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REVIEW ARTICLE

Deconstructing the genitourinary syndrome of menopause

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Abstract The concept of genitourinary syndrome of menopause (GSM) was recently introduced and has been gaining widespread use. While some justifications for its introduction are straightforward, others may be questionable. Numerous unspecific symptoms and signs were included in the definition of the syndrome, but the minimum number required for diagnosis was not established. While the GSM definition is designed to facilitate identifying vulvovaginal and urinary estrogen-deprivation-associated symptoms and signs, several concerns have evolved: (1) the syndrome may result in the underdiagnosis of vulvar and urinary pathology; and (2) serious conditions (e.g., high-grade squamous intraepithelial lesions of the vulva or vulvar intraepithelial neoplasia, differentiated type) may be missed while others may not receive appropriate treatment (e.g., lichen sclerosus, overactive bladder). In addition, the transformation of urogenital symptoms and signs into a syndrome may create an iatrogenization of menopause, which, consequently, can lead to demand for (and offer of) a panacea of treatments. This can be detrimental to the care of women who require focused therapy rather than global treatment addressing a variety of genitourinary conditions, not all of which even require any form of intervention. Women's needs may be better served by having a more precise urogenital diagnosis.

Keywords Genitourinary syndrome of menopause · Vulvovaginal atrophy · Urogenital symptoms · Vulvar conditions · Vulvar lichen

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Aging and menopause-related urogenital changes

As life expectancy increases, women spend more years in menopause. In Western countries, with the advances of dietary quality, hygienic measures, vaccinations, medical care, reduced parity, and better life conditions, women can expect to live >30 years in menopause. In parallel, people invest and demand more in terms of well-being and decreasing the effects of aging. All organ systems are affected by aging, and the urogenital tract is no exception. It endures sudden and dramatic changes due to the cessation of the effect of ovarian estrogens. Most studies on the effect of estrogen deprivation (including causes other than natural menopause) have addressed the vagina; few address the vulva [1].

In the vagina of a menopausal patient, mucosal thinning and loss of vaginal rugae frequently occur. Findings include reduced vaginal secretions, shortened vaginal length and width, elevated vaginal pH, and more frequent colonization by enteric bacteria [2–4]. Vulvar changes associated with menopause include thinning of the skin and vestibular mucosa, decreased subcutaneous fat, laxity of the introitus, and diminished sensitivity. Contrary to the common atrophy associated with lichenoid dermatoses, menopausal atrophy

reduces the width of the labia minora, whereas its length is conserved [1, 2].

Vulvar dermatoses are more common in postmenopausal women [5]. While some patients are highly symptomatic and easily diagnosed correctly, at least 15% of cases of lichen sclerosus are asymptomatic and unrecognized [5]. Vulvar changes may thus be attributed to natural menopause. Distinguishing such changes from those associated with vulvar dermatoses can be a challenge [1], especially for clinicians less experienced in vulvar diseases.

The urinary tract can also undergo serious changes in the postmenopausal period. Estrogen deprivation leads to changes in periurethral tissues (decrease in collagen) and urethral mucosa (atrophy). These changes frequently lead to urinary frequency, nocturia, urinary incontinence, and an increase in urinary tract infections (sometimes globally referred to as urethral syndrome). The frequency of these symptoms is probably overlooked [6, 7]. As a consequence, the incidence of urinary incontinence, especially urge incontinence, increases dramatically with menopause [8, 9].

Urogenital signs/symptoms and the genesis of the genitourinary syndrome of menopause

The genitourinary syndrome of menopause (GSM) is a term proposed by the International Society for the Study of Women's Sexual Health and the North American Menopause Society to include all genital and urinary signs and symptoms possibly associated with menopause [10] with the intention of facilitating communication between clinicians and patients. It was believed to be a more medically accurate, all-encompassing, publicly acceptable, and a less embarrassing term than atrophic vaginitis or vulvovaginal atrophy [10, 11]. Four concepts were used to support this new designation:

1. Vaginitis implies infection/inflammation
2. Urinary signs and symptoms are usually overlooked
3. Atrophy has negative connotations
4. Vagina is not generally a well-accepted term by women and the media

In a recent survey among Portuguese gynecologists, the majority agreed with the first two points and disagreed with the latter two [12].

It is generally agreed that the term vaginitis may not always be adequate, as inflammation is not a systematic finding. In some cases, only a paucity of cells is encountered. Sometimes, an excess of leukocytes and increased numbers of parabasal cells are identified on wet-mount microscopy, Gram staining, or cytology. However, these findings are not specific of vaginal atrophy, as it also can be found in multiple other diagnoses, including aerobic vaginitis, desquamative inflammatory vaginitis, and lichen planus [13] . All such symptoms may be incorrectly lumped together and called atrophic vaginitis when no infection or inflammation is present [1, 14]. However, these arguments do not preclude the use of the term vaginal atrophy—a term that is easily understood.

Urinary symptoms are probably overlooked in many cases, as women are often embarrassed or ashamed to discuss them or accept them as a natural consequence of aging; or the busy clinician fails to address them. This is, indeed, a valid argument. However, the same could—or should—be used for vulvar symptoms. Whereas the GSM addresses urinary symptoms, it ignores vulvar issues, as is discussed herein.

The term atrophy was considered inappropriate when discussing the vulva for the GMS based on the *Merriam-Webster Dictionary* [15] definition: "a decrease in size or wasting away of a body part or tissue; wasting away or progressive decline, as from disuse." Simplistically, atrophy was considered inappropriate in this context, as the condition does not derive from disuse. However, other dictionaries, such as the *Medical Dictionary of Health Terms*, define atrophy as "a wasting away of an organ or tissue due to undernourishment, disease, or aging" [16]. Atrophy is also considered to carry a negative connotation. However, some women may also react negatively to being told they have a "syndrome," particularly the "syndrome of menopause," which may be perceived as pejorative. Now, not only are they menopausal, they also have a syndrome rather than an age-related change.

It is preposterous that in the twenty-first century a community of health professionals uses the argument that "vagina" is not a well-accepted term by women and social media. This view is a myopic interpretation of reality. Mass and social media have a relevant role in educating the general population on medical and healthcare issues. The medical community should be committed to diffusing accurate and adequate information about the human body, and anatomical terms should be applied in this effort—including correct names of genitalia [11]. It is important for women to understand female anatomy. No evidence or data were presented in the final GSM document supporting the opinion that "vagina" is not a well-accepted term. One can accept that in communities that are more conservative, the use of this word can be embarrassing or even offensive. What must be shown to such societies is that these are normal, accepted medical terms for organs that are in no way disrespectful to women.

Classifying the genitourinary changes of menopause as a syndrome is questionable. As a principle of coherency, one can look at its definition in the same *Merriam-Webster Dictionary* [15]: "a group of signs and symptoms that occur together and characterize a particular abnormality or condition." Given that genitourinary changes encountered in menopausal women are almost universal [1, 17], this should not be considered a "particular abnormality or condition."

This newly defined "syndrome" is intended by the GSM authors to be acceptable to all clinicians and the more conservative elements of the population [18]. However, only a minority of relevant societies was represented during GMS composition. For instance, great emphasis was given to urinary tract symptoms, but no urologic society had a relevant place in the discussion. Furthermore, scientific societies devoted to vulvovaginal diseases did not participate in the GSM creation.

GSM in practical terms

A broad set (19) of common and nonspecific symptoms and signs are covered by GSM. Sexual (dys)function is overrepresented in the panel of symptoms: decreased arousal and problems with orgasm or desire are symptoms of sexual dysfunction in all age groups and are not specific to menopause. Likewise, signs are also unspecific for menopausal changes, especially concerning the vulva. At least five of the 11 signs listed as part of the GSM are specific, common features of lichen sclerosus [5, 19]. pH and wet mount are mentioned as possible supportive findings of the diagnosis of the GSM. However, these tools most often lead directly to specific pathology that requires attention and intervention, such as severe atrophy, bacterial vaginosis, and aerobic vaginitis [14, 20]. Also, the definition of GSM does not indicate how many symptoms and/or signs must be present to attain a diagnosis [10] and is too vague to be clinically useful. The authors clearly state that symptoms must be bothersome and must not be confused with another diagnosis. However, almost all menopausal women with any genitourinary symptoms fit into the GSM compendium. Will the untrained clinician easily distinguish color changes and pallor, labia minora reabsorption, and loss of elasticity associated with lichen sclerosus from that associated with menopause? How many women will find the term GSM on the Internet and find an easy explanation for their symptoms? As a consequence, many women will not be evaluated by a health care provider with enough expertise to diagnose vulvar dermatosis or bladder pain syndrome. Adding to the complexity of the question, some women will have symptoms derived from hypoestrogenism as well as from other conditions associated with aging.

Risks of general use of the GSM: each specific diagnosis should be separately addressed

Since the GSM may lead to iatrogenization of menopause (rather than viewing it as a natural, physiological, age-related situation), there would be an increase in demand for treatment, and effective and safe treatment options are available. Estrogen replacement (topical or systemic) reverts vaginal atrophy but does not significantly affect other vulvar conditions and urinary symptoms that are not associated with atrophy [21]. Hence, the inclusion of urinary symptoms in the new syndrome may not lead to better management of these conditions. Instead, rather than receiving a specific diagnosis (overactive bladder, stress or urge urinary incontinence, bladder pain syndrome, etc.) and adequate, tailored treatment, women may receive a general diagnosis and potentially inappropriate treatments.

This new syndrome can prompt a demand for new treatments [22, 23]. Therapies like selective estrogen receptor modulators (alone or combined with estrogens) or repeated vaginal laser treatments will eventually be used at the expense of established and safe treatment options [24]. There are as yet few absolute contraindications for estrogen use, especially if used topically [25]. Even in hormone-dependent breast cancer patients, where estrogen use is strongly contraindicated, there is now reassuring data that ultralow-dose topical estriol can be used safely [26], with excellent results in improving vaginal microflora [27], quality of sex life, and urinary function [28]. Furthermore, vaginal atrophy may benefit from other treatments [20, 22, 29].

Likewise, failure to properly diagnose vulvar diseases such as lichen sclerosus, lichen planus, lichen simplex chronicus, high-grade squamous intraepithelial lesions of the vulva, vulvar intraepithelial neoplasia, differentiated type, vulvar cancer, and vulvodynia may lead to denial or postponement of appropriate treatment. Therefore, appropriate assessment of the genitals (including the vulva) and lower urinary tract is mandatory for providing the most appropriate individualized and ethical treatment.

In conclusion, the GSM seems to add little in terms of female well-being. Rather than contributing to the acceptance of menopause, it is transformed into a disease—and at the expense of overlooking true disease.

Practice points

- Although the GSM aims at facilitating the diagnosis and management of vulvovaginal and urinary symptoms associated with menopause, it may be too soon to adopt it in its present form.
- Vulvovaginal and urinary symptoms associated with menopause do not belong in the definition of a syndrome.
- An individualized approach to women with vulvar, vaginal, or urinary symptoms is needed; symptoms can only be attributed to hypoestrogenism after exclusion of other specific causes.
- The GSM can lead to treatment standardization and overuse, which may be inappropriate for some women.

Research agenda

- Appropriate tools and questionnaires are needed to assess each component (lower genital tract, lower urinary tract) in the GSM.
- A number of criteria (symptoms and/or signs) that define GSM must be established.
- The interaction between comorbid conditions that may be menopause/age related and may aggravate components of the GSM (e.g., pelvic floor disorders) must be properly established.
- A consensus panel comprising a large number and diversity of societies concerned with women's well-being should be carried out.

Compliance with ethical standards

Competing interest The authors have no conflicts of interest.

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