

GSM (Genitourinary Syndrome of Menopause) – why should we Care?

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ABSTRACT

It is estimated that nearly 60% of women in menopause experience a condition called genitourinary syndrome of menopause (GSM) but the majority of these women do not bring up this concern with their health care provider. Studies also show that only 7% of healthcare providers ask women about this condition. This may be due to embarrassment or thinking this is a normal part of aging; both by patients and healthcare providers. This condition is progressive and may affect many aspects of a woman's health including dyspareunia and subsequent decreased libido, as well as an increased risk of vaginal and urinary tract infections, pelvic organ prolapse and incontinence. Women may stop exercising due to discomfort and increase their risk of obesity related health problems as well as emotional health issues. It may also cause women to avoid coming in for their gynecologic exams with the potential of a missed or delayed diagnosis of a serious medical condition. This article is intended to address the signs, symptoms and significant impact this condition can have for women as well as help healthcare providers learn to ask about this, diagnose it, understand the impact it may have on women's health and review various available treatment options.

Key words: Genitourinary syndrome of menopause; Vulvovaginal atrophy; Atrophic vaginitis

ABBREVIATIONS: FDA: U.S. Food and Drug Administration; GSM: Genitourinary syndrome of menopause; SERM: Selective estrogen receptor modulator; STI: Sexually transmitted infection; UTI: Urinary tract infection

INTRODUCTION

It has been called vulvovaginal atrophy or atrophic vaginitis. The newer term, genitourinary syndrome of menopause or GSM was introduced by the International Society for the Study of Women's Sexual Health (ISSWSH) and the North American Menopause Society (NAMS) in 2014. It is defined as "a collection of signs and symptoms associated with estrogen deficiency that can involve changes to the labia, introitus, vagina, clitoris, bladder and urethra" [1].

What GSM means clinically is the tissue of the vagina and vulva become thin and dry and this often leads to a sensation of burning, itching and often pain and dryness during sex. Sometimes it can get so bad that women are unable to have sex (penile/vaginal intercourse) which of course can contribute to low sex drive.

(Disclaimer - this article is primarily addressed to heterosexual women but this condition can affect women regardless of sexual preference or practices).

GSM is caused by decreased estrogen; estrogen helps the tissue stay lubricated and elastic. As women age and enter menopause and have decreased estrogen, the vaginal and vulvar tissue starts to thin and weaken and have less elasticity and lubrication. Even the length of the vagina itself can shorten and the entrance to the vagina (introitus) narrows, often causing pain or difficulty with intercourse.

This can also happen before menopause for other reasons such as when a woman is breastfeeding, had surgery, radiation or chemotherapy affecting her ovaries or due to other medical conditions or medications which may cause low estrogen.

It may sound like GSM just causes vaginal dryness and discomfort, but it can actually affect many aspects of a woman's health; not only physically but psychologically and sexually.

One of the things I am seeing frequently in my gynecologic practice is women who have entered menopause and may have made it past

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the hot flashes and night sweats but are now noticing more dryness and pain with intercourse. When we talk about it, some of my patients admit to avoiding any intimate contact with her partner as she worries that this may lead to sex. Eventually he often starts to feel rejected and the relationship itself suffers.

Unfortunately, even medical providers with training in women’s health and gynecology often don’t get much education on the vulva and usually even less on sexual health. Although we may ask women as they age about hot flashes or night sweats we are often guilty of not asking important questions such as “Are you noticing any vaginal dryness or trouble lubricating during sex?” or inquiring if these changes are affecting a woman’s sexual relationship. One study of over 3000 women with symptoms of GSM showed that only 7% of providers asked about this [2].

It is estimated that although nearly 60% of women in menopause experience GSM, the majority of these women don’t discuss this concern with their health care provider [3]. This may be due to embarrassment, cultural reasons, or even thinking this is a normal part of aging and that nothing that can be done. Even we, as providers, may either overlook these changes or possibly also think they are a normal part of aging.

In addition to pain with sex which in turn affects a woman’s sex drive, GSM can cause discomfort to the point where a woman may stop being as physically active, affecting her physical and emotional health. It can contribute to more frequent vaginal and urinary tract infections due to an increase in vaginal pH and changes in the vaginal microflora. The underlying connective tissue also thins and is more susceptible to inflammation or infection. Pelvic organ prolapse with urinary retention and/or urinary incontinence may also occur [4].

A diagnosis of GSM should include a good history; ask about onset, duration, prior treatment, potential vulvar irritants (Table 1), other medical conditions or medications, previous surgery including prior cancer or cancer treatments. Vaginal infections should be ruled out and sexually transmitted infections (STIs) should also be considered.

Clinically, the external genitalia may appear pale and thin although with inflammation, sometimes the tissue can be erythematous with excoriations. In severe cases, the labia minora may be essentially

nonexistent; having fused to the labia majora. The introitus may narrow and a urethral caruncle is often seen. There is loss of vaginal rugae and decreased elasticity of the vagina which can make distention of the vagina with a speculum, very painful for many women. The cervix may sometimes be difficult to visualize; not only due to pain with opening of the speculum, but it may become flush with the vaginal wall and the cervical os itself may become stenotic.

Nitrazine paper applied to the introitus can help confirm a diagnosis of vaginal atrophy. A normal well-estrogenized vagina will have a pH ranging from 3.5 to 5.0. In the absence of infection (e.g.; bacterial vaginosis) or semen from recent intercourse, a pH>5.5 or higher is seen with vaginal atrophy [5].

Biopsies are recommended to confirm diagnosis of any suspected vulvar disorder or any lesion of the vulva that does not respond to treatment.

There are a variety of different treatment options for GSM. The choice of treatment may depend on the severity of symptoms and should include a discussion of risks/benefits/effectiveness, address a patient’s preference as well as review any concerns she may have regarding hormonal treatment. I begin by discussing non-hormonal options (Table 2) such as vaginal lubricants and moisturizers with my patients, but also give them information regarding vaginal estrogen and other prescription therapies.

Many women find that using lubricants with intercourse helps make sex more comfortable. The brands commonly found over the counter are usually water-based lubricants. Many menopausal and perimenopausal women find that these absorb fairly quickly and don’t provide enough comfort. Silicone-based lubricants tend to last longer and provide more lubrication. Coconut, vitamin E, avocado or olive oils work well but any oil based lubricant should not be used with condoms as they weaken latex and some women find they may be more prone to vaginal infections with these.

There are also non-hormonal products called vaginal moisturizers. As women age, most of us notice that our skin gets thinner and dryer and needs more moisture. Such changes also happen to the

Table 1: Vulvar Hygiene.

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| <p>Things to avoid: Tight fitting clothing Synthetic underwear Scented soaps/body wash/bubble bath Scented detergents Laundry softener/dryer sheets Baby wipes/flushable wipes Feminine hygiene sprays/douches/wipes Dyed/colored toilet paper Constant use of pantliners Washcloths/scrubbies/loofahs</p> <p>Instead Try: Loose fitting clothing Cotton underwear in daytime No underwear at night Fragrance-free pH neutral soaps/detergents Tub bath without additives and at comfortable temperature Use fingertips for gentle vulvar washing ideally with water only Try sport water bottle/perineal bottle/bidet Gently pat vulva dry</p> |
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Table 2: Non-Hormonal Options For GSM.

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| <p>Lubricants -water based KY Astroglide Good Clean Love Sylk Pjur YES</p> <p>-silicone based Uber lube Eros Pink ID Millenium Wet Platinum Pjurmed Premium Glide</p> <p>-oil based Elegance Women’s Lubricants Oils (olive, coconut, avocado, Vit E, Crisco)</p> <p>Moisturizers Replens RepHresh Luvena Lubrigyn Sylk Natural Intimate Moisturizer Yes Vaginal Moisturizer Femallay Moisturizing Suppositories</p> |
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vagina and vulva; just like we may use a daily moisturizer in other areas of the body, women can also use a vaginal moisturizer either daily or two to three times per week. Many of these products contain ingredients like those found in facial products such as hyaluronic acid which helps tissue retain moisture and stay lubricated [6].

There are a variety of prescription treatments available for GSM (Table 3). Low-dose vaginal estrogen is the gold standard treatment for GSM but women (and their health care providers) can still be reluctant to consider this. It doesn't help that the product information has to list possible risks including cardiovascular disease, breast cancer and dementia. NAMs (the North American Menopause Society) has suggested this "black box warning" be removed from vaginal estrogen products as the amount of hormone absorbed into the body when used vaginally, is very low and does not have the same potential health risks as systemic estrogen [7].

Table 3: Prescription Treatments For Gsm.

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| Vaginal Estrogen Ring | |
| -Estring (7.5 mcg estradiol released qd) | Inserted by pt or clinician every 90 days |
| Vaginal Estrogen Insert | |
| -Vagifem/Yuvafem (10 mcg estradiol) | Insert 1 tablet vaginally qhs for 2 weeks, then twice weekly |
| -Imvexxy (4 mcg and 10 mcg estradiol) | Insert vaginally qhs for 2 weeks, then twice weekly |
| Vaginal Estrogen Cream | |
| -Estrace (100 mcg estradiol per gram) | Insert 0.5 to 1 gm vaginally qhs for 2 weeks, then twice a week |
| -Premarin (0.625 mg conjugated estrogen per gram) | Insert 0.5 to 1 gm vaginally qhs for 2 weeks, then twice a week |
| Ospemifene (Osphena) - SERM | |
| | 60 mg daily oral tablet |
| Prasterone (Intrarosa) - DHEA | |
| | 6.5 mg nightly intravaginal suppository |

Even women taking systemic estrogen for vasomotor symptoms of menopause may still experience GSM and benefit from local treatment. If a woman's primary concern is GSM, local, rather than systemic estrogen is recommended as it has been shown to be more effective for this and have lower risks. [8] Vaginal estrogen has also been shown to be more effective in the treatment of recurrent UTIs [9] and improvement of incontinence while systemic estrogen may actually worsen incontinence [10].

Vaginal estrogen is available in various prescription forms including creams, intravaginal tablets or inserts and a vaginal ring. In general it is recommended to treat daily for the first two weeks, then decrease administration to twice weekly. It can often take four to six weeks to notice an improvement and sometimes longer.

Although the vaginal estrogen inserts or ring have been shown to have the least systemic absorption [11], I find for my patients with significant atrophy, these forms of vaginal estrogen may initially not be adequate. I often start with vaginal estrogen cream. Even though the systemic absorption may be a bit higher, it is still quite low and the cream may be applied to the vulva as well. I prefer using the more bioidentical estradiol cream (Estrace) but find that the amount recommended by the manufacturer is usually too much (2 gm-4 gm) and may have higher systemic absorption. I start with 0.5 gm to 1 gm in most of my patients; as in systemic hormone therapy, the lowest effective dose is recommended. Some women may need to start with slightly higher doses, then decrease the amount as the vulvovaginal tissue health improves or transition to the vaginal

inserts or ring. (Somewhat confusingly, there is also a vaginal ring called Femring that provides systemic estrogen to help treat hot flashes and also works locally to treat GSM, but the ring used for GSM (Estring) has very minimal absorption.

Systemic estrogen can increase the thickness of a woman's uterine lining (the endometrium) and potentially lead to uterine cancer or a precancerous thickening (hyperplasia). If a woman is taking systemic estrogen (and still has her uterus), she also needs to take progesterone to help prevent the uterine lining from getting too thick. But when a woman is using only local vaginal estrogen, she does not also need to take progesterone because the amount of estrogen absorbed into the body is extremely low and doesn't appear to increase the risk of uterine cancer (although endometrial safety has not been studied beyond twelve months of use). NAMS has suggested removing the boxed warning on vaginal estrogen but caution that women are still advised to call their provider if they do have any bleeding as this can potentially be a warning sign of uterine cancer or hyperplasia.

Even women with a breast cancer history or other potential contraindications to systemic estrogen may consider using vaginal estrogen. It is still recommended to try non-hormonal options first but for many women this is just not enough. In 2016, the American College of Obstetricians and Gynecologists issued an opinion stating that vaginal estrogen could be considered for women currently undergoing treatment of breast cancer or with a personal history of breast cancer who are unresponsive to nonhormonal treatment and that data does not show an increased risk of cancer recurrence [12]. Although some women are understandably still worried about the potential risk, other women may feel that this is a quality of life issue for them and are relieved to know that this is a treatment option. If vaginal estrogen is considered, it is often advised to consider the vaginal estradiol inserts or the low-dose estradiol ring due to the fixed amount of medication and the lack of significant systemic absorption. The vaginal inserts called Imvexxy come in a very low dose form of 4 mcg which may be preferable if there is concern about systemic absorption. It is usually advised to discuss this first with a woman's oncologist or primary care provider.

Women on aromatase inhibitors for breast cancer treatment are often advised not to be on vaginal estrogen although a 2019 meta-analysis of eight studies showed no increase in serum estradiol levels after eight weeks of local hormone treatment in women on aromatase inhibitors which appears reassuring [13].

A newer product called prasterone was FDA approved in 11/16. It is a nightly vaginal insert which is plant derived and appears very effective in the treatment of vaginal dryness and painful intercourse. Through intracellular steroidogenesis, it is converted into estrogen and testosterone in the cells of the vagina. It appears to be very low risk in terms of low to no absorption of hormones into the bloodstream and may eventually be found to be a good option for women who have contraindications to systemic estrogen, but the FDA currently still requires the warning that it has not been studied in women with breast cancer and, as with vaginal estrogen preparations, should not be used in women with undiagnosed abnormal genital bleeding [14].

Ospemifene is an oral, non-hormonal method to treat moderate to severe dyspareunia associated with vulvovaginal atrophy. It is a selective estrogen receptor modulator (SERM) and is taken daily. Not an actual hormone, it is an estrogen agonist/antagonist, acting

on estrogen receptors in the vagina to treat vaginal dryness and subsequent pain with intercourse. It may be helpful in women who are either unwilling or unable to use vaginal estrogen. Side effects include hot flashes/night sweats and it may increase the risk for thromboembolic complications. It may theoretically increase the risk of uterine cancer as well although, as with the vaginal estrogen studies, it appears to be safe in studies up to one year of use. It appears to have antiestrogenic effects on the breast but is not approved for women with breast cancer [15,16].

Other non-hormonal options for GSM now include physical procedures like laser therapy; reported to help vaginal dryness by causing microabrasions in the vaginal tissue stimulating neovascularization and promoting increased collagen production. While these procedures may be promising, they are currently not FDA approved, are costly and usually require more than one treatment with possible need for retreatment in the future.

In addition to dyspareunia, vaginal and bladder infections, prolapse and incontinence, women with GSM often notice significant pain with pelvic exams and pap smears. Insertion of the speculum can be quite painful; especially if the vaginal introitus has narrowed significantly. The actual opening of the speculum may be even more painful; especially if a woman is no longer sexually active. The vaginal tissue is thin and loses elasticity. It is important to understand these changes and do the best we can to help a woman be more comfortable so she does not avoid coming to see us.

Helpful techniques include using a lubricated narrow Pedersen or a pediatric speculum if necessary. I sometimes will apply topical lidocaine jelly to the introitus and/or speculum first. I also may use only one gloved, lubricated finger for the pelvic exam. If a woman is very anxious or visibly contracting her pelvic floor muscles, I will ask her to squeeze as hard as she can around my gloved finger, then ask her to breathe and relax as I gently insert my finger a bit more. I always ask my patient to let me know if I am causing her pain and that I will stop at any time if she tells me to. This may help her relax allowing a more thorough exam as well as allow a woman some control over an often uncomfortable and intimidating procedure.

In a woman with very severe atrophy who is unable to tolerate any exam or any attempt at penile insertion, it is often helpful to try treating with vaginal estrogen for four to six weeks as well as have her work with a vaginal dilator to assist in gently stretching the tissue. There are many companies that sell graduated vaginal dilators. There is also the Milli which is a patient controlled dilator that expands one millimeter at a time (Table 4). It can be helpful to refer a patient to a good pelvic floor physical therapist if she would like additional instruction and assistance with dilator use and relaxation.

My motivation for writing this article was to let women and their health care providers be more familiar with GSM and the

Table 4: Dilator Resources.

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| http://www.vaginismus.com http://www.soulsource.com http://middlesexmd.com http://www.coopersurgical.com http://www.cmtmedical.com Other dilator options: Milli (a unique expanding dilator) http://www.millimedical.com FeMani Vibrating Massage Wand http://Femaniwellness.com |
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treatment options available. This is a progressive disease and unfortunately isn't often addressed by us or our patients until it becomes severe. We, as medical providers, need to be aware that this is an issue for many women and understand the impact it may have on a woman's overall health as well as her sexual health and quality of life. We need to look for it, ask about it and be familiar with options that can help. It can greatly relieve a woman to know that although these can be normal changes associated with aging, she does not have to live with them or be embarrassed to ask for treatment options. (Table 5 includes a list of retail websites where women may purchase lubricant/moisturizers, vibrators). I hope this article will help us as providers, realize the extent that this condition can affect a woman's life and empower us to know we can offer her some relief.

Table 5: Retail Websites.

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| www.middlesex.md www.goodvibes.com www.evesgarden.com www.adamandeve.com www.babeland.com www.target.com (sexual health) www.walgreens.com (sexual lubricants) www.cvs.com (sexual health) www.sexualityresources.com |
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Conflicts of Interest

No conflicts of interest exist

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 15. <https://hcp.osphena.com/>
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