (eg, hands free). It is worn in preparation for sexual activity.

Short-Acting Drugs for On-Demand Treatment

Oxytocin

OXT could work synergistically with sex hormones to facilitate muscle contractions during orgasm. OXT from the paraventricular nucleus of the hypothalamus is secreted into the blood stream during arousal and orgasm; thus, it is considered a facilitator of arousal and orgasm.[290] Results of a clinical trial with OXT were discussed in the section on arousal.

OTHER—PERSISTENT GENITAL AROUSAL DISORDER: A SERIOUS CONDITION WITH MINIMAL DATA

Persistent genital arousal disorder (PGAD) is a clinical condition characterized by excessive and unremitting feelings of genital arousal in the absence of perceived sexual desire. Leiblum and Nathan[291] defined this syndrome according to the following criteria: (i) physiologic sexual arousal (genital and breast vasocongestion and sensitivity) persists for an extended period (from hours to days) and does not remit on its own; (ii) the signs of physiologic sexual arousal do not remit with ordinary orgasmic experience; (iii) the signs of physiologic sexual arousal are experienced in the absence of subjective feelings of sexual desire and arousal; (iv) the symptoms of sexual arousal can be triggered by sexual-related stimulus but also by non-sexual cues or no stimulus at all; and (v) these symptoms are perceived as intrusive

and unwanted, leading at least to some degree of distress. PGAD must be distinguished from hypersexuality (a symptomatic cluster characterized by out-of-control sexual thoughts and behaviors, accompanied by subjective feelings of sexual desire)[292] and clitoral priapism (engorgement of the clitoris that is experienced with significant pain).[293] PGAD is considered a serious condition with unknown prevalence and indeterminate etiology. Most assumptions on PGAD are based on anecdotal evidence; for this reason, existing findings must be regarded as provisional.

Despite limited evidence, some attempts were made to characterize women with PGAD. Findings on the psychosocial characterization of women with PGAD showed that these women present a negative appraisal of genital sensations,[294] are more likely to be depressed and to have panic attacks, or to present a history of sexual victimization.[295] In addition, women with PGAD were shown to present a sexually conservative thinking style accompanied by a maladaptive cognitive and emotional functioning during sexual activity.[296] Scores on a well-recognized self-report measure of female sexual functioning (the FSFI) showed that women with PGAD are not sexually dysfunctional but lack a satisfactory sexual life.[294]

Some etiologic factors, varying in nature (ie, biological, psychosocial, pharmacologic, etc), have been proposed. This variety suggests that PGAD might be assigned to a set of clinical conditions in which unwanted genital sensations are a common and salient feature.[297] Studies on the biological underpinnings of PGAD stress the role of physical abnormalities such as the existence of a peri-clitoral mass,[298] pelvic varices,[299] or Tarlov cysts[300] in the etiology of PGAD. Alternative evidence points to the effects induced by pharmacologic agents; PGAD symptoms were shown to initiate with venlafaxine[301] or with the discontinuation of an SSRI.[302] In addition, PGAD symptoms sometimes occur under the spectrum of clinical conditions such as restless leg syndrome and overactive bladder syndrome.[303] Soy intake[304] and sleeping[305] also were shown to induce PGAD symptomatology. A psychological conceptualization highlighting the role of the cognitive and emotional appraisal of genital phenomena by women with PGAD on the onset and/or maintenance of the genital symptoms has been further proposed.[306] It is likely that biological vs psychological factors account for different subsets of cases and variants. However, the exact proportion in which this happens is unknown.

With only minimal data on the etiology of PGAD, treatment targets become hard to define. Improvement of PGAD symptoms has been seen with duloxetine, pregabalin,[307] and varenicline.[308] Electroconvulsive therapy also has been successfully applied.[308] CBT targeting anxiety management, response prevention, and dyadic issues has been shown to improve sexual and emotional symptoms.[309] Because the mechanisms underlying PGAD are not completely known, practitioners are encouraged to direct the treatment to the probable cause of the disorder after a careful assessment. As an alternative approach, clinicians could eventually focus on the management of the distress caused by PGAD.[18]

Although recognized as a serious condition, PGAD still lacks an empirically supported framework. However, it is worth noting that some women presenting persistent genital arousal symptoms enjoy this state and do not seek treatment, reporting a satisfactory sexual life.[291] Acknowledging the factors (biological and/or psychological) discriminating women with from women without distress to persistent genital arousal symptoms could be a key issue to the understanding of PGAD. Another area that remains unexplored is that of the central and peripheral processing of sexual stimuli in women with PGAD. It was advocated that spontaneous genital arousal—at least in some women—could be a result of an unconscious processing of sexual stimuli leading women to appraise a potential sexual situation as being devoid of sexual meaning.[306] Another way of assisting women with PGAD would be through sexual education. Informing on this disorder is a way of capturing women's attention, increasing the chances of searching for help.

PGAD Recommendations

PGAD is a serious condition affecting women's emotional well-being. No RCT has been conducted on any of the potential treatments. There is only anecdotal evidence indicating that a set of organic and pharmacologic conditions might underpin PGAD. Some psychosocial markers also were shown to characterize women with PGAD. Eventually, these could be integrated with the organic approaches in a comprehensive treatment design. It also would be desirable to implement educational and informative activities to guide women in their searching for clinical help.

CONCLUSION

Since the prior ICSM consultation there have been significant advances in the assessment and treatment for women with FSD. Within this same period, the FDA withdrew a draft guidance, first issued in 2000, for conducting pharmacologic clinical trials in FSD treatments and most recently has issued a new draft guidance (Low Sexual Interest, Desire, and/or Arousal in Women: Developing Drugs for Treatment). The document outlines the FDA's current thinking about how best to design phase III trials for drugs to treat low sexual interest, desire, and/or arousal in women. Moreover, there has been recognition from the regulatory agencies of the suffering of women with sexual dysfunction. The FDA hosted a 2-day meeting in October 2014 to listen to the voices of women with HSDD and researchers working in this area (Patient-Focused Drug Development Public Meeting and Scientific Workshop on Female Sexual Dysfunction). These efforts at advocacy and education moved the bar forward such that HSDD and in the future all FSDs will be considered genuine conditions and not dismissed as lifestyle issues. Although we might argue about the best methods of

treatment, we can all agree on the suffering that women and their partners experience from these distressing problems. In fact, the FDA guidance specifically acknowledges that there is a medical need for drugs to treat women with sexual dysfunction.

This report has artificially disentangled the biological, psychological, and sociocultural components that affect the assessment and treatment of HSDD, FSAD, and FOD. Our goal was to provide an evidence-based review of these separate components to illuminate the most effective approaches when combined with an integrated biopsychosocial approach. Ultimately, efficacious assessment and treatment will be maximized with honest discussion between an HCP and a woman that validates her experience and results in evidence-based solutions that are tailored to the specific problem.

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