New Terminology—Old Problem!

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- Discuss the reason behind the development of this new terminology
- Review the Old Terminology for which Genitourinary Syndrome of Menopause (GSM) is replacing
- Outline a Primary Care physician (PCP) approach to GSM
- Assist the PCP in recognizing the clinical presentation of GSM
- Explore the step wise treatment options for GSM
- Empower the PCP to feel comfortable with initiating treatment for GSM
Taboo Words? or Are They?

Original Terms:

Vulvovaginal Atrophy (VVA)
Atrophic Vaginitis

- **So Why The Need to Change?**
  - Vulvovaginal Atrophy is a term which describes a clinical appearance but does not include symptoms.
  - General public uncomfortable with using word “vagina” or “vaginal”

Who Changed It?...
SPECIAL FEATURE

Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women’s Sexual Health and The North American Menopause Society

David J. Portman, MD,1 Margery L.S. Gass, MD, NCMP2 on behalf of the Vulvovaginal Atrophy Terminology Consensus Conference Panel

Abstract

Background: In 2012, the Board of Directors of the International Society for the Study of Women’s Sexual Health (ISSWSH) and the Board of Trustees of The North American Menopause Society (NAMS) acknowledged the need to review current terminology associated with genitourinary tract symptoms related to menopause.

Method: The 2 societies cosponsored a terminology consensus conference, which was held in May 2013.

Results and Conclusions: Members of the consensus conference agreed that the term genitourinary syndrome of menopause (GSM) is a medically more accurate, all-encompassing, and publicly acceptable term than vulvovaginal atrophy. GSM is defined as a constellation of symptoms and signs associated with a decrease in estrogen and other estrogens involving changes to the labia majora/minora, clitoris, vestibule/intimae, vagina, urethra and bladder. The syndrome may include but is not limited to genital symptoms of dryness, burning, and irritation; sexual symptoms of lack of lubrication, discomfort or pain, and impaired function; and urinary symptoms of urgency, dysuria and recurrent urinary tract infections. Women may present with some or all of the signs and symptoms, which must be bothersome and should not be better accounted for by another diagnosis. This term was presented and discussed at the annual meeting of each society. The respective Boards of NAMS and ISSWSH formally endorsed the new terminology—genitourinary syndrome of menopause (GSM)—in 2014.

Key Words: Atrophic vaginitis — Genitourinary syndrome of menopause — Menopause, urinary urgency — Vulvovaginal atrophy — Women’s sexual health.

BACKGROUND

The terms vulvovaginal atrophy (VVA) and atrophic vaginitis have been considered by many to be inadequate and inaccurate for describing the range of menopausal symptoms associated with physical changes of the vulva, vagina, and lower urinary tract associated with estrogen deficiency. VVA describes the appearance of the postmenopausal vulva and vagina without specifying the presence of associated symptoms. Atrophic vaginitis connotes a state of inflammation or infection, neither of which is a primary component of VVA. Furthermore, the word atrophy, as used in both terms, has negative connotations for middle women, and the word vagina is not a generally accepted term for public discourse or for the media. Neither term includes reference to the lower urinary tract. A growing need for more accurate and inclusive terminology led to planning of the consensus conference.

Successful precedents for changing medical terminology are known. For example, the term fibrocystic breast syndrome...
TABLE 1. Components used to develop new terminology

<table>
<thead>
<tr>
<th>Anatomy</th>
<th>Descriptors</th>
<th>Problem</th>
<th>Life Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vagina</td>
<td>Vulvovaginal</td>
<td>Atrophy</td>
<td>Midlife</td>
</tr>
<tr>
<td>Vulva</td>
<td>Genital</td>
<td>Alterations</td>
<td>Aging</td>
</tr>
<tr>
<td>Labia</td>
<td>Gynecologic</td>
<td>Changes</td>
<td>Menopause</td>
</tr>
<tr>
<td>Vestibule</td>
<td>Reproductive</td>
<td>Condition</td>
<td>Perimenopause</td>
</tr>
<tr>
<td>Urethra</td>
<td>Sexual</td>
<td>Disease</td>
<td>Postmenopause</td>
</tr>
<tr>
<td>Bladder</td>
<td>Urogenital</td>
<td>Disorder</td>
<td></td>
</tr>
<tr>
<td>Genitourinary</td>
<td>Urinary</td>
<td>Deficiency</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Urologic</td>
<td>Dysfunction</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Syndrome</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vaginitis</td>
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</tr>
</tbody>
</table>

Terms in bold are the words selected by the panel to develop new nomenclature.

urogenital sinus tissue, as are the vulvar vestibule and the upper vagina. Androgen receptors are also widely distributed in the vestibule and within its glands, making urogenital tissues responsive not only to estrogen but to androgens as well. Urinary frequency and urgency are common midlife complaints: incontinence occurs in 15% to 35% of women

OVERVIEW OF ARTICLE

Conclusion of Consensus Conference
- Final two proposed new terms where presented for an open discussion at 2 scientific meetings:
  - Annual Meeting of NAMS – October 2013
  - Annual Meeting of ISSWSH – February 2014

Conclusion of Scientific Meetings
- New Terminology Approved:

Genitourinary Syndrome Of Menopause
GENITOURINARY SYNDROME OF MENOPAUSE
(Formerly Known As Vulvovaginal Atrophy & Atrophic Vaginitis)

Well, What Is It?

- "Chronic, progressive vulvovaginal, sexual, and lower urinary tract condition..."
- Involves multiple symptoms
- Due to hypoestrogenism secondary to the menopausal state
- > 50% of postmenopausal women affected

<table>
<thead>
<tr>
<th>External genital</th>
<th>Urological</th>
<th>Sexual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs and symptoms</td>
<td>Complications</td>
<td>Signs and symptoms</td>
</tr>
<tr>
<td>Vaginal atrophy and pressure</td>
<td>Labial atrophy</td>
<td>Frequency</td>
</tr>
<tr>
<td>Dryness</td>
<td>Vulvar atrophy and lesions</td>
<td>Urgency</td>
</tr>
<tr>
<td>Irritation/burning</td>
<td>Atrophy of Bartholin glands</td>
<td>Polyuria</td>
</tr>
<tr>
<td>Tenderness</td>
<td>Intravaginal erosion of urethra</td>
<td>Urosepsis</td>
</tr>
<tr>
<td>Painful sexual intercourse</td>
<td>Alkaline pH (5-7)</td>
<td>Dysuria</td>
</tr>
<tr>
<td>Discomfort during intercourse</td>
<td>Reduced vaginal and cervical secretions</td>
<td>Hematuria</td>
</tr>
<tr>
<td>Suprapubic pain</td>
<td>Pelvic organ prolapse</td>
<td>Recurrent urinary tract infection</td>
</tr>
<tr>
<td>Leukorrhea</td>
<td>Vaginal vault prolapse</td>
<td></td>
</tr>
<tr>
<td>Erythema</td>
<td>Vaginal atrophy and shortening</td>
<td></td>
</tr>
<tr>
<td>Erythema</td>
<td>Internal elements</td>
<td></td>
</tr>
<tr>
<td>thinning of pubic hair</td>
<td>Thinning of vaginal epithelium</td>
<td></td>
</tr>
<tr>
<td>Thinning of pubic hair</td>
<td>Patellar inoculation membrane</td>
<td></td>
</tr>
<tr>
<td>Thinning of pubic hair</td>
<td>Fusion of labia minora</td>
<td></td>
</tr>
<tr>
<td>Patellar inoculation membrane</td>
<td>Labial atrophy</td>
<td></td>
</tr>
<tr>
<td>Fusion of labia minora</td>
<td>Laxity of labia minora</td>
<td></td>
</tr>
<tr>
<td>Labial atrophy</td>
<td>Labial atrophy</td>
<td></td>
</tr>
</tbody>
</table>

Clinical Manifestations of GSM

External Genitalia

Urological

Sexual
Embryonic Development:

Urogenital sinus

Mullerian duct = uterus and upper 4/5 of vagina once fused

Sinovaginal node (Muller tubercle)

Vaginal vestibule, and lower 1/5 of the vagina, urinary bladder, trigone, and urethra formed by all the above.

PATHOPHYSIOLOGY

Urinary symptoms
✓ Pain passing urine
✓ Frequency, urgency

Genital symptoms
✓ Dryness
✓ Itch, irritation, burning, itching

Sexual symptoms
✓ Decreased lubrication
✓ Discomfort or pain
✓ Bleeding after sex
✓ Decreased arousal, orgasm or desire

Vulvovaginal Atrophy (VVA)
Genitourinary Syndrome of Menopause (GSM)

CHANGES IN VAGINAL TISSUE
Due to hypoestrogenic state
Postmenopausal Changes in the Vaginal Epithelium

- Premenopausal
- Erectile tissue
- Folds or rugae
- Muscular coat
- Inner lining contains large amount of glycogen
- Postmenopausal
- Loss of folds
- Loss of inner lining and glandular function

Bardocz G, Jr.: A Profile of the Menopause. Kent, UK: Wells Medical Limited; 1995:49 (Fig. 6-4).

Atrophy: The Clinical Picture

- 2 years since natural menopause
- No estrogen therapy
  - Loss of labial and vulvar fullness
  - Pallor of urethral and vaginal epithelium
  - Minimal vaginal moisture
  - Loss of urethral meatal turgor

Vaginal histology

H & E, magnification × 10

Premenopause
Well-estrogenized epithelium, multi-layered with good blood supply; superficial cells rich in glycogen

Postmenopause
Estrogen-deficiency atrophy with marked thinning of the epithelium, reduced blood supply and loss of glycogen
FUSION OF LABIA MAJORA AND MINORA


THE PRIMARY CARE PHYSICIAN’S APPROACH TO GSM
"You have not because you ask not." James 4:2

#SayQuotable

"YOU GOT TO ASK!"

"YOU GOT TO LOOK!"

- Inspect the external genitalia
  - Mons pubis
  - Clitoris
  - Labia majora & minora
  - Urethra meatus
  - Vestibule
  - Introitus

- Inspect the internal genitalia
  - Vaginal walls
  - Cervix
“YOU GOT TO TALK!”

- Discuss your findings:
  - Patient focused
  - Care-giver focused
  - Patient & Care-giver focused

- Explain what your findings mean:
  - Clinically (Diagnosis/Treatment)
  - Personally (for the patient)
  - *Physician comfort and confidence important

“YOU GOT TO DO!”

- Take Action
  - Expectant management
  - Conservative treatment
  - Medication administration

- Refer
  - Gynecologist
  - Physical Therapist
  - Oncologist
You Can Do It

You Can Do It

Determine Severity of Symptoms

STEP WISE APPROACH TO TREATMENT OF GSM

1. Low Dose Vaginal Estrogen
2. Nonhormonal Vaginal Lubricants
3. Long Acting Vaginal Moisturizers
4. Ospemifene
5. Laser/Vaginal DHEA*
### TABLE 1. Examples of nonhormonal therapeutic options for dyspareunia secondary to VVA

<table>
<thead>
<tr>
<th>Lubricants</th>
<th>Moisturizers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Water based</strong></td>
<td></td>
</tr>
<tr>
<td>Astroglide Liquid</td>
<td>Replens</td>
</tr>
<tr>
<td>Astroglide Gel Liquid</td>
<td>Me Again</td>
</tr>
<tr>
<td>Astroglide</td>
<td>Vagisil</td>
</tr>
<tr>
<td>Just Like Me</td>
<td>Feminase</td>
</tr>
<tr>
<td>K-Y Jelly</td>
<td>K-Y SILK-E</td>
</tr>
<tr>
<td>Pre-Seed</td>
<td>Luvena</td>
</tr>
<tr>
<td>Slippery Stuff</td>
<td>Silken Secret</td>
</tr>
<tr>
<td>Liquid Silk</td>
<td></td>
</tr>
<tr>
<td><strong>Silicone based</strong></td>
<td></td>
</tr>
<tr>
<td>Astroglide X</td>
<td></td>
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<tr>
<td>ID Millennium</td>
<td></td>
</tr>
<tr>
<td>K-Y Intrigue</td>
<td></td>
</tr>
<tr>
<td>Pink</td>
<td></td>
</tr>
<tr>
<td>Pjur Eros</td>
<td></td>
</tr>
<tr>
<td><strong>Oil based</strong></td>
<td></td>
</tr>
<tr>
<td>Elegance Women’s Lubricants</td>
<td></td>
</tr>
<tr>
<td>Olive oil</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: VVA, vulvovaginal atrophy.

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### TABLE 2. Vaginal EE products for postmenopausal use in the United States and Canada

<table>
<thead>
<tr>
<th>Composition</th>
<th>Product name</th>
<th>FDM-approved dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>Enexal Vaginal Cream&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Initial: 2-4 g/d for 1-2 wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintenance: 1 g/d intra-vag&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Conjugated estrogen</td>
<td>Premarin Vaginal Cream&lt;sup&gt;4&lt;/sup&gt;</td>
<td>For VVA: 0.5 g/d for 21 d then off 7 d, or twice/wk&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td>Estrone</td>
<td>Exemestan Vaginal Cream&lt;sup&gt;4&lt;/sup&gt;</td>
<td>(0.625 mg active stEROId)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Initial: 1 tablet for 2 wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintenance: 1 tablet b.i.d. (tablet containing 0.3 mg of estradiol, equivalent to 4.0 mg of estrone, for VVA)</td>
</tr>
</tbody>
</table>

Abbreviations: EE, estrogen therapy; FDM, Food and Drug Administration; VVA, vulvovaginal atrophy.

<sup>1</sup>Available in the United States but not Canada.
<sup>2</sup>Available in Canada but not the United States.
<sup>3</sup>Some FDM-approved dosages of conjugated estrogen and estradiol creams are greater than those currently used in clinical practice that are proven to be effective.
<sup>4</sup>Some FDM-approved dosages of estrone vaginal tablets, used by many women, may be adequate for many women.
<sup>5</sup>From Enexal<sup>10</sup>, Premarin<sup>11</sup>, Exemestan<sup>12</sup>, Estrone<sup>13</sup>, Feering<sup>14</sup>, Vagifem<sup>15</sup>, Bachman G, et al. 16
VAGINAL ESTROGEN BLACK BOX WARNING

- On all estrogen classed medications, including HT
  - No distinction between route
  - No distinction between dose
- Warning based on WHI trial & other studies specific to systemic ET or EPT
- Study findings not relevant to low dose vaginal estrogen
  - Minimal if any systemic absorption
  - Low PM blood estradiol levels compared to systemic estrogen

VAGINAL ESTROGEN BLACK BOX WARNING

- Observation studies and short term RCTs for low dose vaginal estrogen demonstrate:
  - No evidence of increased VTE risks, breast cancer, stroke, heart disease, or dementia
- Current box warning is inappropriate and based on extrapolated results from systemic MHT
- Health care providers and patients deterred from using, based on findings
- VAGINAL ESTROGEN BLACK BOX REVISION RECOMMENDED!!!
A citizen’s petition filed in 2016

600 signatures – clinicians, patients, medical & professional organization representatives

“FDA reconfirmed that ALL estrogen products will have black box warning”
Oral treatment for vulvovaginal atrophy and dyspareunia

Osphena® — the only FDA-approved, non-estrogen, oral pill for moderate to severe painful sex due to menopause.

Important Safety Information and Indication:

Osphena® works like estrogen in the lining of the uterus, but can work differently in other parts of the body. Taking estrogen alone or Osphena may increase the chance for getting cancer of the lining of the uterus. Vaginal bleeding after menopause may be a warning sign of cancer of the lining of the uterus. Your healthcare provider should check any unusual vaginal bleeding to find out the cause, as well as tell them right away if this happens while you are using Osphena.

Innovative treatment option for GSM

Fractional Laser Treatment of Vulvovaginal Atrophy

Two Renewal Mechanisms in One
- Ablation
- Thermal effect
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