

Clinical Practice Guidelines for Managing Genitourinary Symptoms Associated With Menopause

MONICA CHRISTMAS, MD, NCMP,*
ANNABELLE HUGUENIN, MBBS, LLB (Hons),†
and SHILPA IYER, MD*

*Department of Obstetrics and Gynecology, University of Chicago Medicine, Chicago, Illinois; and †Department of Obstetrics and Gynecology, Royal Women's Hospital Melbourne, Victoria, Australia

Abstract: Genitourinary syndrome of menopause encompasses the group of urogenital signs and symptoms resultant from hypoestrogenism, including genital dryness, burning or irritation, sexual discomfort, pain or dysfunction, and urinary urgency, dysuria, and recurrent urinary tract infections. Genitourinary syndrome of menopause can have a profound impact on well-being, functioning, and quality of life in

postmenopausal women. Treatment includes vaginal moisturizers and lubricants geared towards providing symptomatic relief; hormonal treatments which promote epithelial thickening and production of vaginal secretions; and pelvic floor physical therapy along with behavioral therapies that address pelvic floor hypertonicity and psychosocial factors.

Key words: postmenopause, genitourinary symptoms, vulvovaginal atrophy, hormone therapy, dyspareunia, atrophic vaginitis

Correspondence: Monica Christmas, MD, NCMP, Department of Obstetrics and Gynecology, University of Chicago, 5841 S. Maryland Avenue, Chicago, IL 60637. E-mail: mchristmas@bsd.uchicago.edu

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Introduction

Hypoestrogenism, most commonly due to menopause, can have a profound impact on quality of life and function.¹ While many of the problematic symptoms of

hypoestrogenism improve over time, those impacting the genitourinary system are often persistent and usually do not improve without intervention. Genitourinary symptoms fall into 3 categories: genital, sexual, and urinary symptoms. Historically, a variety of terms, like vulvovaginal atrophy and atrophic vaginitis, were used to describe the physiologic changes to the genital tract related to estrogen deficiency. However, the older terminology was not inclusive of the often associated urinary symptoms and sexual function issues and did not incorporate symptom bother. Recognizing the need to standardize terminology, the North American Menopause Society and the International Society for the Study of Women's Sexual Health convened a terminology consensus conference in 2013, where the term genitourinary syndrome of menopause (GSM) was coined.² GSM encompasses the group of urogenital signs and bothersome symptoms resultant from hypoestrogenism, including genital dryness, burning, or irritation; sexual discomfort, pain, or dysfunction; and urinary urgency, dysuria, and recurrent urinary tract infections.

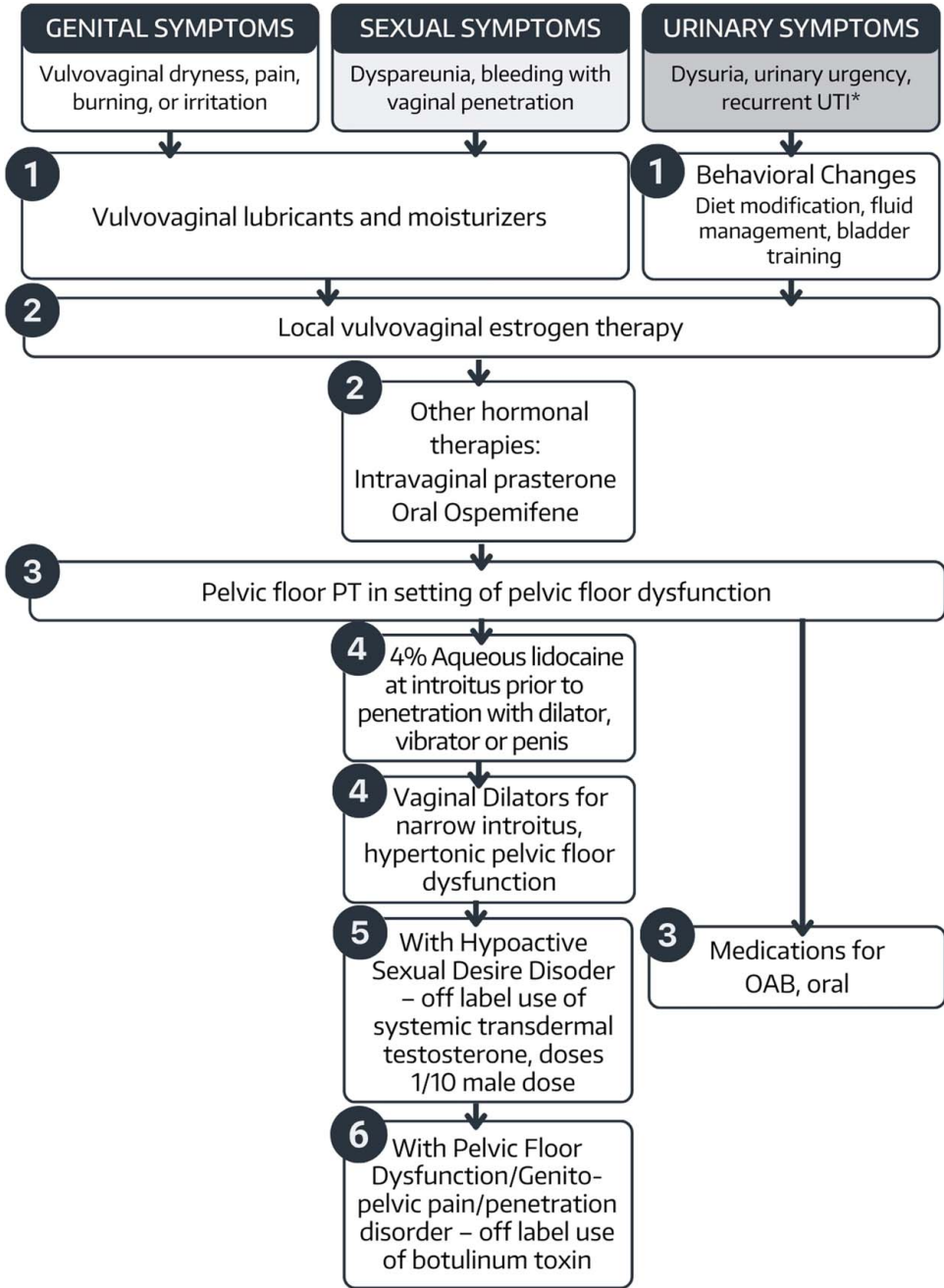
Over half of those in postmenopause report some, if not all, the genitourinary symptoms included in a diagnosis of GSM, with some studies reporting up to 80% prevalence of at least 1 symptom of GSM.³ Numerous studies have found GSM-related symptoms can have a profound impact on well-being, functioning, and quality of life in postmenopausal women.^{4,5} Moreover, many postmenopausal women relay they are reticent to initiate discussions about their genitourinary symptoms with their clinician but feel it is an issue that should be addressed within the healthcare encounter.⁵

There is a myriad of treatments for GSM-related symptoms, including over-the-counter moisturizers and lubricants geared toward providing symptomatic relief; hormonal treatments, which promote

epithelial thickening and production of vaginal secretions; and pelvic floor physical therapy along with behavioral therapies that address pelvic floor hypertonicity and psychosocial factors. In addition, off-label use of vaginal laser therapy, as well as botulinum neurotoxin A injections, are often employed to manage refractory cases.^{3,6}

Despite the high prevalence of genitourinary symptoms associated with menopause, studies have shown that symptoms are often underdiagnosed and undertreated.³ We compiled a comprehensive, evidence-based approach to the treatment of GSM. The guideline is divided into the 3 categories that genitourinary symptoms fall under: genital, sexual and urinary. However, we recognize some people will experience symptoms in all 3 categories, as they are often interconnected. In addition, amelioration of symptoms may hinge on treatment of the underlying atrophic tissue changes. Because GSM is chronic, when early symptoms go undertreated, more severe pelvic floor dysfunction can ensue, leading to pain with sitting and other normal daily activities or inability to withstand any form of vaginal penetration.⁷ Treatment is based on the presence of bothersome symptoms, as physical findings and objective measures (ie. pH, VMI) have not been shown to correlate with symptom severity.⁸ A step-by-step approach to treatment is provided; however, shared decision-making between the clinician and patient is paramount to compliance and optimal outcomes.⁶

Details on appropriate history and physical examination are provided elsewhere (ref Goetsch and Clark) but are briefly mentioned here. Extensive discussion of the treatment of sexual dysfunction in GSM and hormonal therapies for GSM are also found elsewhere (ref Gaddam, reference Pinkerton). This paper is intended as an overview and general approach to the management of GSM (Fig. 1).



Additional management recommendations: Antibiotics for recurrent UTI*

FIGURE 1. A stepped approach to GSM management. Key: The boxes directly below the shaded symptom headings show a potential stepped approach to symptom management with the boxes labeled #1, the first step in the management sequence under the symptom heading, the boxes labeled #2, the second step in the management sequence under the symptom heading, and so on. Where the treatment box extends across all 3 symptoms, genital, sexual, and urinary, the treatment is recommended for all 3 symptoms. GSM indicates genitourinary syndrome of menopause; OAB, overactive bladder; UTI, urinary tract infections.

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Signs and Symptoms of Vulvovaginal Atrophy

For those with bothersome symptoms related to signs of hypoestrogenism and vulvovaginal atrophy (VVA), the first step to management is performing a thorough history and physical exam that will assure a correct diagnosis of GSM, and once that is established, allow targeted clinical management. VVA is a process resulting from the postmenopausal reduction in circulating estrogen, which causes reduced epithelial blood flow. Consequently, the epithelium thins become more fragile with loss of tissue elasticity and is accompanied by a reduction in vaginal secretions.⁹ Although menopause is the most common cause of hypoestrogenism, other factors unrelated to the natural menopause transition can result in estrogen deficiency as well (Table 1). Despite menopause being a natural, ubiquitous process, it is unclear why some women have little to no symptomatology and others experience pervasive distressing symptoms.

The constellation of physical exam findings of VVA includes hypopigmentation and erythema of the vaginal mucosa, loss of vaginal rugae and labia minora, evidence of friability such as petechiae and fissures, decreased elasticity, narrowing and shortening of the vagina, and urethral eversion or prolapse. A speculum exam should be done; however, it may be challenging especially in a patient with severe hypertonicity or in those with vaginal stenosis secondary to surgery or radiation. Often the use of a pediatric speculum or vaginoscopy can be utilized to aid in

visualization. Lidocaine application to the vestibule may facilitate examination.

A careful history will elucidate whether patients are using “feminine hygiene” products or taking prescription medications that may exacerbate symptoms. Avoidance of products that contain perfumes, alcohol, preservatives, and other irritants, such as feminine hygiene washes, soap, bubble bath, douches, lubricants, powders, fragrant panty liners, and spermicides, is recommended.⁶ Comorbid conditions, medications, or psychosocial factors that may affect sexual function may be elucidated and addressed.

TABLE 1. Causes of Hypoestrogenism

Type	Cause
Conditions	Natural Menopause (including primary ovarian insufficiency and premature menopause) Hypothalamic amenorrhea Postpartum state Breastfeeding Pituitary tumors
Iatrogenic	Pharmacologic agents Gonadotropin-releasing hormone antagonist/agonist Leuprolide Nafarelin Selective estrogen receptor modulators Aromatase inhibitors Danazol medroxyprogesterone Surgical menopause (bilateral oophorectomy with or without hysterectomy) Chemotherapy Pelvic radiation therapy

Ref: Gandhi et al,²⁶ 2020 NAMS³ GSM. GSM indicates genitourinary syndrome of menopause; NAMS, North American Menopause Society.

Other common vulvovaginal conditions should be evaluated, such as vulvovaginal candidiasis, bacterial vaginosis, trichomonas, foreign bodies, lichen sclerosis, lichen planus, or neoplasia (Table 2). Further evaluation of suspicious and persistent lesions is indicated, as GSM typically does not present with isolated lesions.⁶

Once a diagnosis of GSM is secured and other disorders ruled out, management should proceed based on (1) the constellation of presenting bothersome symptoms, (2) signs of genitourinary tissue friability or diminished integrity, (3) patient's preference for, or contraindication to, hormonal versus nonhormonal therapies, and (4) ultimate treatment goals of the patient.

Management of Genital and Sexual Problems of GSM—Vulvovaginal Dryness, Burning, Irritation and Dyspareunia

LUBRICANTS AND MOISTURIZERS FOR GENITAL SYMPTOMS AND DYSPAREUNIA IN GSM

Dyspareunia, pain with intercourse, is a common consequence of hypoestrogenism due to physiologic changes to the genitourinary tract. Often associated with post-coital bleeding, it is exacerbated by thinning of the vaginal epithelium and lamina propria, loss of tissue elasticity, atrophy of smooth muscle, and reduction in vascular support contributing to decreased vaginal transudate and glandular secretions.¹ If the primary symptom of GSM is vaginal dryness, burning, irritation, or dyspareunia, treatment considerations should always include a lubricant or a moisturizer. The basis of treatment with vaginal moisturizers or lubricants for dyspareunia entails targeting therapy to break the cycle of pain. If dyspareunia is purely due to vulvovaginal atrophic dryness, treatment is relatively

TABLE 2. Other Vulvovaginal Conditions Associated With Genital Symptoms

Condition
Lichen sclerosis
Lichen planus
Lichen simplex
Desquamative inflammatory vaginitis
Contact dermatitis
Vulvovaginal candidiasis and vaginitis
Cicatricial pemphigoid
Idiopathic overactive bladder
Detrusor overactivity associated with neurologic and medical conditions (ie. diabetes, interstitial cystitis)
Vulvodinia/Vestibulodynia
Psychological disorders
Malignancy
Trauma
Foreign body

uncomplicated. In mild cases, conservative management with the use of an over-the-counter vaginal moisturizer and lubricant may be enough to improve symptoms. Table 3.

There is a paucity of high-level data supporting the efficacy of vaginal moisturizers and lubricants; however, there is some evidence they improve VVA and dyspareunia.^{10,11} It is recommended that vaginal moisturizers be used on a regular basis, at least 2 to 3 times per week, but can be used daily to help bring more moisture to the vaginal mucosa.¹² The mechanism of action involves adherence of the moisturizer, which carries up to 60 times its weight in water, to mucin and epithelial cells on the vaginal mucosa, thereby improving the fluid content of the vaginal epithelium until it sloughs off.¹¹ In addition to water, they contain plant-based or synthetic polymers to facilitate adherence to the vaginal walls, along with other additives to maintain ideal viscosity, pH buffering, and preservation.¹¹ There is some evidence that hyaluronic acid-based moisturizers may have some benefits. A systematic review of 5 small randomized controlled trials aimed to evaluate the effects of hyaluronic

TABLE 3. Summary of Over-the-counter Nonhormone Vaginal Moisturizers and Lubricants

	Benefits	Drawbacks
Moisturizers (use daily or every few days independent of sexual activity)		
Hyaluronic acid-based	Rehydrates vaginal tissues	Does not restore or reverse cellular
Polyacrylic acid-based	Provides a protective coating over	or pH changes due to GSM
Polycarbophil-based	vaginal mucosa	May contain glycerin
Vitamin E oil or suppositories	May be used with other	May be associated with mild
Vitamin D suppositories	nonhormonal and hormonal	irritation
	therapies	
	Compatible with condom use	
Lubricants (used by both/all partners or applied to device/toy prior to sexual or vaginal penetrative activity)		
Water-based		
	Compatible with latex and silicone	Hyperosmolar
	Less risk of vaginal candidiasis	Dries out quickly
	Inexpensive	May contain glycerin or parabens
	Some products may not decrease	
	sperm motility	
Silicone-based		
	Compatible with latex	Iso-osmolar
	Does not dry out as easily as water-	More expensive
	based	Difficult to wash off
		Incompatible with silicone and
		rubber (ie. vibrators or dilators)
		Impairs sperm motility
		Some products may increase the
		risk of vaginal candidiasis
Oil-based (vegetable, olive,		
coconut, vitamin E oil)	Inexpensive	Erodes condoms
	Natural	Impairs sperm motility
		Increased colonization with
		candida species

GSM indicates genitourinary syndrome of menopause.

acid-based moisturizers in treating symptoms due to vaginal atrophy (atrophic vaginitis, vaginal dryness, and dyspareunia) found that hyaluronic acid had similar efficacy, safety, and tolerability compared to vaginal estrogen.¹³ Consequently, regular use of vaginal moisturizers may provide an acceptable alternative for women with bothersome symptoms and contraindications to hormonal treatments. An overview of available moisturizers and lubricants is outlined in Table 3.

While vaginal moisturizers should be used on a regular basis regardless of sexual activity and are purported to provide longer relief of symptoms by improving hydration of the vaginal mucosa, a lubricant is intended for use with sexual activity to reduce friction against atrophic vulvar and vaginal tissue associated with penetration,¹² but some patients may also

use lubricants for dryness not associated with sexual activity. Lubricants provide short-term relief of dyspareunia due to atrophy. Lubricants are used before sexual activity to reduce friction against atrophic vulvar and vaginal tissue associated with penetration.¹² There are 3 categories of lubricants: water-based, silicone-based, and oil-based. Although these products are unregulated, a few studies have sought to examine efficacy. A single-center, randomized, double-blind, crossover trial of postmenopausal women with a history of breast cancer found participants experienced greater relief of dyspareunia with the use of a silicone-based lubricant versus water-based.¹⁴ In general, the lubricant is applied directly to the penis, vagina, or device, such as a vibrator, dildo, or dilator, immediately before or during intercourse. Although, vaginal moisturizers

and lubricants may provide relief for mild symptoms, the benefit is limited at best, as these over-the-counter products do not treat the underlying atrophy.

ESTROGEN THERAPY FOR GENITAL SYMPTOMS AND DYSPAREUNIA IN GSM

High-level placebo randomized controlled trials have demonstrated clear efficacy of estrogen therapy (ET) in improving all GSM-related symptoms due to vulvovaginal atrophy³; however, clinically meaningful benefit for individual symptoms has not been determined for many GSM symptoms. Typical measures for efficacy include change in the most bothersome symptom (scale 0 to 3: none, mild, moderate, and severe, respectively). Most RCTs show a mean decrease in symptom severity of 1.2 to 1.7 points (scale 0 to 3) from baseline over 12 weeks with an approximate decrease in placebo groups from 0.8 to 1.3 points, giving a mean improvement over placebo 0.4 to 0.5 points for all studies.¹⁵ There are a myriad of US Food and Drug Administration (FDA) approved ET that can be administered through oral and transdermal routes. Low-dose, local vaginal estrogen therapy (ET) is preferred over systemic HT for GSM due to VVA because vaginal delivery of estrogen is associated with better efficacy and with minimal systemic absorption leading to decreased oncological and thromboembolic risk.¹⁶ Vaginal formulations include creams, tablets, inserts, and a low-dose vaginal ring (Table 4). Each has similar efficacy; however, the cream, pill, and insert are used daily for the first 2 weeks followed by twice weekly maintenance, while the ring is only placed every 90 days. The ring may be left in place during intercourse.

As with the low-dose, local estrogen therapies, there are numerous systemic ET options, including an oral pill, transdermal patch, emulsion, spray, and two higher dose vaginal rings. Systemic ET is

indicated when there are concomitant vasomotor symptoms, premature menopause, or when osteoporosis prevention is a consideration. However, systemic ET alone does not always improve genitourinary symptoms associated with menopause. If vaginal symptoms persist after initiating systemic HT, then the addition of a low-dose vaginal ET is often needed.¹⁶ Protection of the endometrial lining is not required with the use of low-dose, local ET; however, a progestogen or tissue-selective estrogen complex is required if the uterus is present in those using systemic ET.¹⁶

Estrogen therapy appears to be one of the most effective treatments for addressing moderate to severe dyspareunia due to underlying VVA and is recommended when the patient has not had an adequate response to nonprescription therapies.¹⁶ The available options for administration are outlined in Table 4. Local vaginal ET is preferred for moderate to severe dyspareunia. However, when systemic HT is warranted, transdermal ET options may be best, as oral ET is associated with increased sex hormone-binding globulin along with reduced bioavailability of testosterone, which may further exacerbate a low libido in a patient that already has sexual dysfunction.¹⁶

OTHER HORMONAL THERAPIES FOR MODERATE TO SEVERE DYSPAREUNIA IN GSM

The FDA has also approved 2 daily nonestrogen therapies, prasterone, an intravaginal dehydroepiandrosterone insert, and oral ospemifene, a selective estrogen receptor modulator, for the treatment of dyspareunia due to VVA (Table 4). The dehydroepiandrosterone insert is metabolized to active androgen in the peripheral vaginal tissues and then aromatized to form estrogens.¹⁷ The conversion to active hormone occurs intracellularly, thereby limiting the effect to the cells locally with minimal systemic absorption and no estrogenic stimulation

TABLE 4. Hormone Therapy Options for Management of Genitourinary Syndrome of Menopause

Product type	Brand name	Generic available	Recommended dosing		Remarks
			Loading dose	Maintenance dose	
Vaginal Cream					
Estradiol-17 β	Estrace	Estradiol	0.5-1 gm daily for 1-2 wk	0.5-1 gm 1-3 times weekly	FDA recommended dose: loading dose 2-4 gm daily; maintenance dose 1 gm 1-3 times weekly
Conjugated estrogen	Premarin	No	0.5-1 gm daily for 1-2 wk	0.5-1 gm 1-3 times weekly	FDA recommended dose: 0.5 g twice weekly OR cyclic dosing VVA – 0.5-2 gm daily for 21 d, then off 7 d Dyspareunia – 0.5 gm daily for 21 d, then off 7 d
Vaginal Insert					
Estradiol hemihydrate	Vagifem	Yuvafem	10 μ g daily for 2 wk	Twice weekly	
Estradiol-17 β	Invexxy	No	4 or 10 μ g daily for 2 wk	Twice weekly	
DHEA/prasterone	intrarosa	No	6.5 mg daily		
Vaginal ring					
Estradiol-17 β	Estring	No	Device containing 2 mg releases 7.5 μ g daily for 90 d		
Estradiol acetate	Femring	No	Device containing 12.4 mg releases 0.05 mg daily OR Device containing 24.8 mg releases 10 mg daily for 90 d		The systemic vaginal estrogen ring is used to treat GSM in those who also have moderate to severe VMS. A progestogen should be prescribed in those with in-situ uterus to reduce the risk of endometrial hyperplasia or endometrial cancer.
Oral tablet					
SERM	Ospheña	No	60 mg daily		May increase VMS but typically diminishes after the first month.

DHEA indicates dehydroepiandrosterone; FDA, Food and Drug Administration; GSM, genitourinary syndrome of menopause; SERM, selective estrogen receptor modulator; VMS, vasomotor symptoms.

to the endometrium. Studies have shown improvement in vaginal lubrication, arousal, orgasm, and pain. Safety in patients after breast or other hormonally derived cancers has not been well established; however, there is some limited safety data that is promising.¹⁷

Likewise, oral ospemifene is not approved for use in women with a history of breast cancer in the United States, as it has not been adequately studied in this population. However, an antiestrogenic

effect on breast tissue was seen in pre-clinical trials, and in Europe, it is approved for use in women with a history of breast cancer who have completed treatment.³ Ospemifene is the only oral product available on the market to treat moderate to severe dyspareunia due to VVA. Although, for many, the ease of vaginal dosing is preferred, for others, the messiness of creams and inserts, along with discomfort associated with vaginal placement, contribute to noncompliance.

Oral ospemifene is ideal for those who wish to avoid the potential inconveniences associated with intravaginal therapies.

TESTOSTERONE PLUS VAGINAL ET FOR HYPOACTIVE SEXUAL DESIRE DISORDER (HSDD) IN GSM

Off-label use of systemic transdermal testosterone can be considered for the management of HSDD in postmenopausal women; however, the use of transdermal or vaginal testosterone for the treatment of GSM is not recommended.^{3,18} There is limited evidence showing vaginal testosterone improves dyspareunia and vaginal dryness in postmenopausal women; however, increases in serum estradiol and testosterone levels have been seen in some trials, raising concerns about efficacy and safety, especially in those with a history of breast cancer.^{3,19} More long-term, adequately powered, randomized, placebo-controlled trials are warranted. Until these studies are forthcoming, we only recommend the addition of transdermal systemic testosterone to vaginal ET for those with persistent HSDD after the treatment of GSM (see Kingsberg et al).

VAGINAL LASER THERAPY FOR VAGINAL DRYNESS AND DYSPAREUNIA IN GSM

Vaginal laser therapy has garnered enthusiasm as an alternative nonhormonal treatment option for dyspareunia associated with hypoestrogenism, particularly in those with contraindications to vaginal estrogen or other hormonal therapies. The hypothetical mechanism of action is the creation of microtrauma to the vaginal epithelium, which in turn promotes blood flow and encourages collagen synthesis and thickening of the vaginal epithelium.²⁰ Studies of efficacy are limited to a small number of blinded sham-controlled RCTs, and the majority do not show benefit.^{21–23}

However, concerns around the safety and efficacy of vaginal laser have led the

US FDA, the North American Menopause Society, and the American College of Obstetricians and Gynecologists (ACOG), among other organizations, to issue warning statements against the use for the treatment of GSM.^{3,20,24} In addition to the concerns, there is no consensus around the frequency or duration of treatment, an important issue as the treatments are expensive and typically are not covered by insurance. Currently, vaginal laser therapy is not recommended for the treatment of any components of GSM due to lack of scientific evidence supporting safety and efficacy.^{3,20}

PHYSICAL THERAPY, VAGINAL DILATORS FOR MODERATE TO SEVERE DYSPAREUNIA RELATED TO PELVIC FLOOR DYSFUNCTION IN GSM

Genito-pelvic pain/penetration disorder (GPPPD) encompasses the relationship between dyspareunia and vaginismus, which is defined by fear and anxiety of penetration that commonly triggers tightening and tensing of the abdominal and pelvic floor muscles.²⁵ VVA, due to menopause, commonly causes dyspareunia leading to vaginismus, which over time, results in hypertonicity of the pelvic floor musculature, often perceived as a blockage of the vaginal canal. Treatment of the underlying atrophy is recommended; however, if GPPPD persists after adequate treatment, additional therapy is warranted. GPPPD is a vicious cycle marked by dyspareunia leading to avoidance, decreased libido, and progressive vaginal dryness.²⁶ Management hinges on treatment of the underlying condition, recognizing that a multifactorial approach is often needed.

Pelvic floor physical therapy is a therapeutic modality to address pelvic floor dysfunction in those with hypertonicity. Physical therapists with specialized training in pelvic floor physical therapy employ a multitude of modalities geared to help relax the pelvic floor muscles. Suc-

cessful treatment involves combining pelvic floor physical therapy with behavioral health modalities, such as sex therapy, cognitive behavioral therapy, and hypnotherapy, to yield the best outcomes.²⁷ When access to care or embarrassment is an obstacle, internet-based, self-guided interventions can be useful.

Vaginal dilators and vibrators may be used to mechanically stretch the vaginal tissues and aid in relaxation of the pelvic floor muscles. Dilators come in graded sets of static, cylindrical rods or individually and are available in a wide array of materials, including silicone, latex, plastic, and glass.²⁷ Some have additional features like cooling, heating, and vibrating. In addition to static dilator sets, a single, dynamic, battery-operated dilator has been cleared by the FDA. The diameter is controlled electronically by the user. It can be placed at the smallest diameter, 15 mm, and incrementally expanded by 1 mm up to a maximum diameter of 40 mm, without removal from the vagina. Daily practice is recommended by increasing the size of the dilator as tolerated until the vagina can comfortably accommodate a dilator comparable to the size of their partner's erect penis or to the size of a vibrator or dildo. Typically, this equates to a size 5 (4-inch circumference) or 6 (5-inch circumference); however, for those who have larger partners, dilation up to a size 7 or 8 is needed.²⁷ Behavioral interventions and frequent follow-up aid in overcoming anxiety around vaginal dilation and help support compliance and ultimate progression to intercourse.²⁷ Dilation recommendations vary; however, consistent dilation each week over a year is recommended, with some encouraging dilators being kept overnight for the first month.²⁷

OFF-LABEL THERAPIES FOR REFRACTORY DYSPAREUNIA IN GSM
Refractory cases of dyspareunia may respond to off-label use of botulinum neurotoxin A injections into the pelvic

floor muscles, which inhibits acetylcholine release at the neuromuscular junction, resulting in pelvic floor relaxation. A review of 13 small studies found the use of botulinum neurotoxin A was associated with some success in treating refractory disease and had some benefit in lessening pain due to vaginal dilation.²⁸

Application of topical lidocaine to the vestibule before dilation or vaginal penetration has been shown to reduce dyspareunia, especially when used in conjunction with a lubricant or as an adjunct or alternative to hormonal therapy.²⁹ Improvement of dyspareunia after applying topical lidocaine to the vestibule suggests there may be a neurologic component in addition to underlying atrophy.

GSM and Urinary Symptoms

The term GSM includes the urinary urgency, frequency, dysuria, and recurrent urinary tract infections (UTIs). The decision to include urinary symptoms was based on a narrative literature review and expert opinion.² While acknowledging the overlap with urinary symptoms, aging, and menopause, the panel did not address which symptoms might be attributable to aging versus those related to menopause. Overactive bladder (OAB) is defined by the International Continence Society as “a symptom complex of urinary urgency, usually with frequency and nocturia, in the absence of other pathology such as infection or stones”.³⁰ OAB is associated with increasing age and is common, affecting 29% of women in the United States and up to 43% in non-White communities.³¹ Urinary symptoms in aging women are likely related to both decreased estrogen in peri-menopause and postmenopause, as well as neurological and vascular changes from overactive bladder, a multifactorial etiology.

Dysuria, or discomfort with urination, can mean both burning when urine touches the vaginal skin or discomfort during voiding. Dysuria with voiding is commonly

related to an overactive bladder, UTIs, or inflammation. Dysuria triggered by external skin burning and irritation is often related to VVA. It is often difficult for patients and clinicians to pinpoint these differences. The prevalence of recurrent UTIs increases in women in peri-menopause and postmenopause. Low estrogen levels in peri-menopausal and postmenopausal women lead to changes in the vaginal epithelium from decreased vascularity, as well as changes in the vaginal microbiome, specifically reduction in lactobacillus and increased pH, thereby increasing the susceptibility to uropathogens and bladder infections.³² Current treatment recommendations focus on the alleviation of the most bothersome symptoms to patients, often involving treatment of the underlying atrophy, along with any structural, neurologic, or infectious contributing factors. Treatment guidelines outlined here address all causes of urinary symptoms, as it is difficult to separate urinary symptoms from hypoestrogenism versus OAB.

The American Urological Association (AUA)'s initial evaluation of lower urinary tract symptoms of urinary frequency, urgency, and dysuria includes obtaining a history, physical exam, and a urinalysis.³³ A thorough history should elicit and differentiate between urinary urgency, frequency, nocturia, enuresis, and incontinence. Patients with neurological diseases such as spinal cord injuries or multiple sclerosis need a more detailed evaluation and will not be included here. Chronic medical conditions such as hypertension and diabetes can also lead to increased urinary urgency and frequency especially if poorly controlled. Symptoms often improve once blood pressure and glycemic control have been obtained. Gross hematuria, microscopic hematuria, and any vaginal or rectal bleeding should raise a red flag, as bleeding can signify malignancy or kidney stones and need prompt evaluation.

In addition to taking a complete history, voiding diaries are also useful tools to assess fluid intake and voiding patterns. A voiding diary typically measures fluid intake and voids over a 1-to-3-day period. Likewise, bladder stimulants like caffeine and alcohol, along with the volume of fluid, should be assessed.⁶ Often, behavioral changes based on fluid intake patterns can help to improve symptoms.

Historically, a post-void residual (PVR) was suggested before treatment for urinary symptoms. In 2019, the AUA amended its guidelines and noted the PVR to be optional.³³ There is no standard definition for an abnormal PVR or at what PVR women are more likely to have symptoms. The Lower Urinary Tract Dysfunction Network found that PVR was similar in women with lower urinary tract symptoms and those without.³⁴ However, if urinary retention is suspected to be the cause of urinary urgency and frequency, a PVR is a helpful diagnostic tool. Lastly, a urinalysis should be obtained in patients with urinary symptoms to assess for an underlying UTI or evidence of hematuria that would require further workup.

BEHAVIORAL, DIETARY CHANGES, AND PELVIC FLOOR MUSCLE THERAPY FOR URINARY SYMPTOMS OF GSM

Behavioral therapy includes fluid management, urge avoidance, and bladder retraining to break habits of preemptive voiding. Fluid management can be evaluated with a voiding diary where the patient records what they are drinking at what times, the number of voids, and the volume of voids throughout the day. Limiting fluids before sleeping can reduce nocturia, and drinking to thirst can reduce polydipsia. There is some evidence to suggest that caffeine, carbonation, alcohol, and artificial sweeteners increase urinary frequency and urgency, and reducing these bladder irritants can

improve symptoms. The literature is contradictory, but there is some evidence underlying these dietary changes in managing urinary frequency and urgency.³⁵

Pelvic floor muscle therapy (PFMT) is performed by physical therapists with specialized training in the pelvic floor, focusing on strengthening pelvic floor muscle tone and control to improve bladder symptoms. A recent literature review of PFMT on OAB symptoms found an overall beneficial effect. Because PFMT regimens are heterogeneous, it is difficult to compare data across trials, but there is little risk and some benefit.³⁶ A meta-analysis looking at the effect of PFMT on OAB found that pelvic electrical stimulation resulted in the greatest improvement in urinary frequency, urgency, and incontinence when compared with PFMT with biofeedback.³⁷

SYSTEMIC HORMONE THERAPY FOR URINARY SYMPTOMS OF GSM

There appears to be no benefit in systemic HT for urinary symptoms of GSM, including urinary urgency, frequency, dysuria, or prevention of recurrent UTIs. In fact, use has been associated with worsening urinary incontinence and new onset incontinence.³⁸ Therefore, systemic HT should not be used to treat GSM-related urinary symptoms, and those considering systemic HT for other symptoms, such as vasomotor symptoms, should be counseled regarding the risk of worsening or new onset urinary incontinence.

VAGINAL ESTROGEN THERAPY FOR URINARY SYMPTOMS OF GSM

Overall, low-dose, vaginal ET improves symptoms of urinary frequency, urgency, dysuria, and prevention of recurrent UTIs.³⁸ There are several options available to patients (Table 4). A 2019 guideline for treating recurrent UTIs from the American Urogynecologic Society advocated for the use of vaginal estrogen due to its low-risk profile with or without the

addition of a short course of daily, low-dose antibiotics to suppress recurrence.³⁹

OVERACTIVE BLADDER MEDICATIONS FOR URINARY SYMPTOMS OF GSM

After or alongside behavioral or dietary changes, medications can be added to treat OAB symptoms. In addition, low-dose, local vaginal ET can also be used alone or in conjunction with OAB medications. There are currently 2 categories of medications available including anticholinergic medications and Beta3 agonist medications including mirbegron and vibegron. Anticholinergic medications have side effects such as dry mouth, constipation, and dry eyes. They have also been increasingly associated with cognitive changes in patients.⁴⁰ The AUA has a treatment guideline that is easy to use for further guidance.³³

For patients with persistent symptoms, the AUA outlines a treatment pathway that includes third-line therapies, including percutaneous tibial nerve stimulation, onabotulinum toxin A, and sacro neuromodulation.⁴¹ Treatment with third-line therapies often requires referral to a specialist in urogynecology or urology.

OTHER TREATMENTS FOR OVERACTIVE BLADDER IN GSM

Newer treatment modalities have recently gained some attention. Ospemifene, a selective estrogen receptor modulator, FDA-approved for the treatment of dyspareunia in postmenopausal women, has been shown to improve OAB symptoms in small clinical trials. Data supporting Ospemifene for the treatment of OAB is not yet recommended; however, if it is already being used for dyspareunia, women may see some improvement in their urinary symptoms.⁴²

Like Ospemifene, some small clinical trials have shown some improvement in OAB symptoms with vaginal laser in postmenopausal women, but no large-scale randomized placebo-controlled

trials have been done. There currently is not enough evidence to suggest treatment for urinary symptoms with laser therapy.⁴³

Conclusion

Genitourinary symptoms associated with menopause are common and often impact the quality of life and impair daily function. Clinicians should screen all menopausal patients. Symptoms are highly responsive to treatment and should be treated early to improve quality of life and function. A personalized, multimodal approach to treatment is necessary as symptoms may involve genital, urinary, and sexual function (Fig. 1).

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