

Female Sexual Dysfunction: Disorders of Desire, Arousal and Orgasm

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Podcast: AUA on female sexual dysfunction**Key Points:**

- Epidemiologic studies consistently show that 42-45% of adult women report some symptoms of female sexual dysfunction (FSD), but only 10-17% are bothered by their symptoms to meet criteria for formal diagnosis of FSD.
- Inquiry on sexual wellness should be a routine component of urologic care for women. The presence of a sexual problem and concomitant distress merits evaluation or at minimum referral for further discussion and management.
- Desire, arousal, and orgasm dysfunctions are the result of sexually inhibitory factors (which may be psychosocial or physiochemical) overwhelming sexually excitatory ones. Treatment may involve psychotherapeutic and/or pharmaceutical interventions to eliminate inhibiting factors and/or support sexual excitation.
- There are two FDA-approved medications for pharmacotherapy of hypoactive sexual desire disorder (HSDD) – flibanserin and bremelanotide - both influence neurotransmission within the central nervous system (CNS) to encourage sexual excitation

Sexual dysfunction may occur in conjunction with urinary incontinence and pelvic organ prolapse. Appropriate consideration and counseling should be given to treatment of incontinence and pelvic organ prolapse (POP), as medical and surgical treatments may impact sexual function.

1. Introduction

Since the publication of data from the US National Health and Social Life Survey in 1999,¹ several epidemiological studies have examined the prevalence of FSD in both the USA and abroad. The largest of these is The Prevalence of Female Sexual Problems Associated with Distress and Determinants of Treatment Seeking (PRESIDE) study involving 31,581 US women aged 18 to 102 years, which found that 44% reported any sexual problem (desire, arousal, orgasm). Low desire was the most common problem reported by 39% of women, low arousal by 26%, and orgasm problems by 21%.² From these data it is clear that many women experience sexual symptoms; however, this same study indicated that just 12% of women reported

concomitant sexual problems and related distress.

The broader relevance of these national statistics is affirmed by other international studies including the Natsal in Britain and the GeSiD in Germany,³ which have demonstrated remarkably similar numbers of women affected by FSD symptoms and associated bother. It is important to note that the population featured in the PRESIDE study was overwhelmingly white and well-educated: smaller epidemiologic studies that feature more diverse populations suggest that women of color, sex-gender minority, or lower socioeconomic status are more likely to experience FSD.

Inquiry on sexual symptoms should be a routine component of urologic care for women. The presence of a sexual problem and concomitant distress merits evaluation or at minimum referral for further discussion and management. In this document we review and discuss disorders of desire, arousal, and orgasm in women as well as sexual function in patients with incontinence, prolapse and a history of pelvic mesh.

2. Hypoactive Sexual Desire Disorder (HSDD) in Women

2.1 Anatomy and Physiology

Sexual desire is a cognitive and emotional process, a function of neuroanatomy and physiology. Various neuroactive chemicals – including dopamine, melanocortin, norepinephrine, oxytocin, and testosterone – encourage sexual excitation; others – including serotonin, prolactin, and opiates – are sexually inhibitory. The activity of these chemicals on hypothalamic and mesolimbic pathways in the brain is modulated by learning, experience and behavior, medication and other drugs, or other neuropsychiatric disease processes. The balance of these excitatory and inhibitory forces regulates sexual interest and response, as summarized by the Sexual Tipping Point framework (www.mapedfund.org).^{4,5}

2.2 Diagnosis

HSDD is characterized by any of the following, associated with bothersome emotional distress, for a minimum of 6 months:

- Lack of motivation for sexual activity, as manifested by:
 - Decreased or absent spontaneous sexual desire/thoughts/fantasies
or
 - Decreased or absent responsive desire to erotic cues/stimulation
or
 - Inability to maintain desire or interest through sexual activity
- Loss of previously present desire to initiate or participate in sexual activity that is not secondary to avoidance of sexual pain.

HSDD can be lifelong or acquired, generalized or situational. Individuals with lifelong low or absent desire for sex may be (self-identified or not) asexual; in the absence of distress about low/absent sexual desire the patient should not be diagnosed with HSDD.⁶ Women who are distressed by an absence or diminution of sexual desire merit diagnosis and treatment.

According to the PRESIDE study, approximately 10% of adult women in the USA reported HSDD, with higher rates among those who are post-menopause.² PRESIDE and other epidemiologic studies confirm HSDD to be the most common female sexual complaint. While sexual function is important to patients, they are often reluctant to broach such a sensitive and potentially taboo subject without an overt invitation to do so. Ubiquity statements and validated tools such as the Decreased Sexual Desire Screener (DSDS) are helpful for eliciting

sexual complaints and obtaining the history necessary for diagnosis of HSDD.⁶

Past medical history and medications (both past and present) are all relevant to the diagnosis of HSDD. Frequently contributory conditions include: menopausal status; history of endocrinopathy, or the use of medications that affect the activity of sex hormones (e.g. combined oral contraceptives, spironolactone, aromatase inhibitors, etc.), neuropsychiatric disease or the use of neuroactive medications (e.g. selective serotonin reuptake inhibitors, antipsychotics).

In addition to eliciting the relevant medical, surgical, and sexual history, a physical exam assessing the vulvar and vaginal tissues is helpful. The genital exam may identify signs of hormone insufficiency, decreased sensation, or co-morbid pain that may not be identified by history alone. Laboratory and imaging tests are not diagnostic of HSDD, but may be indicated to narrow the differential diagnosis or identify comorbid conditions that are contributory to the problem.⁷

2.3 Treatment

Based on our understanding of the neurophysiology of sexual desire (Section 2.1), all treatments for HSDD are aimed at encouraging pro-sexual stimuli and discouraging those that are inhibitory of sexual interest. This may be achieved through pharmaceutical or psychotherapeutic interventions.

Systemic and cultural barriers to routine and reliable sexual education in the USA have resulted in widespread misapprehension of what constitutes normal sexual desire and which behaviors are likely to provide pleasurable sensation during sexual activity. Patients may need to be informed that it is normal for desire to be responsive as well as spontaneous, that motivation and reward from sexual activity promote sexual desire, and that any limiting or aversive factors (physical or psychological)⁸ should be addressed.

This education may be accomplished as part of the routine urologic history and physical exam. For further psychotherapeutic intervention, referral to a sex educator or therapist for solitary or couple's counseling may be very helpful. Resources to identify qualified sex educators/therapists are provided by the American Association of Sex Educators, Counselors, and Therapists (AASECT.org) and the Society for Sex Therapy and Research (sstarnet.org).

2.4 Pharmacotherapy

There are two FDA-approved medications for pharmacotherapy of HSDD, both of which influence neurotransmission within the central nervous system (CNS) to encourage sexual excitation. Both medications were met with considerable skepticism on the part of the popular and professional press, for reasons that are arguably as much sociocultural and economic as they are scientific.⁸ Currently, they are only approved for use in pre-menopausal women, but clinical trials are ongoing and anticipated in other populations, including post-menopausal women and men, as the mechanism of action is equally relevant to the pathophysiology of HSDD regardless of patient age or sex.

Flibanserin (Addyi)® is a multifunctional serotonin agonist and antagonist, with associated noradrenergic and dopaminergic activity. Taken at a dose of 100mg at bedtime, it has been shown in a series of large RCTs to result in a statistically significant and clinically meaningful improvement in the level of sexual desire and decrease in distress compared to placebo, for approximately half of the women who take it.⁹ It may take up to 8 weeks for efficacy to emerge, and 12 weeks for maximal benefit to be achieved. Like other CNS agents, it can be sedating:^{10,11} to compensate for this side effect, patients must be counseled to take the medication before bed as prescribed, and to avoid ingestion of alcohol within 2 hours of doing so.¹² The initial boxed warning in which women were counseled that they needed to abstain from alcohol if using flibanserin has

been removed.¹³

Bremelanotide (Vyleesi®) is a melanocortin receptor agonist, self-administered via pre-filled autoinjector at a dose of 1.75mg SC, at least 45 minutes prior to anticipated sexual activity. In the RECONNECT study, composed of 2 replicate RCTs, there were statistically and clinically significant improvements in level of sexual desire and decreased distress compared to placebo. The most common adverse effect is nausea, which affected 40% of study participants, with variable degrees of severity. Due to associated, transient rise in blood pressure, bremelanotide is contraindicated in patients with uncontrolled hypertension and/or cardiovascular disease, and should not be administered more than once daily. Initially developed as a sunless tanning agent in the 1980s, it is also associated with hyperpigmentation, which may be avoided by limiting use to < 8x/month. ¹⁴

2.5 Testosterone Supplementation for HSDD

Testosterone has been used for HSDD for many years and has demonstrated efficacy for treatment of HSDD in post-menopausal women in four 24-week clinical trials.¹⁵ Testosterone is not FDA-approved for women, and remains an off-label treatment that can be challenging to dose appropriately. Commercially available formulations, packaged to provide the daily recommended dose for men, dispense approximately 10x the dose that is appropriate for women. Transdermal formulations (patches, creams, gels, sprays) are the preferred choice as they provide the most physiologic form of replacement therapy. Other modes of administration, such as intramuscular formulations or subcutaneous pellets, are not recommended. Overdose¹⁶ carries risks of acne, breast pain, headache, hirsutism/androgenic alopecia, deepening of voice, and clitoromegaly. Patients on testosterone must be appropriately monitored with baseline and follow-up serum testosterone levels, for dose within the upper-normal reference range of a premenopausal woman. Expert opinion recommends titration to a goal serum free T between 0.6-0.8 ng/dL, which is the normal pre-menopausal range.^{17,18} Symptomatic improvement is generally seen within 12 weeks; if symptoms of HSDD are not improved after 6 months of treatment, testosterone therapy should be discontinued. In principle, effective treatment with testosterone may be continued indefinitely, but long-term safety data to support this is lacking. Similarly, there is a lack of data regarding the risks/benefits of testosterone treatment in pre-menopausal women. Testosterone supplementation should be avoided during pregnancy, when androgen exposure may pose risk of fetal anomalies.¹⁹ For more information please see the International Society of the Study of Women's Sexual Health Global Consensus Position Statement on the **Use of Testosterone Therapy for Women**.¹⁶

Table 1: Medications used for the treatment of HSDD

Medication	Flibanserin	Bremelanotide	Testosterone (1%)
Indication	Premenopausal women	Premenopausal women	Post-menopausal women (off label)
Timing	Daily	As needed	As needed
Dose	100mg (1 tab) qHS	1.75mg (single-dose autoinjector) --At least 45 min before sexual activity --No more than 1x/day --No more than 8x/month	5-10mg/day --Titrate dose to goal serum free T (0.6-0.8 ng/dL) ²⁰
Side effects	Sedation, hypotension, dizziness, syncope, insomnia	Nausea, flushing, headache, hypertension	Acne, alopecia, hirsutism, vocal change, clitoromegaly
Contraindications	CYP4A4 inhibitors, hepatic impairment	Poorly controlled hypertension, naltrexone	Pre-existing symptoms of virilization

3. Female Sexual Arousal Disorder (FSAD)

Sexual arousal may be considered as both a physiologic, genital process and a neuropsychological state of erotic awareness. Our psychiatric colleagues understandably emphasize the latter and eliminated the diagnosis of FSAD from the DSM in its latest edition, in favor of a combined Female Sexual Interest/Arousal Disorder (FSIAD). The invention of this new diagnosis was justified by the purported difficulty of differentiating problems of desire and arousal, and that disturbances in mental arousal are rarely separable from disordered desire. However, mental awareness is only part of human sexual arousal response, and female genital arousal is often desynchronized with women's perceived experience.²¹ Urologists are well positioned to help women understand and mitigate distressing issues of impaired genital arousal.

In an effort to reconcile these divergent disciplinary perspectives and the preponderance of scientific evidence, ISSWSH has proposed that **Female Sexual Arousal Disorder (FSAD) be subdivided into two categories:** Female Cognitive Arousal Disorder (FCAD) and Female Genital Arousal Disorder (FGAD), with the following characteristics:²²

- **FCAD** is defined as persistent (≥ 6 months) and distressing difficulty attaining or maintaining adequate mental excitement for sexual activity, resulting in problems feeling emotionally engaged or "turned on". This may or may not be co-morbid with FGAD or HSDD, and is best addressed by behavioral and psychotherapeutic interventions.
- **FGAD** is a persistent (≥ 6 months) and distressing difficulty to attain or maintain an appropriate genital response in response to adequate sexual stimulation. FGAD should not be diagnosed in the situation where a woman is not experiencing arousal but is also not receiving sexual stimulation that is aligned with her preferences. FGAD is a problem of pelvic anatomy and physiology, and thus falls within the urologic scope of care. For this reason, the remainder of this section will focus specifically on the pathophysiology, diagnosis, and treatment of Female Genital Arousal Disorder.

3.1 Anatomy and Physiology

Much is made of the significant differences between male and female bodies and sexualities, but from the particular perspective of genital arousal response, these differences are overstated. Fundamentally, **female and male genitalia** are anatomically homologous with consequent physiologic similarities, as follows:

The female vulva, vagina, and cervix are, like the penis, complexly innervated by the pelvic (parasympathetic), hypogastric (sympathetic), and pudendal (somatic) nerves.²³⁻²⁴ Similar to male genital arousal, the physiology of female genital arousal relies on parasympathetic stimulus overcoming baseline sympathetic tone. With parasympathetic activation, vasodilation and engorgement of the genital tissues occurs. As the clitoral corpora cavernosa are intrapelvic structures, their erection is readily overlooked on gross evaluation; more easily appreciated is the increase in vaginal lubrication that follows from genital hyperemia increasing oncotic pressure within the vaginal submucosa.^{23,24,25} This increased blood flow provokes a fluid transudate, released by mucosal aquaporins into the vaginal lumen. Finally, the pelvic muscles relax, lengthening the vagina and elevating the cervix. Collectively, these changes facilitate vaginal penetration.^{24,26}

3.2 Diagnosis

Female genital arousal is reliant on the nervous system, peripheral vasculature, and the vulvovaginal epithelium.²⁷ Disease processes that compromise these organ systems and their function can impair arousal response in women. Common conditions that may impair genital sexual response include: diabetes mellitus, metabolic syndrome, peripheral vascular and cardiovascular diseases. Pelvic surgery, chemotherapy, or

radiation may also cause iatrogenic disruption of the neurovascular mechanisms that regulate genital blood flow or scarring that limits vaginal lengthening and lubrication.⁷ In the wake of the recent COVID-19 pandemic, research has shown reduction of FSFI scores specifically impacting domains of arousal, lubrication, and satisfaction, suggesting that the vasculopathy characteristic of COVID-19 disease may be a contributory to FSD, though interpretation of this data is complicated by the psychosocial burden of the pandemic, which fell disproportionately on women.²⁸ When these are part of a patient's past medical history, a high index of suspicion for and inquiry about reduced or absent genital sensitivity, engorgement, and/or lubrication with sexual stimulation are appropriate.²⁹

A targeted physical exam, focused on the quality of the vulvovaginal tissues and sensory response, is essential to identify any contributory mucosal abnormality, whether from adhesion, inflammatory, infectious or hormonally-mediated vestibulodynia. While Doppler ultrasound, thermography, and plethysmography are sometimes used to evaluate genital engorgement in research studies of female sexual arousal, these modalities have no defined clinical application at this time.³⁰ Vaginal cultures and vulvar biopsies may be indicated to characterize dermatoses of uncertain etiology. Administration of the Female Sexual Function Index (FSFI), a validated questionnaire that includes subsections about arousal and lubrication, may be helpful for monitoring patient progress in response to treatment, but is of limited diagnostic utility, as it predates our current distinction between FCAD and FGAD and erroneously implies that lubrication is functionally separate from arousal. The FSFI also does not contain assessment of distress so cannot be used in place of a careful history to make a diagnosis of sexual dysfunction.³⁰

Epidemiologic studies of FSAD suffer from a similar confusion, utilizing different definitions for sexual arousal, and thus giving different reports of disease frequency. In the PRESIDE study, 3.3% of pre-menopausal women and 7.5% of per-menopausal women reported distress due to genital arousal difficulties, suggesting that the changes associated with genitourinary syndrome of menopause contribute substantially to overall disease burden.²

3.3 Treatment

FGAD is most treatable when it occurs secondary to an identifiable dermatosis or vaginitis; these conditions may be effectively corrected with the local application of hormones, antimicrobial agents, or topical steroids, as appropriate. Unfortunately, some chronic dermatoses, adhesions, peripheral vascular or nervous pathologies are not readily corrected or reversed, and can only managed²⁷

The only FDA-cleared device for treatment of FGAD is the Eros-Clitoral Therapy Device, which applies suction to the exposed glans clitoris to promote engorgement.³¹ Since its approval in 2000, the "sex tech" industry has burgeoned, and there are many similar vulvar/clitoral suction and/or vibratory devices available without a prescription, some of which are advertised as scientifically studied and "doctor approved"³² (e.g. Dame Products). Most of these are presented simply as pleasurable toys, whose potential therapeutic value as neurovascular agents is overlooked. This popular characterization of female arousal aids as toys, rather than treatments, has significant economic implications, as their expense is not covered by health insurance or health savings accounts.

Following the success of PDE5i in the treatment for erectile dysfunction in men, several studies tested the potential benefits of these medications in women. Sildenafil reliably increases vulvar and vaginal blood flow³³ and thus, may benefit patients whose arousal disorder is comorbid with vascular disease. However, this measured physiologic change is not consistently interpreted by study participants as an increase in their level of sexual arousal.³⁴ Some evidence exists that this lack of synchrony between genital and subjective arousal is an inherent characteristic of female sexuality.²¹ However, these findings may also be artifactual, a limitation of

past disease definitions, flawed research protocols, and/or absence of valid outcome measures.³⁵ Regardless, in the absence of any clear demonstration of efficacy, PDE5i are not FDA approved for the treatment of FSAD at this time.

Unfortunately, a lack of scientific evidence for safety and efficacy has not limited the market for therapies that are purported to improve female arousal response, which includes energy-based (laser and radiofrequency) devices, platelet-rich-plasma (PRP) and stem-cell injections, and herbal treatments. Many of these treatments claim to restore or regenerate normal tissue morphology and function; all are commercially available, poorly regulated, and potentially hazardous, without any reliable evidence of efficacy for the treatment of FGAD currently. Patients should be advised accordingly, and only administered these interventions in clinical trials. ^{36,37}

4. Female Orgasmic Disorder (FOD)

4.1 Definition

Female Orgasmic Disorder is characterized by a persistent or recurrent, distressing compromise of orgasm frequency, intensity, timing, and/or pleasure, associated with sexual activity for ≥6 months. Parameters include: frequency, where orgasm occurs less often or is absent (anorgasmia); intensity, where orgasm occurs with reduced intensity (muted orgasm); timing, where orgasm occurs either too late (delayed orgasm) or too early (spontaneous or premature orgasm) than desired by the woman; and pleasure, where orgasm occurs with absent or reduced pleasure (anhedonic orgasm, pleasure dissociative orgasm disorder (PDOD²²). FOD may be present lifelong or acquired, generalized or situational. It is important to recognize that the type and intensity of stimulation required to reach sexual climax is highly variable and idiosyncratic: studies have described vaginal, clitoral, and cervical orgasms. The majority of women do require clitoral stimulation for orgasm, and FOD should not be diagnosed in the absence of adequate stimulation (e.g. vaginal penetration alone).

The prevalence of FOD (orgasm concerns plus distress) in American women is estimated at 4.7%.²

4.2 Risk Factors and Pathophysiology

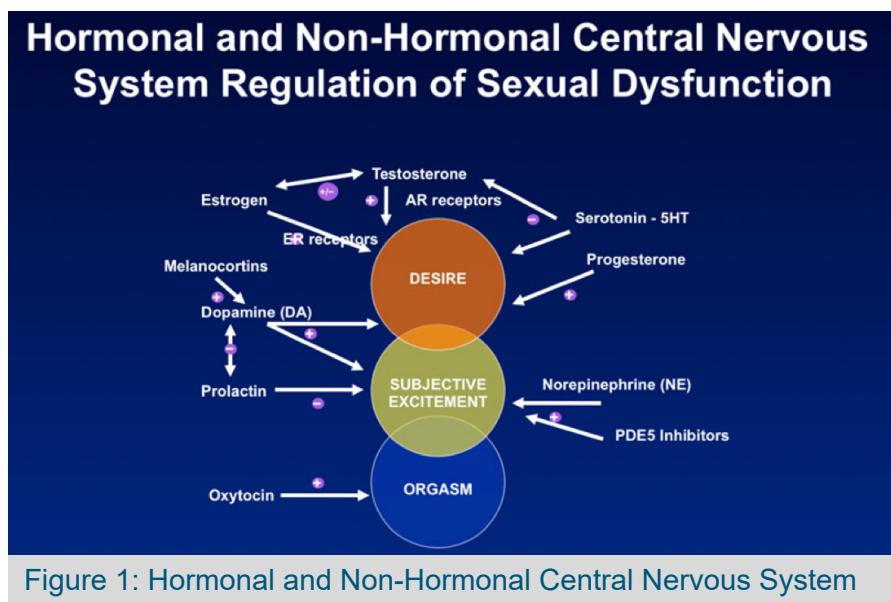


Figure 1: Hormonal and Non-Hormonal Central Nervous System Regulation of Sexual Function

Orgasm is a physiologically complex process, involving anatomical, hormonal, psychological, and situational

variables. All of these are implicated and potentially contributory to FOD.

FOD, similar to FSAD and HSDD, may be the result of insufficient sexual excitatory processes (dopamine, oxytonin, melanocortin and norepinephrine), or of increased sexual inhibitory processes (opioid, endocannabinoid, and serotonergic systems) (Figure 1).^{38,39,40,41}

Sexual excitation and inhibition imbalance causing FOD may result from psychosocial issues such as ineffective sexual communication, a traumatic relationship experience, mood disorder, fatigue, past trauma and abuse history, cultural and religious prohibitions and feeling excess pressure to have sex. Common psychological etiologies include spectating (obsessive self-observation and critique during sex), unresolved conflict with the partner, religious guilt, and fear of pregnancy. FOD may also be related to partner sexual dysfunctions (e.g. erectile dysfunction or premature ejaculation).⁴²

Organic factors resulting in FOD include medications such as selective serotonin reuptake inhibitors (SSRI)-induced sexual dysfunction. Medical problems related to FOD include diabetic neuropathy, multiple sclerosis, genital cutting, genital or pelvic surgery (e.g. radical cystectomy, hysterectomy), pelvic trauma, and hormonal issues such as low testosterone, low estrogen, or hypothyroidism.⁴³ Clitoral phimosis is a common and underrecognized condition that may compromise orgasm by reducing pleasurable sensation from the glans clitoris.

4.3 Diagnosis and Evaluation

The clinical diagnosis of FOD is established by a history that includes biopsychosocial evaluation. In addition, physical exam is essential to rule out contributory anatomic and physiologic causes. As with the other female sexual disorders, hormonal testing (potentially including but not limited to estradiol, testosterone, sex hormone binding globulin, prolactin, thyroid hormone, and pituitary gonadotropins) should be considered.^{43,44}

4.4 Treatment

The underlying cause of FOD is often multifactorial, thus treatment should be multifaceted, addressing psychological and somatic causes.

Sex therapy offers psychological and behavioral interventions to improve orgasmic function. Psychological approaches to improving orgasmic function focus on the woman exploring psychological factors such as low desire, poor arousal, depression, anxiety, fatigue, emotional concerns, past trauma and abuse history, cultural and religious prohibitions, feeling excess pressure to have sex, or a partner's sexual dysfunction such as erectile dysfunction or premature ejaculation.²⁹

Behavioral strategies for FOD include practices with supratentorial effects (e.g. mindfulness meditation, fantasy material, masturbation training) and pelvic effects (e.g. Kegel exercises, exploration of sexual positions and devices (e.g. vibrators) that optimize genital stimulation).^{43,44}

As orgasm may be solitary or an experience shared with others, cultivating self-awareness and emotional intelligence, or knowledge of one's own mood or sense of being, as well couple-based interventions such as sensate focus therapy and couple's counseling are helpful for orgasm function.^{43,44}

There are no FDA-approved pharmacological treatments for FOD.

Options for medications used off-label for FOD as well as FSAD are bremelanotide and flibanserin. This is believed to be beneficial due to the same mechanism of action as it is used for hypoactive sexual desire disorder - through influence on neurotransmission within the central nervous system (CNS) to encourage sexual excitation. As previously described, the mechanism of action is equally relevant to the pathophysiology of HSDD regardless of patient age or sex and thus can be used off-label in pre or post menopausal women

and men.

In addition, changes to medications that are implicated in causing or exacerbating orgasm dysfunction can be helpful. FOD in women using SSRI agents may respond to a weekend drug holiday or to a gradual decrease in dose. Both of these strategies may result in a recurrence of symptoms (depression, anxiety) or SSRI withdrawal symptoms, so patients must be appropriately counseled and closely monitored. Alternatively, the SSRI can be substituted with a dopaminergic and noradrenergic anti-depressant such as bupropion.⁴⁵ Another strategy is to continue the daily SSRI and add a second agent such as bupropion.⁴⁶

There is some evidence that PDE5I may improve orgasmic function in women on SSRIs.⁴⁷ In a small randomized control trial women taking sildenafil had statistically significant improvement in the orgasm domain of the FSFI.⁴⁷ Additional medical treatments that have been reported include dopamine agonists, oxytocin, and alpha-2 receptor blockers such as yohimbine hydrochloride; evidence to support the use of these treatments is scant and their use is considered experimental at this time.⁴³

When reversible structural causes of FOD are identified, such as clitoral phimosis, surgical treatment is appropriate.⁴⁸

5. Persistent Genital Arousal Disorder (PGAD)

5.1 Definition

Persistent genital arousal disorder (PGAD) is characterized by persistent or recurrent, unwanted or intrusive, distressing feelings of genital arousal or being on the verge of orgasm (genital dysesthesia), not associated with concomitant sexual interest, thoughts, or fantasies. PGAD may be associated with limited resolution, no resolution, or aggravation of symptoms by sexual activity with or without aversive and/or compromised orgasm, aggravation of genital symptoms by certain circumstances, despair, emotional lability, catastrophization and/or suicidality and inconsistent evidence of genital arousal during symptoms.^{49,50} Both **men** and women can experience PGAD, but it is most commonly described and recognized in female patients. Women with PGAD are often ashamed for having these persistent and bothersome feelings in their genitals. In fact, women with PGAD sometimes have suicidal thoughts related to their unrelenting symptoms.⁵¹

Persistent genital arousal disorder is not included in the DSM-IV-TR or the DSM 5; however, it has been included in the ISSWSH nomenclature and recently published a consensus paper.^{49,52} This well-recognized clinical diagnosis may be classified as lifelong if the PGAD has been present throughout the person's life or as acquired if the PGAD develops variably in later life. The prevalence of PGAD is unknown, but it is estimated to affect about one percent of the female population.⁵⁰ Interestingly, a questionnaire on PGAD given to women attending a walk-in sexual health clinic in London indicated that as many as one in three women reported at least one symptom of spontaneous genital arousal in the absence of desire or excitement.⁵³

5.2 Risk Factors and Pathophysiology

PGAD may be associated with psychiatric and psychological-related pathophysiologies. Women with PGAD have described that stress worsens PGAD symptoms, whereas distraction and relaxation strategies lessen PGAD symptoms.^{54,55}

PGAD may be associated with pathophysiologies including vascular, neurologic, pharmacologic, and hormonal etiologies. Arterial vascular causes may be secondary to pelvic arterio-venous malformations with unregulated arterial communications to the genitalia. Venous vascular causes may be secondary to pelvic congestion syndrome with ovarian venous incompetence and large varices draining the genitalia. PGAD has been associated with central neurologic causes such as Tourette's Syndrome, epilepsy, post-blunt CNS

trauma, post-neurosurgical intervention for arterio-venous malformation, and cervical and lumbosacral surgical interventions.⁵¹ Peripheral neurologic causes may be secondary to pudendal nerve entrapment and hypersensitivity or small fiber neuropathy of the pudendal nerve including its dorsal branch to the clitoris. Pharmacologic causes include use of certain anti-depressants, such as trazodone, or secondary to sudden withdrawal of selective serotonin re-uptake inhibitors (SSRIs) as occurs in SSRI discontinuation syndrome. Hormonal causes include initiation and discontinuation of hormone therapy in post-menopausal women. **Many cases of PGAD are idiopathic.**^{54,55}

5.3 Diagnosis and Evaluation

Women with PGAD should undergo detailed history, psychological evaluation, physical examination and laboratory testing. Physical examination and diagnostic testing should be directed towards identifying the region of origins, in particular regions 1, 2 and 3. This can be done with a comprehensive physical exam, labs, neurological testing and end organ anesthesia testing.

Table 2

Region 1	End organ (clitoral, vestibular, urethral or vulva pathology)
Region 2	Pelvic/perineum (overactive/hypertonic pelvic floor dysfunction, vascular pathology, pudendal nerve pathology)
Region 3	Cauda equina (sacral tarlov cysts, lumbar disc disease)
Region 4	Spinal Cord
Region 5	Brain (medications or organic i.e epilepsy, AVM, aneurysm)

Initiation and discontinuation of hormone therapy in post-menopausal women has been associated with onset of PGAD.⁵⁴⁻⁵⁵ A history of hormone use and serum assay for hormone levels may be warranted including estrogen, testosterone, FSH, LH, TSH, and prolactin.⁵⁶

Clitoral ultrasound studies may be used to diagnose arterial vascular causes secondary to pelvic arterio-venous malformations leading to unregulated arterial communications to the genitalia. Pelvic ultrasound and transvaginal ultrasound may be used to exclude venous vascular causes secondary to pelvic congestion syndrome with ovarian venous incompetence and large varices draining the genitalia.⁵⁷⁻⁵⁸

Neurologic consultation, EEG, CT scans, and MRI's⁵⁷ may be indicated if there is concern about central neurologic causes such as those detailed above.

5.4 Treatment

The treatment for PGAD is complex and requires a multidisciplinary approach with the goals of reducing distress and bother to the patient which can include surgery, medication, psychological, pelvic floor physical therapy. The International Society for the Study of Women's Sexual Health consensus papers recommends tailoring treatment to the underlying cause of PGAD symptoms.⁵² Due to absence of large scale studies and poor understanding of the physiology of this condition, many of these must be considered empiric treatments.⁴²⁻⁵⁴⁻⁵⁵⁻⁵⁹⁻⁶⁰⁻⁶¹⁻⁶²⁻⁶³⁻⁶⁴⁻⁶⁵

Psychological-based treatments engage the management of depression or focus on efforts to maximize relaxation through strategies such as distraction and/or hypnosis. Pharmacologic strategies have included use of tricyclic or SSRI antidepressants (clomipramine, paroxetine), anti-seizure medications (carbamazepine), the opioid agonist tramadol, and varenicline (a partial agonist at the nicotinic receptor subtype that decreases the ability of nicotine to stimulate the release of mesolimbic dopamine) and low dose zolpidem. Discontinuing trazodone, SSRIs or excess herbal estrogen products may provide relief. Women with PGAD secondary to arterial-venous malformation may be cured by selective embolization. Women with PGAD secondary to pelvic venous incompetence might benefit from embolization of the incompetent ovarian vein. Release of pudendal nerve entrapment has resulted in PGAD symptom improvement. Surgical options are available for regions 1, 2 and 3 and should be utilized if patients have failed conservative therapy. These can include vestibulectomy, clitoral lysis of adhesions (region 1), surgical release of the pudendal nerve (region 2) and spinal surgery (region 3). An additional strategy for treating PGAD is application of a TENS (transcutaneous electrical nerve stimulation) unit or utilizing pudendal neurostimulation.⁴²⁻⁵⁴⁻⁵⁵⁻⁵⁹⁻⁶⁰⁻⁶¹⁻⁶²⁻⁶³⁻⁶⁴⁻⁶⁵

6. Effects of Incontinence, Prolapse and Mesh on Female Sexual Function

6.1 Prolapse and Incontinence

6.1.1 Epidemiology

Difficulties with sexual function may occur in conjunction with urinary incontinence and pelvic organ prolapse. One in five community dwelling women report urinary incontinence or prolapse as a reason for sexual inactivity. Prolapse is more likely than urinary incontinence to result in sexual inactivity. However, overall sexual satisfaction appears to be independent of the presence of (or use of therapy for) urinary incontinence or prolapse.⁶⁶ Readers are referred to the Core Curricula on **Pelvic Organ Prolapse, Urethral Diverticula, Overactive Bladder**, and **Urinary Incontinence** for more specific details on evaluation or prolapse and incontinence.

Prolapse

Prolapse may develop in the anterior compartment (cystocele), posterior compartment (rectocele) or apex (uterovaginal prolapse or vaginal vault prolapse if the patient has had a hysterectomy). Patients often have prolapse of multiple compartments and patients with more severe prolapse are more likely to complain it interferes with sexual activity.⁶⁶

Urinary Incontinence

Urinary incontinence may be divided into stress incontinence (**SUI**) and urge incontinence (**UII**). Urine leakage during intercourse is known as coital incontinence. There are 2 types of coital incontinence: climacturia or orgasmic urinary incontinence, which is urinary incontinence at the moment of orgasm, and penetration urinary incontinence, which occurs with vaginal penetration. Bladder overactivity is conventionally implicated in orgasmic incontinence and SUI in penetration incontinence, though pelvic muscle spasm during orgasm suggests a likely role for SUI in climacturia as well. Data suggest that urinary leakage during intercourse is more common in women with genuine stress incontinence.

It is important to differentiate coital incontinence from passage of fluid from the female periurethral glands or Skene's glands; this is sometimes referred to as female ejaculation (FE). Small case series using ultrasound and histological evaluation have found the presence of glandular structures encircling the urethra which stain positively for prostate specific antigen (PSA) and the androgen receptor (AR).^{67,68} Female ejaculation may vary from a small quantity of whitish secretions from this glandular tissue or squirting of a larger amount of diluted and changed urine. Both phenomena may occur simultaneously and are two different physiological components of female sexuality. The prevalence of FE has been reported to be between 10-54%.^{69,70} It is rarely reported in the literature and reports of high prevalence are based mostly on subjective questionnaire research⁷¹ with inherent selection bias.

6.1.2 Diagnosis

Prolapse

Patients with prolapse may report pressure, heaviness or bulge. **Prolapse** exam should be performed in the lithotomy position with Valsalva to assess the full-extent of prolapse. If a patient complains of bulge not evident in lithotomy the patient should be asked to stand in a modified squat and the exam repeated.

Incontinence

Patients who report incontinence should be asked whether it occurs with urge or with stress activities. Patients who report coital incontinence should be asked if it occurs with penetration and/or with orgasm. Stress incontinence can be visualized on exam with a cough stress test. Urge incontinence may be assessed with history and in appropriate patients urodynamics may be helpful. If patients are unsure if a vaginal fluid is urine or vaginal secretions, a pyridium pad test may be performed which would stain urine orange but not affect vaginal secretions.

6.1.3 Treatment

Treatment for prolapse and incontinence has been shown to have mixed effects on sexual function, with some studies showing improvement, some showing no change and others finding deterioration. The preponderance of evidence as summarized in recent meta-analyses suggests that sexual function tends to be stable or improved after incontinence and/or prolapse surgery although there is substantial heterogeneity and follow up tends to be scant.^{72,73}

Prolapse

Although many studies show improvement in sexual function with prolapse surgery, posterior colporrhaphy,

which can narrow the introitus, has been associated with worsening sexual function and increased dyspareunia.⁷⁴ When performing a posterior colporrhaphy it is important to ensure adequate caliber of the vaginal canal.

When considering abdominal approaches vs vaginal approaches, consideration should be given to vaginal length. There is evidence that abdominal approaches such as abdominal sacrocolpopexy may conserve more vaginal length and be preferable in women who are sexually active or with shorter vaginal length.⁷⁵

Incontinence

Urgency incontinence can be treated with behavioral modification, medications such as anticholinergics and beta-3 agonists, chemodenervation with botox, and neuromodulatory treatments such as sacral neuromodulation and peripheral tibial nerve stimulation (PTNS). Medical therapy with both oral and transdermal anticholinergics has been shown to have a positive effect on female sexual function in overactive bladder patients, while there is less data on the effects of beta agonists as this is a newer class of medication.^{76,77,78} Neuromodulation has also been shown in a small series to improve sexual function independent of improvement in urinary symptoms.⁷⁹ It has been hypothesized that neuromodulation may strengthen pelvic floor muscle tone with bulbocavernosus contraction placing pressure on the deep dorsal vein of the clitoris preventing venous escape and resulting in clitoral engorgement. This suggests a possible novel treatment for female sexual dysfunction.

Conservative options for stress incontinence include pelvic floor physical therapy and injection of urethral bulking agent. Surgical options include vaginal approaches such as a midurethral sling which is the most-common surgical treatment for **SUI** and abdominal approaches such as a Burch urethropexy. Controversy exists regarding the impact of midurethral slings on female sexual function, while many studies show an improvement in sexual function there is concern that the peri-urethral dissection may disrupt peri-urethral glands, nerve innervation periurethrally and of the anterior vagina, and thereby affect sexual function. A meta-analysis examining overall female sexual function and specifically orgasmic function found that 67% of midurethral sling procedures resulted in no change or improvement in overall sexual function postoperatively, whereas only 33% of studies analyzed for orgasm function showed improvement after the procedure. For transvaginal tape, both overall sexual function and orgasm scores improved whereas for transobturator tape, overall sexual function improved significantly while mean orgasm score did not. The authors felt this lack of significant improvement in orgasm scores might be due to disruption of the periurethral tissue.⁸⁰ Coital incontinence can be treated similar to the underlying incontinence - with orgasmic incontinence being treated similar to urgency incontinence and penetration incontinence being treated similar to stress incontinence.

6.2 Mesh and Sexual Dysfunction

On April 16, 2019 the **FDA issued an order** that all companies producing mesh intended for surgical correction of pelvic organ prolapse in the transvaginal compartment to immediately stop selling their products. This cease and desist order precluded companies from selling and distributing transvaginal mesh, but did not include mesh used for mid-urethral slings (MUS) or trans-abdominal mesh used for hysteropexy or sacrocolpopexy. A prior lack of consensus on the perioperative complications of sexual dysfunction in these patients makes it difficult to define these signs and symptoms; the dysfunctions can include dyspareunia, pain in the sexual partner with penetration, decreased sexual satisfaction, and change in orgasmic capacity. A recent meta-analysis published in 2017 on sexual function after MUS surgery revealed that approximately 67% of mid-urethral sling procedures resulted in either unchanged or improved sexual function post-operatively.⁸¹ Overall sexual satisfaction likely improves after a mid-urethral sling or prolapse procedure

with trans-abdominal mesh due to improvement in leakage during sexual activity as well as improvement in comfort when there is no longer the sensation of a vaginal bulge noted with prolapse.

Prior reported incidences of de-novo dyspareunia after MUS surgery for stress urinary incontinence (SUI) have been as high as 20% overall.⁸² Dyspareunia rates after surgical correction for pelvic organ prolapse are variable and appear to be highest with transvaginal mesh procedures.⁸³ A recent meta-analyses on POP surgery suggested a lower rate of de novo dyspareunia of up to 9%.⁷² Interestingly, there is scarce data consensus on sexual function after transabdominal mesh procedures for pelvic organ prolapse (POP).

A majority of the literature shows no statistical change in orgasm function after sling procedures for SUI, however a recent meta-analysis showed an orgasm improvement rate of 33% after a bulk of studies was analyzed for sexual function after sling surgery.⁸¹ Several studies analyzed for orgasmic function after transvaginal mesh surgery showed no statistically significant improvement in orgasm in those women undergoing prolapse repair.

There is a critical lack of published data on sexual function in women who have undergone transabdominal or transvaginal mesh for incontinence or prolapse repair. Therefore, there is also a critical lack of consensus on the definition of sexual function and dysfunction in these women as well. More prospective study designs are needed to discern sexual complications in women undergoing surgical correction of prolapse or incontinence, especially as the FDA continues to regulate the use of surgical mesh in these female patients.

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