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Review

Continuing Education

Genitourinary Syndrome of Menopause

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Genitourinary syndrome of menopause (GSM) occurs in approximately 50% of menopausal women but is both underrecognized and undertreated despite numerous treatment options. Vaginal dryness, irritation, dyspareunia, urinary frequency, and urinary urgency are some of the more common symptoms that can have a negative effect on women's lives and relationships. Treatment options can include over-the-counter moisturizers and lubricants that can be composed of water or silicone or have an oil base. However, women and health care providers need be aware of the effects of excipients in these products so that the therapy does not cause vaginal irritation. US Food and Drug Administration (FDA)–approved treatment options include vaginally administered estrogen products as well as dehydroepiandrosterone (prasterone) and the selective estrogen receptor modulator ospemifene. The prescription options have proven efficacy and safety and can be considered for use by women with a history of cancer following collaboration with the oncologist. Despite the FDA warning that recommends vaginal lasers not be used for vaginal rejuvenation, vaginal lasers have also been used as a treatment for GSM, but studies on their safety are limited. This article reviews GSM, including its impact, diagnosis, and treatment.

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INTRODUCTION

Menopause is the natural progression in a woman's reproductive life when she outlives ovarian production of estrogen. The significant reduction in circulating estrogen has far-reaching effects throughout the body, including the brain, skin, hair, joints, and the genitourinary system. Vulvovaginal atrophy (VVA) refers to the changes in the genitals associated with a hypoestrogenic state but does not include the coinciding changes to the urinary system. Therefore, menopausal symptoms that affect the genitourinary tract are now referred to as the genitourinary syndrome of menopause (GSM). Symptoms include vulvovaginal dryness, burning, and irritation, which can lead to painful intercourse and difficulty reaching arousal and orgasm. In addition, women may also develop dysuria and urinary urgency and be at risk for recurrent urinary tract infections, vaginitis, and sexually transmitted infections.[1] Unlike other bothersome symptoms of menopause such as hot flashes or mood changes, which usually lessen or resolve with time, GSM is progressive without treatment. Symptoms of GSM are common, affecting 27% to 84% of postmenopausal women, yet may be significantly undertreated with approximately 7% of those affected reporting use of prescribed therapies.[1,2] This article reviews the etiology and treatment options for women with GSM, including over-the-counter options, prescriptions, and energy-based therapy.

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PATHOPHYSIOLOGY OF GSM

GSM is the result of a hypoestrogenic state that occurs following menopause or primary ovarian insufficiency. Estrogen has many effects on the vulva and the vagina, including maintaining blood flow, supporting the tissues and microbiome, and protecting against pathogens.[3] The vulvovaginal area is sensitive to the physiologic changes of menopause because of the numerous estrogen receptors that are located throughout the vulva and vagina, including the autonomic and sensory neurons in the vagina.[2] Likewise, there are estrogen receptors throughout the lower urinary tract, urethra, bladder, and pelvic floor muscles.[2] Low levels of estrogen result in a higher diversity of vaginal bacteria, an elevated vaginal pH, clitoral atrophy, and a shortened and narrowed vagina, which causes the urethra to become more prominent.[2] The vulvar and vaginal epithelium becomes thin and more susceptible to trauma, and the tissue may appear dry, friable, and pale with petechiae, ulcerations, or tears.[2] Furthermore, this thinning will cause the underlying connective tissue to be exposed and increase the likelihood of inflammation or infection.[4] However, despite the tissue appearing dry, there can be an increase in vaginal discharge that may be brown or yellow in color.[2]

Most likely, the pathophysiology of GSM is due to a decrease in both estrogen and androgens. In addition to estrogen receptors, women have androgen receptors in the vulva and vagina, with a higher density of estrogen receptors in the vagina and more androgen receptors in the vulva.[2] Not only are androgens necessary for the biosynthesis of estrogen, but both estrogen and testosterone are necessary for vascular responsiveness and signaling pathways during sexual arousal.[5]

HOW GSM AFFECTS WOMEN

Several studies have examined the impact of GSM on women. The REVIVE study was an internet-based survey that assessed the perceptions, experiences, and needs of 3768 postmenopausal women in 4 different European countries.[6] The

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Quick Points

- Genitourinary syndrome of menopause (GSM) is grossly undertreated despite having a high prevalence among menopausal women.
- GSM has a negative impact on women, and health care providers do not adequately screen for it.
- Over-the-counter options can include lubricants, moisturizers, and some vitamins.
- Prescription options are safe and effective and include vaginal estrogen, ospemifene, testosterone, and prasterone.
- Although there are limited studies, vaginal lasers are another treatment option for GSM.

study found that 30% to 40% of the women surveyed experienced 2 or more symptoms, with vaginal/vulvar dryness being the most common symptom.[6] Furthermore, 66% to 74% of the women reported that their symptoms interfered with their sexual satisfaction, 62% to 70% of the women reported reduced sexual spontaneity, and 53% to 69% reported a loss of intimacy.[6] The VIVA survey, which included 500 postmenopausal women in the United States, examined attitudes about and knowledge of vaginal atrophy.[7] The VIVA survey found that 48% of the women reported vaginal discomfort of which the most common symptoms were vaginal dryness (85%) and dyspareunia (52%).[7] Although 76% of the women reported that they would be comfortable discussing their symptoms with a health care provider, 40% waited one year or more after their symptoms started, and 37% of the women did not seek help.[7] More recently, the 2017 EMPOWER survey examined if there was any progress in women's understanding of VVA and its treatment.[8] Unfortunately, most women regarded VVA as a normal part of aging; only 19% of the women recognized VVA as a medical condition.[8] Health care providers initiated a conversation regarding GSM at 15% of the visits, and 44% of the women initiated a discussion of their symptoms with their health care provider.[8] VVA had a significant negative impact on their quality of life, especially with regard to sexual activity, and 13% of women stated that they would like to have more sexual activity if they did not have vaginal dryness, itching, and/or pain.[8] Of the women surveyed, 50% had treatment for VVA. Within the group who were treated, 33% to 51% were satisfied with local vaginal estrogen products, and 41% to 45% were satisfied with lubricants and moisturizers.[8] Reasons for dissatisfaction included lack of efficacy, inconvenient applications, and concerns regarding adverse effects and risks of treatment.[8]

ASSESSMENT AND DIAGNOSIS OF GSM

The diagnosis of GSM is based on the history and physical examination findings. Table 1 lists the objective and

Table 1. Signs and Symptoms of the Genitourinary Syndrome of Menopause

Body System	Objective Signs	Subjective Symptoms
Vulvovaginal	Thinning/graying of pubic hair	Dryness
	Labial atrophy/reduced subcutaneous fat	Irritation
	Tissue appears dry and pale with petechiae and may have ulcerations and/or tears	Burning
		Itching
	Loss of vaginal rugae	Discomfort
	Decreased elasticity of the vaginal tissue	
	Recurrent vaginitis	
	Discharge	
	Elevated pH	
	Prolapse	
Urinary	Urethral caruncle	Frequency
	Frequent urinary tract infections	Urgency
	Prominent urethral meatus	Dysuria
	Incontinence	
Sexual	Vaginal stenosis	Dyspareunia
	Postcoital bleeding	Decreased lubrication
	Clitoral atrophy and phimosis of the prepuce	Decreased arousal
		Decreased libido
		Decrease in sensation

subjective vulvovaginal, urinary, and sexual signs and symptoms of GSM. Normalizing symptoms of GSM and discussing its high prevalence may facilitate the woman's comfort. Current health history, including any history of dermatologic disorders, medications, vulvovaginal hygiene, and use of bladder irritants, should be elucidated.[9] Questions specific to GSM are those about vulvovaginal symptoms, including dryness, pruritus, and changes in discharge, as well as urinary symptoms such as frequency, urgency, and history of recurrent urinary tract infections. In addition, health care providers should obtain a sexual history and ask about pain with sexual activity, loss of lubrication, and difficulty with arousal and orgasm. Treatments that have been tried should be reviewed. The impact of these symptoms on quality of life, relationships, and body image should be examined.

Screening tools that can increase a health care provider's awareness and diagnosis of GSM are available. The Day-to-Day Impact of Vaginal Aging questionnaire is a patient-reported screening tool used to assess the impact of vaginal symptoms on function and well-being.[10] The US Food and Drug Administration (FDA) recommends use of the Most Bothersome Symptom Approach for GSM symptom evaluation.[11] This tool asks women to rate the severity of 4 common GSM symptoms: vaginal dryness, vaginal soreness, vulvovaginal irritation, and vaginal discharge.[11] If the woman is sexually active, additional questions ask about dyspareunia.[11] The Most Bothersome Symptom Approach is helpful for evaluating change in severity of symptoms after intervention.[11]

A physical examination is performed to look for objective signs of GSM, including thinning or absent pubic hair, thinning of the vulvar skin, both erythema and pallor of the vulvovaginal tissue, loss of vaginal rugae, and fissures.[3] Urethral caruncle, prolapse, and polyps are also associated with GSM. The examination should include asking permission to show the woman the physical findings with a handheld mirror. Microscopy is performed to assess for an increased proportion of parabasal cells, mixed flora, and an increase in white blood cells.[2] Evaluating the vaginal pH and maturation index is helpful but not necessary for a diagnosis. Likewise, there is no laboratory test to negate or confirm the diagnosis of GSM. Treatment is advisable for any woman who endorses bothersome GSM symptoms, even if the physical findings do not correlate with the individual's report of severity.

DIFFERENTIAL DIAGNOSES OF GENITORURINARY SYNDROME OF MENOPAUSE

There are numerous differential diagnoses to consider when assessing for GSM, as many disorders can cause vulvovaginal pruritus, irritation, or dyspareunia. Differential diagnoses include infections, contact irritants, trauma, radiation, and dermatologic conditions. The most common differential dermatologic diagnoses that affect menopausal women are reviewed.

Lichen sclerosus is a vulvar inflammatory disease of unknown etiology that is more common in prepubertal and menopausal women compared with reproductive-age women. Presenting symptoms include vaginal pruritus and dyspareunia. Whereas women with GSM may have pale and thinned tissue on their genitals, women with lichen sclerosus have white plaques and papules that can be present on the labia majora, labia minora and perineum. Another distinguishing feature of lichen sclerosus is architectural changes such as a reabsorption of the labia minora and scarring of the clitoral hood. A vulvar biopsy is recommended if there is uncertainty about the diagnosis or if there are any visible lesions in the vulvar area. Inadequately treated lichen sclerosus is associated with an increased risk of squamous cell carcinoma.

Pruritus, irritation, and skin color change can be secondary to infection or contact dermatitis. Microscopy or a yeast culture can assist in the assessment and diagnosis of a yeast infection. Vulvovaginal hygiene history can help identify possible irritants and correlation with onset of symptoms.

Vulvodynia is vulvar pain of at least 3 months' duration without a clear identifiable cause and can be an independent finding or a symptom of VVA related to GSM. Although vulvovaginal pain and dyspareunia are symptoms common to both vulvodynia and GSM, a key finding in persons with vulvodynia is pain with light touch, sitting, or wearing certain clothing. GSM can cause daily vulvovaginal itching or irritation but will typically not cause acute daily pain. The cotton swab test is helpful for pain mapping and diagnosis of vulvodynia.[3]

Desquamative inflammatory vaginitis (DIV) is present in up to 8% of women who experience recurrent vaginitis.[3] The etiology is unknown but is more common in women who are hypoestrogenic, such as during the postpartum period, perimenopause, or menopause. Symptoms include copious vaginal discharge that may be yellow to brown with a displeasing odor, an increase in white blood cells on microscopy, and dyspareunia. DIV is a diagnosis of exclusion, but the odor and copious discharge differentiates it from GSM. If a health care provider initially treats a woman for DIV with estrogen for what they presume to be GSM, there is usually only slight improvement, which is another clue that the underlying condition may be DIV.

Lastly, pelvic floor hypertonus can cause dyspareunia and erythema at the points of pelvic floor muscle attachment. The pelvic floor muscles contribute to core stability. Thus, exploration of back, knee, or hip pain or diagnoses that may have caused the pelvic floor muscles to become hypertonic is warranted. Internal palpation of all the pelvic floor muscles to identify any trigger points or areas of pain that may be due to a buildup of lactic acid can be performed with permission.

It is important to remember that other disorders can occur simultaneously with GSM and a woman will need treatment for both. If there is any uncertainty in the diagnosis or if a woman is not responding to the treatment as expected, referral to a health care provider who is an expert in women's sexual health or menopause for a further evaluation is recommended.

OVER-THE-COUNTER TREATMENT OPTIONS

First-line therapy for GSM includes over-the-counter options that may be effective for women with mild to moderate

symptoms. These products include moisturizers, lubricants, vitamins, and probiotics.

Moisturizers and Lubricants

Moisturizers are intended for long-term use. The FDA recognizes that the vagina is a biologically active organ and has therefore classified moisturizers as class II medical devices, which makes them subject to testing and strict manufacturing standards.[12] Women can apply moisturizers to the entire vulva daily, and the product is intended to remain on the body for 60 minutes.[13] Moisturizers are available with water, silicone, oil, or hybrid bases.

Lubricants are short-acting and intended for sexual play and may be classified as medical devices.[13] They are also available with water, silicone, oil, or hybrid bases. The most beneficial moisturizers and lubricants have both moisturizing and moisture-sealing qualities, a pH similarto the orifice of penetration, and do not have allergenic, sensitizing, or contact-irritant botanical components.[11]

Water-based products are nonstaining, but emollients and preservatives are added for viscosity, to alter water activity, and to prevent bacterial contamination. These agents can increase osmolality.[13] Osmolality is the measure of the number of dissolved particles per kilogram of solvent, expressed as the mOsm/kg. Osmolality is important for vaginal moisturizers and lubricants because the epithelial cells try to maintain an equilibrium of water content and osmolality determines whether or not water flows into or out of the epithelial cells of the vagina. Glycols that are added as an emollient are the primary component that increases osmolality.[12] The World Health Organization recommends that the osmolality in a lubricant or moisturizer ideally not exceed 380 mOsm/kg, but 1200 mOsm/kg is acceptable.[14] Hypo-osmotic moisturizers and lubricants can damage the epithelial cells by causing too much water to be drawn into the cells, causing them to swell or burst. Hyperosmotic moisturizers and lubricants will cause epithelial damage by drawing water out of the cells, causing the cells to shrink and slough off. The damaged epithelium is then at increased risk for infection or sexually transmitted infections, including HIV and herpes simplex virus.[15] High osmolality can also be toxic to lactobacilli, which may also increase the risk of vaginal infections.[15] Table 2 lists the pH and osmolality of several commonly used water-based lubricants and moisturizers.

Silicone- and oil-based products do not add emollients or preservatives and therefore do not affect pH or osmolality. Topically applied plant-based oils have also been studied for their ability to act as a barrier, help the skin retain moisture, and promote wound healing.[16] However, their specific application on the vulvovaginal area has not been studied. There is interest in their use because some plant constituents have an antioxidant effect that can help with skin barrier homeostasis and anti-inflammation.[16] Olive oil and coconut oil are particularly helpful in permeating the skin because of their high content of monounsaturated oleic acid.[16] In addition, both olive oil and coconut oil have an anti-inflammatory and antioxidant effect, and coconut oil also has an antibacterial effect.[16] However, because of the lack of research, oil- or plant-based products should be used off label with caution. Furthermore, oil-based products may alter the integrity of latex condoms and should be avoided by women who use condoms to prevent pregnancy or sexually transmitted infections.[14]

Additional components of moisturizers and lubricants may include hyaluronic acid, bee products, and cannabinoids. Although studies are lacking that compare hyaluronic acid products with nonhyaluronic acid, hyaluronic acid is often added to vaginal moisturizers and lubricants because it is thought to draw moisture into any area to which it is applied.[1] Bee products have also been used in moisturizers and can have anti-inflammatory, antioxidant, and regenerative effects on the skin, but these products have not been specifically studied in the vulvovaginal tissue.[17] Cannabinoids are sometimes added to vaginal lubricants to increase moisture and enhance sexual arousal and excitation, but there are no studies on this effect or its safety.[9] Although vaginal moisturizers and lubricants can improve the symptoms of GSM, they do not improve health of the vaginal tissue.[18]

Vitamins E and D

Although studies are lacking, both vitamin E and D are over-the-counter options that may be used for treating symptoms of GSM. Vaginally inserted vitamin E enhances the moisture and resiliency of the vaginal walls by preventing tissue damage and increasing blood circulation.[19] Likewise, the vaginal epithelium has vitamin D receptors, and oral vitamin D supplements may aid in differentiation and proliferation of the epithelium.[19]

Probiotics and the Vaginal Microbiome

Recent research suggests there are at least 5 different types of vaginal microbiomes and that menopause does change the species of the vaginal microbiome.[4] Although a lactobacillus-dominated microbiome is often thought to be optimal, the role of lactobacilli is somewhat unclear.[4] Not all types of lactobacilli are beneficial, and it is unknown if lactobacilli promote vaginal health or if they are a marker for vaginal health.[20] It was previously thought that a low estrogen level in the vagina led to lower glycogen content and a subsequent decrease in colonization of lactobacilli.[20] Without a lactobacillus-dominant environment, dysbiosis and an increase in susceptibility to infection follow.[21] However, not all menopausal women lose their vaginal colonization of lactobacilli.[20] Therefore, it is unclear if a decrease in lactobacilli may play a role in GSM. In one cross-sectional study of 88 women, 53% reported a GSM symptom, and the authors found that a lactobacillus-dominant vaginal microbiome was not associated with fewer GSM symptoms.[20] Currently there are no proven therapies to alter the vaginal microbiome for the treatment of GSM, and thus the effectiveness of probiotics requires further research.[9]

PRESCRIPTION TREATMENTS FOR GENITORURINARY SYNDROME OF MENOPAUSE

There are numerous prescription options that are safe and effective for women with severe GSM and for those whose symptoms are not resolved with over-the-counter therapies.

Table 2. Commonly Used Personal Water-Based Moisturizers and Lubricants		
Name	**pH**	**Osmolality, mOsm/kg**
Moisturizers		
Canesintima Intimate Moisturizer	5.63	846
Gynomunal Vaginal Moisturizing Gel	5.84	>2000
Hyalofemme Vaginal Hydrating Gel	4.88	1729
Regelle Long-Lasting Vaginal Moisturizer	2.88	2012
Replens MD Longer-Lasting Vaginal Moisturizer	2.95	2011
Sylk Natural Intimate Moisturizer	4.47	877
Yes Vaginal Moisturizer	4.15	250
Lubricants		
Astroglide Gel Lubricant	4.38	6100
Astroglide Ultra Gentle Sensitive Skin Lubricant	4.56	945
Balance Activ Menopause Vaginal Moisturizing Lubricant	5.64	309
Bioglide Natural Lubricant	4.99	>2000
Durex Play Feel Lubricant	5.48	1563
Durex Sensilube Hydrating Intimate Gel	5.99	16
Good Clean Love Lubricant	4.73	240
Higher Nature V Gel Aloe Vera Lubricant	4.09	1646
ID Glide Lubricant	5.20	3200
Intimate Organics Lubricant	4.86	>2000
Intimy Lubricant	6.19	1501
Klick Natural Glide Lubricant	4.84	>2000
KY Jelly Lubricant	4.49	2007
Pjur Med Natural Glide Personal Lubricant	4.41	>2000
Pjur Woman Nude Lubricant	4.42	>2000
RepHresh Vaginal Gel	3.46	1914
Sass Intimate Dryness Gel	4.99	>2000
Simply Slick Personal Lubricating Lotion	6.68	>2000
System Jo Personal Lubricant	5.86	61
Yes But Anal Lubricant	7.78	330
Yes Baby Sperm-Friendly Lubricant	7.65	333
Yes Baby Vaginal-Friendly Lubricant	4.22	249
Yes Water-Based Intimate Lubricant	4.08	154

Source: Adapted from Edwards and Panay.

Any health care provider with prescriptive authority can prescribe the therapies. Table 3 summarizes and compares the FDA-approved prescription options for GSM.

Vaginal Estrogen

Systemically administered estrogen therapy is useful for treatment of both GSM and vasomotor symptoms, but when the only distressing menopausal symptom is GSM, vaginal estrogen therapy is preferred. In addition, some women using a systemically administered hormone therapy may need additional vaginal estrogen for GSM symptoms.

FDA-approved vaginal estrogen therapy is available as estradiol, estrone, and conjugated estrogens. Vaginally administered estrogen products are available as a cream, pill, suppository, or ring. The vulvovaginal tissue is permeable, and estrogen applied to the tissue is readily absorbed with minimal systemic absorption. The degree of potency and amount of systemic absorption will vary depending on the type of estrogen. Conjugated equine estrogens are the most potent, and estriol is the least potent.[18] A vaginal estrogen cream applied to a larger area of the genitals will have greater absorption compared with a ring or tablet.[18] The upper one-third of the vagina has more potential for systemic absorption compared with the lower one-third of the vagina, and the vaginal epithelium is more absorptive compared with the vulva or vestibule.

There are no significant clinical differences in efficacy among the different formulations and dosages.[2] Furthermore, all the vaginal estrogen FDA-approved products have proven

Table 3. Comparisons of US Food and Drug Administration–Approved Prescription Options for GSM Treatment

Brand (Generic)	Formula	Dose	Comments
Premarin (no generic available)	0.625 mg CEE per 1 g of vaginal cream Comes with one applicator	0.5 g vaginally at night for 21 d, then off for 7 d	Potential for inaccurate dosing
Estrace (estradiol)	0.01% estradiol vaginal cream, 0.1 mg/g Comes with one applicator	1 g vaginally at night for 2 wk, then 3 times per wk	An additional small amount can be applied to areas of irritation externally Women with more severe cases of vaginal narrowing can apply externally with a fingertip and omit the applicator Potential for inaccurate dosing
Vagifem, Yuvafem (estradiol)	Estradiol vaginal pill preloaded in individualized applicators	10 mcg vaginal tablet used nightly for 2 wk, then 2 times per wk	Applicator is smaller than the applicator used for Estrace
Estring (no generic available)	Estradiol ring inserted into the vagina by patient or health care provider	7.5 mcg estradiol released over 90 d Removed and replaced every 90 d	Partner may feel the ring during penetrative intercourse May be difficult to use if the woman has a prolapse May be difficult to insert if the woman has significant vaginal narrowing Some women may find it difficult to remove and reinsert independently
Imvexxy (no generic available)	Estradiol vaginal suppository; no applicator	4 or 10 mcg estradiol tablet Insert vaginally at night for 2 wk, then 2 times per wk	Lowest possible dose of the vaginal estrogen products available
Osphena (ospemifene)	SERM, oral dose	60 mg orally to be taken at bedtime with food	Only oral dose option for GSM treatment Cannot be used in conjunction with another SERM
Intrarosa (prasterone)	DHEA suppository with individual applicators	6.5 mg DHEA nightly	Nightly dosing, no difference between loading and maintenance dosing No Black Box warning

Abbreviations: CEE, conjugated equine estrogen; DHEA, dehydroepiandrosterone; GSM, genitourinary syndrome of menopause; SERM, selective estrogen receptor modulator.

effectiveness in placebo-controlled randomized controlled trials that assessed their effectiveness for treatment of dyspareunia, vaginal dryness, vaginal/vulvar irritation, vaginal soreness, dysuria, or bleeding associated with intercourse.[2] In a systematic review of 24 trials that evaluated the effectiveness of vaginal estrogen compared with placebo for treatment of GSM, all the included studies showed vaginal estrogen products to be superior compared with placebo in the objective endpoints of maturation of vaginal epithelium and pH.[22] In addition, some studies also showed superiority over placebo for treatment of dyspareunia, vaginal dryness, reduced urinary urgency, and cystitis.[22] A post hoc analysis of a double-blind, randomized, placebo-controlled trial that included 205 postmenopausal women found that although vaginal estrogen is effective for women at any menopausal age, women who were younger than 60 years at initiation of treatment had better and quicker GSM symptom relief compared with women older than 60 years when treatment was initiated.[23] Symptom relief for all women using vaginal estrogen therapy starts within a few weeks but may take up to 12 weeks for maximum efficacy.

Safety of Vaginal Estrogen Products

Adverse effects of vaginal estrogen products could include discharge, candidiasis, vaginal bleeding, and risks associated with systematically administered estrogen such as endometrial hyperplasia, endometrial cancer, and deep vein thrombo-

sis. A systematic review of the effectiveness and safety of vaginal estrogen products analyzed 24 clinical trials (n = 4678) and reported very low rates of adverse effects, including vaginal bleeding (n = 35; 0.75%), vulvovaginal mycotic infection (n = 34; 0.73%), endometrial hyperplasia (n = 3, 0.06%) in those using vaginal estrogen versus no cases in women using placebo, and one case of endometrial cancer.[22] However, none of the studies were longer than 52 weeks and therefore did not determine long-term safety data.[22] Among users of vaginal estrogen, rates of endometrial cancer and hyperplasia appear to be consistent with rates of these disorders found in the general population, and therefore concurrent use of progestogen is unnecessary.[2] Furthermore, atrophic vaginal tissue is more absorptive than nonatrophic tissue, and serum estrogen levels may initially rise with treatment; however, with maintenance dosing and a subsequent thicker vaginal epithelium that decreases absorption, blood levels will remain within the normal postmenopausal range.[24]

A large prospective study from the Nurses' Health Study followed postmenopausal women who did not use systemic estrogen over a period of 18 years to compare outcomes of those who used vaginal estrogen products versus those who did not use vaginal estrogen. The participants in the vaginal estrogen group had an average use of vaginal estrogen for 37.5 months. The study found no difference in total myocardial infarction, hip fracture, or cancer in the women who used vaginal estrogen compared with those who did not use vaginal estrogen.[25] After adjusting for major confounders and hysterectomy status, there were no differences in the risk of any cardiovascular disease, including myocardial infarction, pulmonary embolism, stroke, and deep vein thrombosis. There were also no differences in the risk of cancer outcomes, including invasive breast cancer, ovarian cancer, endometrial cancer, and colorectal cancer.[25] Furthermore, the North American Menopause Society's GSM position statement asserts that there is no increase in coronary heart disease, cancer, or increased risk of venous thromboembolism with use of vaginal estrogen.[2] In women who are at high risk for breast cancer because of family history, the North American Menopause Society and the International Society for the Study of Women's Sexual Health consensus recommendation for women at high risk for breast cancer states that because of the low systemic absorption, vaginal estrogen can be considered for treatment of GSM.[18] In addition, although studies are limited, the consensus recommendation also suggests that women who are carriers of the *BRCA* mutation who have had an oophorectomy can also consider the use of vaginal estrogen.[18]

Despite a strong safety profile, all vaginal estrogen products contain FDA Black Box warnings that include statements regarding the risk of stroke, dementia, breast cancer, and endometrial cancer. These statements are based on the risks associated with systemic oral estrogen and estrogen plus progestin therapy as identified in the Women's Health Initiative Observational Study, not vaginal estrogen.[26] The only contraindication for vaginal estrogen therapy is undiagnosed vaginal and uterine bleeding.[2] Furthermore, any woman using a vaginal estrogen product who has postmenopausal bleeding should receive a pelvic examination, pelvic ultrasound, and, if indicated, an endometrial biopsy to assess for endometrial proliferation.[2] These agents should be used with caution by persons with an estrogen-dependent neoplasia or those at increased risk for thrombosis.[2]

Women who are breast cancer survivors are at an increased risk for GSM because many are already menopausal at the time of diagnosis. In addition, treatment for estrogen receptor–positive breast cancer can worsen GSM symptoms. These treatments may include chemotherapy or radiation (which can induce ovarian insufficiency), oophorectomy, and endocrine therapies including gonadotropin-releasing hormone agonists, aromatase inhibitors, or selective estrogen receptor modulators (SERMs).[18] First-line therapy for women with GSM who have a history of estrogen receptor–positive breast cancer should be over-the-counter therapies. If those are ineffective, both the North American Menopause Society and the American College of Obstetricians and Gynecologists support the use of vaginal estrogen therapy if discussed in collaboration with the woman and her oncologist.[18,27] Estrogen preparations with the lowest systemic absorption should be considered, such as estradiol tablets, suppositories, or rings.[18] Obtaining blood levels is not recommended during therapy because currently there is no known safety threshold of serum estradiol in breast cancer survivors.[18] Women using an aromatase inhibitor need counseling and assessment because any systemic absorption of estrogen can negate the effect of the aromatase inhibitor.[18]

Dehydroepiandrosterone (Prasterone)

Dehydroepiandrosterone (DHEA), also known as prasterone (Intrarosa), is another medication available by prescription for treatment of GSM. Prasterone is formulated as a daily vaginal insert and has been approved by the FDA for treatment of moderate to severe dyspareunia in women. The metabolism of DHEA is unique in that it is metabolized by enzymes inside the vaginal mucosal cells into both estrogen and testosterone, a process that is referred to as intracrinology.[28] The cell-specific small amounts of estrogen and testosterone are then able to act locally as paracrine agents in the vagina.[5] Approximately 95% of the produced estrogen and androgen is then inactivated inside the cells and released in the blood for elimination, thereby avoiding hormone exposure to other tissues.[29] Prasterone is also distinctive because it replaces not only vaginal estrogen but also testosterone.[29] Studies have shown prasterone to be effective in treating dyspareunia and improving sexual dysfunction scores. The improvement in sexual dysfunction score is most likely due to the increased sensitivity of vaginal nerve fibers to the androgenic action.[29] The effect of prasterone on the urinary system has not been studied, but it is suggested that because the effects are similar to estrogen, it may be helpful for treatment of dysuria and recurrent urinary tract infections.[30]

Prasterone has not been studied in women with an increased risk of breast cancer or in women with a history of breast cancer.[31] In addition, women who have androgen receptor–positive tumors or those using endocrine therapies for the treatment of breast cancer may not be candidates for use of this product.[31] Currently, there are no studies that compare prasterone with vaginal estrogen for efficacy or hormone levels, and therefore it is unknown if prasterone is

preferable for breast cancer survivors.[31] Similar to the vaginal estrogen products, the use of prasterone by women with a breast cancer history can be discussed in collaboration with the woman and her oncologist. Of note, prasterone does not have an FDA Black Box warning.

Testosterone

Currently there are no FDA-approved testosterone formulations for women, and the only country that does regulate and authorize the use of testosterone for women is Australia. Although systemically administered testosterone is prescribed off label for hypoactive sexual desire disorder in women, there are limited studies that have evaluated the use of systemic testosterone for the treatment of GSM. Androgens regulate the epithelium of the vagina and mucin production, which is important for lubrication and sexual response.[32] However, there are limited data that address the safety and efficacy of testosterone cream for the treatment of GSM. A review of 6 clinical trials examined the safety of intravaginal testosterone used to treat VVA.[33] The studies had between 10 and 80 participants.[33] The review was unable to determine effectiveness or safety of intravaginal testosterone because of the poor research study designs.[33] Further research is needed to determine the role of testosterone in the treatment of GSM.

SERM: Ospemifene

Ospemifene (Osphena) is an SERM and the only FDA-approved treatment for GSM that is taken orally. Ospemifene has proven efficacy for improving the vaginal maturation index, vaginal pH, dyspareunia, and vaginal dryness.[2] Although the lower vaginal pH could reduce the likelihood of a urinary tract infection, there are no published data on ospemifene's exact effect on the urinary system.[34] Vasomotor symptoms occurred in 7.2% of the participants who used 60 mg per day versus 3.2% of those who used 30 mg per day and 2% of the women given the placebo.[35]

Clinical trials have shown that ospemifene has a neutral effect on the breast, but because of the small size and short duration of these trials, the FDA has not approved ospemifene for use in persons with breast cancer.[2] However, the consensus statement by the North American Menopause Society and the International Society for the Study of Women's Sexual Health suggests that ospemifene can be considered for use by women who are not already taking another SERM for breast cancer risk reduction.[18] Of note, ospemifene carries the same FDA Black Box warnings as the vaginal estrogen products.

Lidocaine

Topical lidocaine applied to the vestibule prior to penetrative intercourse can be used for the treatment of GSM.[18] Goetsch et al conducted a double-blind randomized controlled trial of 46 individuals who were survivors of estrogen-deficient breast cancer and who had severe penetrative dyspareunia, clinical evidence of severe VVA, increased sexual distress, and abnormal sexual function scores. The participants were randomized to apply either saline or 4% aqueous lidocaine to the vestibule for 3 minutes prior to vaginal penetration for one month.[36] After one month, all the women received lidocaine for the next 2 months in an open-label trial.[36] Forty-three women completed the double-blinded part of the study, and 41 completed both parts of the study.[36] During the blinded phase, all the women who were randomized to lidocaine reported less pain, and in the open study, 37 of the 41 women reported comfortable penetration.[36] The sexual distress scores decreased, and the sexual function scores improved in all areas except orgasm.[36] Of the 20 women who had previously abstained from intercourse, 17 resumed.[36] Lidocaine can cause discomfort with application and can affect a partner's sensations. However, in the aforementioned study no partners reported penile numbness.[18,36]

Vaginal Laser Treatment

Energy-based therapies are an emerging nonhormonal option for the treatment of GSM. Of the available therapies, vaginal lasers are the most widely used. The mechanism is activation of heat shock proteins and tissue growth factors elicited by heating the vaginal walls.[37] This results in more collagen and vascularization that improves the elasticity and moisture of the vaginal wall.[37] There are 2 types of lasers used: the CO_2 and the erbium-doped yttrium aluminum garnet erbium-doped yttrium aluminum garnet (Er:YAG) laser. The Er:YAG laser has a higher affinity for water compared with the CO_2 laser, which enables a deeper secondary thermal effect and controlled heating of the vaginal wall.[38] The procedures for both lasers are not standardized but typically consists of 3 therapies, 4 to 6 weeks apart.[38] All health care providers are eligible for training in the use of vaginal lasers, and there are no contraindications for women to receive the laser treatment. However, at the time of this writing, insurance companies do not cover the cost of vaginal laser treatment for GSM, which can be prohibitive.

In 2018 the FDA issued a safety communication against the use of vaginal lasers because of potential adverse effects such as vaginal burns, scarring, pain during sexual intercourse, and recurring or chronic pain. A systematic review was performed to examine the safety of vaginal lasers. The authors conducted a literature review and evaluated reports from the Manufacturer and User Facility Device Experience (MAUDE) and Bloomberg Law databases.[39] A total of 29 cases of adverse events were reported in the studies identified in the literature review.[39] Minimal change from baseline or "no treatment effect" was noted in 12 cases (41.4%), 5 cases (17.2%) reported a worsening of symptoms of vaginal pain or dyspareunia, and 12 cases (41.4%) did not report sufficient information to determine the effects of the laser.[39] A review of the MAUDE database found that 78 cases (65%) were complaints regarding equipment malfunction but that no patients were harmed, 5 cases (4%) reported improper handling of the devices by the operator, and 7 cases (6%) documented injury to the operator.[39] Potential complications or adverse effects, the most common being pain (n = 13) and burning (n = 10), were reported in 30 cases (25%).[39] Lastly, after reviewing the Bloomberg Law database, the authors found no claims for laser devices for the treatment of GSM.[39] In conclusion, the

authors found few reports of adverse events, and when they did it was unclear whether the adverse effects were due to a lack of efficacy, progression of the disease, incorrect use of the device, or harm caused by the procedure.[39] Many of the studies supported the effectiveness of the lasers for the treatment of GSM, but most also had small numbers of participants, short follow-up, lack of randomization, no placebo controls, and sponsorship support from laser manufacturers.[39]

The VeLVET Trial, a randomized multicenter trial, enrolled 69 menopausal women with VVA to either fractionated CO_2 laser or vaginal conjugated estrogen cream.[40] Of the 62 women who completed the 6-month protocol, the primary outcome of vaginal dryness, itching, irritation, and dysuria scores did not differ between the 2 groups.[40] There was no difference between the 2 groups in vaginal maturation index findings or the Female Sexual Function Index outcome.[40] Furthermore, there was no statistical difference in participants' perception of symptoms, with 71.9% of participants receiving laser treatments and 82.8% of participants receiving estrogen rating their improvement as "better or much better."[40] There was also no statistical difference between the 2 groups in reports of no difference in their symptoms or dissatisfaction, and no women in the study reported worse symptoms after treatment.

A systematic review and meta-analysis of 8 studies of vaginal laser therapy in female breast cancer or gynecologic cancer survivors with sexual dysfunction was performed to evaluate efficacy.[41] There was a significant improvement in dyspareunia and vaginal dryness at the 1-month, 3-month, and 12-month laser treatments, but the evidence was of low quality.[41] Furthermore, the evidence for efficacy was rated "very low" for the symptoms of vaginal itching, burning, dysuria, and vaginal health index score (VHIS).[41]

Finally, a pilot study that evaluated sexual function of breast cancer survivors with GSM symptoms enrolled 64 participants to receive 3 CO_2 laser treatments.[42] Of the 64 participants, 59 women completed the study, and at the 4-week follow-up, all had an improvement in their sexual function scores measured by the Female Sexual Function Index and the Female Sexual Distress Scale Revised.[42] Thirty-nine women completed the 12-month follow-up and reported no adverse effects.[42]

ADDITIONAL TREATMENT OPTIONS

In addition to the therapies reviewed in this article, some women might benefit from a interprofessional approach. Health care providers may consider a consultation with a sex therapist or pelvic floor physical therapist. Sex therapists can help women who have developed avoidance behaviors or anxiety due to a history of dyspareunia.[31] They can assist a couple in their sexual communication and intimacy.[31] In addition, they may be helpful if the woman's partner has a sexual dysfunction that becomes more problematic when the woman is able to reengage in sexual activity.

Women adequately treated for GSM may continue to have dyspareunia if they have pelvic floor dysfunction. Pelvic floor physical therapists can evaluate and treat pelvic floor dysfunction and assist with strengthening and relaxation of the pelvic floor muscles, which may or may not include dilators. Dilators are available that can expand or are marketed as a set with progressively larger sizes. The therapeutic goal is to assist in mechanical distention of the vaginal tissue and relaxation of the pelvic muscles.[43] Dilators can also decrease anticipatory anxiety by reconditioning the mind-body connection.[43]

DISCUSSION

Despite the many treatment options and their reported safety, GSM is significantly undertreated. The reported barriers to education and treatment of menopausal symptoms by health care providers include confusing messages from the media, inconclusive data about the efficacy of hormone therapy, time restraints, and the FDA Black Box warning on vaginal estrogen products.[44] When knowledge and barriers were compared between primary care clinicians and gynecology clinicians, the latter were more likely to screen, educate, and treat women for VVA.[44] Of particular concern are the women with Medicare insurance who may only choose to see a primary care provider, as assessment for VVA is not part of the routine care in the Medicare annual wellness visit.[44]

Healthcare providers and women can discuss and use shared decision-making to select among treatment options, including both over-the-counter and prescription therapies. The choice is influenced by patient preference, insurance coverage, and cost. Compounded products should be used with caution because of the lack of randomized controlled trials and concerns about potency, quality, and purity.[9] Vaginal lasers are an option for women for whom over-the-counter options were ineffective, who do not want to choose a prescription option, or who prefer to not have the maintenance dosing of the prescriptions. Staying sexually active with or without a partner can promote vaginal health and prevent GSM by maintaining vascularity and elasticity of the tissues.[45] However, sexual activity does not treat GSM, and it is not advisable to recommend continued sexual activity to a woman who is experiencing pain.

Lastly, any woman treated for GSM should have a follow-up visit to discuss the treatment effectiveness. Common pitfalls of therapy may include discontinuation due to cost, application, concerns about safety, and misunderstanding of the longevity of the treatment. Treatment should be thought of as long-term therapy and should continue as long as the benefits outweigh the risks. Women should be counseled that GSM symptoms will return if therapy is discontinued. A systematic review of 9 articles found that with discontinuation of vaginal estrogen products there is a return of signs and symptoms within a few months.[46] Telemedicine is an option for follow-up if the woman's symptoms have improved or resolved. However, if the woman is continuing to have vulvovaginal discomfort or dyspareunia at a follow-up visit, a repeat pelvic examination should be performed to consider other diagnoses that could be concomitant with GSM. If there is concern about the diagnosis or management, a referral to a women's sexual medicine or menopause expert is an option. Both the North American Menopause Society and the International Society for the Study of Women's Sexual Health list experts on their websites. Table 4 lists resources for consultations or referrals.

Table 4. Resources for Consultations and Referrals	
Organization and Specialists	**Website**
International Society for the Study of Women's Sexual Health Provides a list of women's sexual health experts	https://isswsh.org
North American Menopause SocietyProvides a list of menopause experts	https://www.menopause.org
American Association of Sexuality Educators, Counselors, and TherapistsCertified sex therapists	https://AASECT.org
APTA Pelvic Health: An Academy of the American Physical Therapy AssociationPelvic floor physical therapists	https://aptapelvichealth.org/

CONCLUSION

GSM is a common condition that can adversely affect quality of life following menopause and is frequently undertreated. Following treatment, women report improved quality of life, comfort, and pain-free sexual play. These are attainable goals that health care providers can help women achieve. GSM diagnosis, treatment, and education can require a great deal of the health care provider's time, but it is also rewarding to make such an important impact on a woman's life.

CONFLICT OF INTEREST

The author has no conflicts of interest to disclose.

REFERENCES

1. Kingsberg SA, Krychman M, Graham S, Bernick B, Mirkin S. The Women's EMPOWER survey: identifying women's perceptions on vulvar and vaginal atrophy and its treatment. *J Sex Med*. 2017;14(3):413-424.
2. North American Menopause Society. The 2020 genitourinary syndrome of menopause position statement of the North American Menopause Society. *Menopause*. 2020;27(9):976-992.
3. North American Menopause Society. *Menopause Practice: A Clinician's Guide*. 6th ed. North American Menopause Society; 2019.
4. Qi W, Li H, Wang C, et al. The effect of pathophysiological changes in the vaginal milieu on the signs and symptoms of genitourinary syndrome of menopause (GSM). *Menopause*. 2020;28(1):102-108.
5. Simon JA, Goldstein I, Kim NN, et al. The role of androgens in the treatment of genitourinary syndrome of menopause (GSM): International Society for the Study of Women's Sexual Health (ISSWSH) expert consensus panel review. *Menopause*. 2018;25(7):837-847.
6. Nappi RE, Sanitago P, Particco M, Panay N. The REVIVE (Real Women's Views of Treatment Options for Menopausal Vaginal Changes) survey in Europe: country-specific comparisons of postmenopausal women's perceptions, experiences, and needs. *Maturitas*. 2016;91:81-90.
7. Simon JA, Kokot-Kierepa M, Goldstein J. Vaginal health in the United States: results from the Vaginal Health: Insights, Views, & Attitudes survey. *Menopause*. 2013;20(10):1043-1048.
8. Krychman M, Graham S, Bernick B, Mirkin S, Kingsberg SA. The Women's EMPOWER survey: women's knowledge and awareness of treatment options for vulvar and vaginal atrophy remains inadequate. *J Sex Med*. 2017;14(3):425-433.
9. Philips NA, Bachman GA. The genitourinary syndrome of menopause. *Menopause*. 2021;28(5):579-588.
10. Mastroianni J, Thomspon JA, Shifren JL, Zuckerman AL, Pereira K. Improving the identification of genitourinary syndrome of menopause through the utilization of the Day-to-Day Impact of Vaginal Aging questionnaire. *Menopause*. 2020;27(11):1295-1301.
11. Mercier J, Morin M, Reichetzer B, Lemieux MC, Khalifé S, Dumoulin C. Genitourinary syndrome of menopause symptom severity and impact outcome measures: are they reliable and correlated? *Menopause*. 2019;26(6):659-664.
12. Wilhite M. Chapter 59: Vaginal dryness. In: Rakel D, ed. *Integrative Medicine*. 4th ed. Elsevier; 2017:592-599.
13. Edwards D, Panay N. Treating vulvovaginal atrophy/genitourinary syndrome of menopause: how important is vaginal lubricant and moisturizer composition? *Climacteric*. 2016;19(2):151-161.
14. World Health Organization; United Nations Population Fund; Family Health International. *Use and Procurement of Additional Lubricants for Male and Female Condoms: WHO/UNFPA/FHI360 Advisory Note*. World Health Organization; 2012.
15. Ayehunie S, Wang YY, Landry T, Bogojevic S, Cone RA. Hyperosmolar vaginal lubricants markedly reduce epithelial barrier properties in a three-dimensional vaginal epithelium model. *Toxicol Rep*. 2017;5:134-140.
16. Lin TK, Zhong L, Santiago JL. Anti-inflammatory and skin barrier repair effects of topical application of some plant oils. *Int J Mol Sci*. 2017;19(1):70.
17. Kureck-Górecka A, Górecki M, Rzepecka-Stojko A, Balwierz R, Stojko J. Bee products in dermatology and skin care. *Molecules*. 2020;25(3)556.
18. Faubion SS, Larkin LC, Stuenkel CA, et al. Management of genitourinary syndrome of menopause in women with or at high risk for breast cancer: consensus recommendations from the North American Menopause Society and the International Society for the Study of Women's Sexual Health. *Menopause*. 2018;25(6):596-608.
19. Alvisi S, Gava G, Orsili I, et al. Vaginal health in menopausal women. *Medicina (Kaunas)*. 2019;55(10):615.
20. Mitchell CM, Srinivasan S, Zhan X, et al. Vaginal microbiota and genitourinary menopausal symptoms: a cross-sectional analysis. *Menopause*. 2017;24(10):1160-1166.
21. Muhleisen AL, Herbst-Kralovetz MM. Menopause and the vaginal microbiome. *Maturitas*. 2016;91:42-50.
22. Biehl C, Plotsker O, Mirkin S. A systematic review of efficacy and safety of vaginal estrogen products for the treatment of genitourinary syndrome of menopause. *Menopause*. 2019;26(4):431-453.
23. Derzko CM, Röhrich S, Panay N. Does age at the start of treatment for vaginal atrophy predict response to vaginal estrogen therapy? Post hoc analysis of data from a randomized clinical trial involving 205 women treated with 10 μg estradiol tablets. *Menopause*. 2020;28(2):113-118.
24. Crandall CJ, Diamant A, Santoro N. Safety of vaginal estrogens: a systematic review. *Menopause*. 2020;27(3):339-360.
25. Bhupathiraju SN, Grodstein F, Stampfer MJ, et al. Vaginal estrogen use and chronic disease risk in the Nurses' Health Study. *Menopause*. 2018;26(6):603-610.
26. Crandall CJ, Hovey KM, Andrews CA, et al. Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the Women's Health Initiative Observational Study. *Menopause*. 2017;25(1):11-20.
27. ACOG practice bulletin no. 126: Management of gynecologic issues in women with breast cancer. *Obstet Gyencol*. 2012;119(3):666-682.

28. Labrie F. Intracrinology and menopause: the science describing the cell-specific intracellular formation of estrogens and androgens from DHEA and their strictly local action and inactivation in peripheral tissues. *Menopause*. 2018;26(2):220-224.
29. Portman DL, Labrie F, Archer DF, et al; VVA Prasterone Group. Lack of effect of intravaginal dehydroepiandrosterone (DHEA, prasterone) on the endometrium in postmenopausal women. *Menopause*. 2015;22(12):1289-1295.
30. Buck ES, Lukas VA, Rubin RS. Effective prevention of recurrent UTIs with vaginal estrogen: pearls for a urological approach to genitourinary syndrome of menopause. *Urology*. 2021;151:31-36.
31. Crean-Tate KK, Faubion SS, Pederson H, Vencill JA, Batur P. Management of genitourinary syndrome of menopause in female cancer patients: a focus on vaginal hormonal therapy. *Am J Obstet Gynecol*. 2020;222(2):103-113.
32. Parish SJ, Simon JA, Davis SR, et al. International Society for the Study of Women's Sexual Health clinical practice guideline for the use of systemic testosterone for hypoactive sexual desire disorder in women. *J Sex Med*. 2021;18(5):849-867.
33. Bell RJ, Rizvi F, Islam RM, Davis SR. A systematic review of intravaginal testosterone for the treatment of vulvovaginal atrophy. *Menopause*. 2018;25(6):704-709.
34. Archer DF, Carr BR, Pinkerton JV, Taylor HS, Constantine GD. Effects of ospemifene on the female reproductive and urinary tracts: translation from preclinical models into clinical evidence. *Menopause*. 2015;22(7):786-796.
35. Simon JA, Lin VH, Radovich C, Bachman GA; Ospemifene Study Group. One-year long-term safety extension study of ospemifene for the treatment of vulvar and vaginal atrophy in postmenopausal women with a uterus. *Menopause*. 2013;20(4):418-427.
36. Goetsch MF, Lim JY, Caughey AB. A practical solution for dyspareunia in breast cancer survivors: a randomized controlled trial. *J Clin Oncol*. 2015;33(30):3394-3400.
37. Tadir Y, Gaspar A, Lev-Sagie A, et al. Light and energy based therapeutics for genitourinary syndrome of menopause: consensus and controversies. *Lasers Surg Med*. 2017;49(2):137-159.
38. Arunkalaivanan A, Kaur H, Onuma O. Laser therapy as a treatment modality for genitourinary syndrome of menopause: a critical appraisal of evidence. *Int Urogynecol J*. 2017;28(5):681-685.
39. Guo JZ, Souders C, McClelland L, et al. Vaginal laser treatment of genitourinary syndrome of menopause: does the evidence support the FDA safety communication? *Menopause*. 2020;27(10):1177-1184.
40. Paraiso MFR, Ferrando CA, Sokol ER, et al. A randomized clinical trial comparing vaginal laser therapy to vaginal estrogen therapy in women with genitourinary syndrome of menopause: the VeLVET trial. *Menopause*. 2020;27(1):50-56.
41. Athanasiou S, Pitsouni E, Douskos A, Salvatore S, Loutradis D, Grigoriadis T. Intravaginal energy-based devices and sexual health of female cancer survivors: a systematic review and meta-analysis. *Lasers Med Sci*. 2020;35(1):1-11.
42. Quick AM, Zvinovski F, Hudson C, et al. Patient-reported sexual function of breast cancer survivors with genitourinary syndrome of menopause after fractional CO_2 laser therapy. *Menopause*. 2021;28(6):642-649.
43. Krychman M, Liu MC, Meller D. Vaginal dilators: a guide for health care professionals. *Contemp Ob Gyn*. 2020;65(11).
44. Vesco KK, Beadle K, Stoneburner A, Bulkley J, Leo MC, Clark AL. Clinical knowledge, attitudes, and barriers to management of vulvovaginal atrophy: variations in primary care and gynecology. *Menopause*. 2019;26(3):265-272.
45. Krychman ML, Katz A. Breast cancer and sexuality: multi-modal treatment options. *J Sex Med*. 2012;9(1):5-13.
46. Weidlinger S, Schmutz C, Janka H, Gruetter C, Stute P. Sustainability of vaginal estrogens for genitourinary syndrome of menopause - a systematic review [published online March 12, 2021]. *Climacteric*. doi: 10.1080/13697137.2021.1891218.

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