

Genitourinary Syndrome of Menopause

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Overview

- Definition of GSM
- Epidemiology of GSM
- Non hormonal treatments for GSM
- Hormonal Treatments for GSM
- New and Emerging therapies

Definition

Genitourinary Syndrome of Menopause:

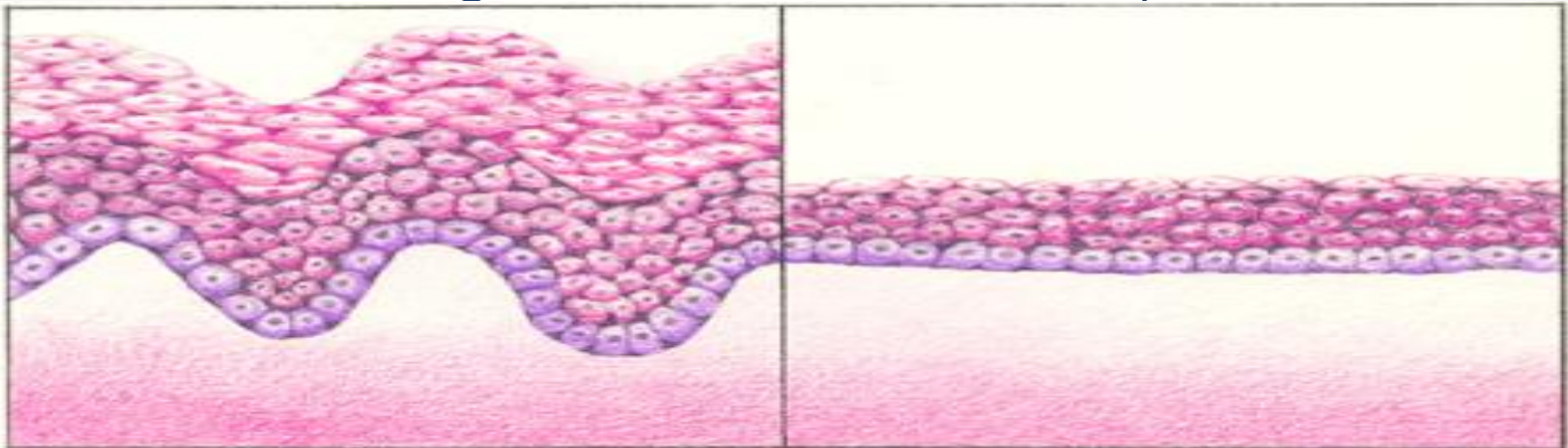
New Terminology for Vulvovaginal Atrophy from the International Society for the Study of Women's Sexual Health and The North American Menopause Society

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.

Menopause 2014

What is GSM?

- Changes in the vaginal and vulvar surfaces that on examination are thin, pale, and dry
 - Related to decreased blood flow from loss of Estrogen
 - Causes decreased acidity of vagina
 - Decreases numbers of lactobacilli
 - Decreasing number of surface epithelial cells



Vaginal Signs and Symptoms

- Dryness and insufficient moistness
- Diminished blood flow
- Dyspareunia
- Itching
- Burning sensation
- Soreness
- Loss of elasticity
- Thinning of the vaginal tissue and alteration of keratinization
- Mucosal defects including petechiae, microfissures, ulceration and inflammation
- Shortening, fibrosis, obliteration of vaginal vault and/or
- narrowing of vaginal entrance
- Smoothing of fornix, flattening of vaginal rugae

• **Slide courtesy of Sharon Parish**

Clinical Examples

Atrophic vaginitis



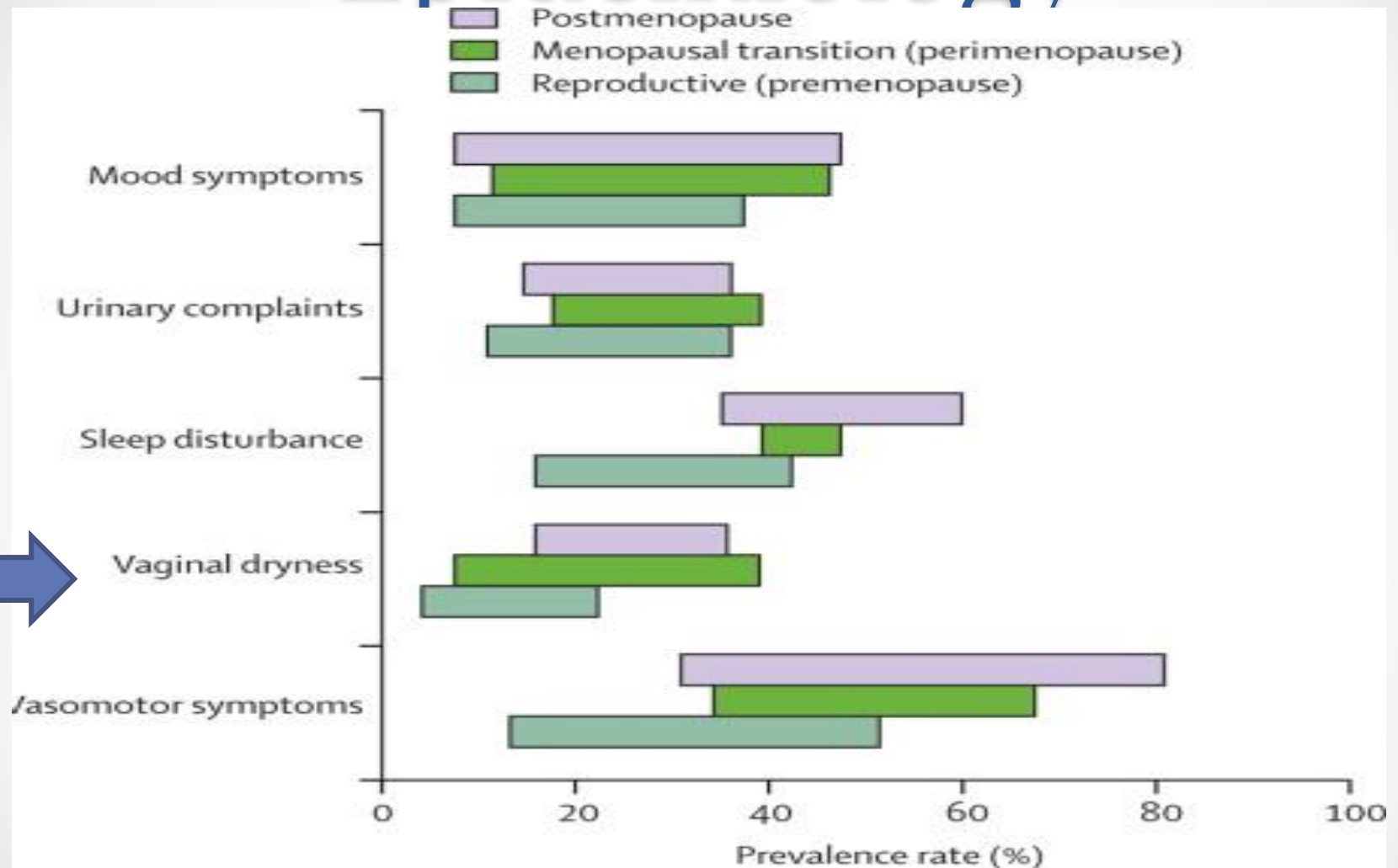
External genitalia show scarce pubic hair, diminished elasticity and turgor of the vulvar skin, decreased introital moisture, and fusion of the labia minora.

Courtesy of Aron Schuftan, MD.

UpToDate®



Epidemiology



Prevalence rates of symptoms 51 population studies showed wide ranges of prevalence rates. Rates of vasomotor symptoms, vaginal dryness, and sleep disturbances are higher for women in menopausal transition and postmenopause than for women in reproduct...

Nelson H, 2008

Surveys of PM Women

- Numerous
 - VIVA, REVEAL, HealthyWomen, CLOSER, REVIVE, Women's Voices in Menopause
- Largest in US: REVIVE

Real Women's Views of Treatment Options for Menopausal Vaginal Changes
3,046 women with symptoms of VVA.

- * 85% of partnered women had "some loss of intimacy"
- * 59% indicated VVA symptoms detracted from enjoyment of sex
- * 47% of partnered women indicated VVA interfered with their relationship
- * 29% reported VVA had a negative effect on sleep
- * 27% reported VVA had a negative effect on their general enjoyment of life

Only 7% reported that their healthcare practitioner initiated a conversation about VVA

Evaluation

- History
 - Onset, duration, quality of sx
- Physical Exam
 - Do not miss other common dermatoses!
 - Examine the vulva
 - Speculum exam
 - Wet mount
 - Expect 1 WBC over 1 epithelial cell
 - pH=5
 - Important to re-examine after treatment if any concern about the dx

Treatment Non-Hormonal

- Moisturizers
 - Replens
 - Rephresh
 - Vagisil
 - Feminease
 - Luvena
- Lubricants
 - Water based: K-Y, Astroglide, liquid
 - Silicone Based: Pink, Pjur Eros
- Oil Based
 - Elegance Women's
 - Olive Oil
 - Coconut Oil



Cost and How to Use

Product	Ingredients	Use	Price	Studies
Replens	Polycarbophil Glycerin, mineral oil	Every 3 days	\$17.5/14 app	Yes
Me again	Hyaluronic acid Propylene glycol, paraben	7 days > 2/wk	\$18/8 app	HA-yes
KY Liquibeads (ovules)	Dimethicone , Gelatin, Glycerin, Dimethiconol	?		No
KY long lasting	Various polymers Glycerin, mineral oil	?	\$16/6 app	No
Emerita personal moisturizer	Aloe Vera Gel, Calendula, Vitamin E, Ginseng, Chamomile, Allantoin	As needed	\$16/4 oz	No
Moist Again	Carbomer , aloe vera glycerin, chlorhexidine	As needed	\$7/4 oz	No
Hyalofemme	Hyaluronic acid	7 days > 2/wk	\$17/30gram	HA-yes
Pre-seed	Hydroxyethylcellulose , Pluronic, Arabinogalactan	As needed	\$20/9 app	Yes

Slide Courtesy of Sharon Parish

Non hormonal Treatments

What's the Data?

- Very Few Studies have looked at the effect of OTC moisturizers and VVA
- Best Studied Tx is Replens
 - 15/39 women in RCT
 - Sig improvement in sx of dryness, pain, itching
 - few women had IC during trial but all reported decreased dyspareunia
- Bygdeman M Maturitas 1996
- Nachtigall LE. Fertil Steril 1994

Hormonal Management

- **Most Important Principal**
 - Local is better than Systemic!
- **Improvements in**
 - atrophic symptoms (including dyspareunia)
 - lower urinary tract symptoms
 - gross vaginal mucosal appearance
 - decreases in vaginal pH
 - increases in the number of vaginal lactobacilli
 - favorable shifts in the vaginal and/or urethral cytology
 - Also preferred to systemic estrogen

Suckling J Cochrane Database Syst Rev 2006
NAMS Menopause 2013

Vaginal Estrogen Products

Formulation	Composition (Product Name)	Dosing
**Cream	17 β estradiol (Estrace®) Conjugated estrogens (Premarin®)	Initial: 2-4 g/d for 1-2 wk Maintenance: 1 g/d (0.1 mg active ingredient/g) 0.5-2 g/d (0.625 mg active ingredient/g)
Tablet	Estradiol hemihydrate (Vagifem®)	Initial: *10 mcg/d for 2 wk Maintenance: 10 mcg twice/wk
**Ring	17 β estradiol (Estring®)	Device contains 2 mg Releases 7.5 mcg/d for 90 d

*Ultra-low-dose vaginal estradiol tablets (10 μ g) as effective as low-dose tablets (25 μ g) and more effective than placebo (*Simon J, et al. Obstet Gynecol. 2008;112:1053-1060*).

**FDA approved for Dyspareunia

• Slide Courtesy of Sharon Parish

Safety of HT

- Vaginal E2 does result in increases of circulating estrogen
- There is little evidence to support use of progesterone for endometrial protection
- One study showed premarin @0.3mg qod with 1/20 women inc proliferation
Handa et al Obstet Gynecol 1994
- No evidence of endometrial proliferation attributed to vaginal tables or ring*
- No need for routine ultrasonography

Simon J et al *Obstet Gynecol* 2010

Naessen and Rodriguez-Macias K *Am J Obstet Gynecol*. 2002

More Hormonal Tx

- **Ospemefine**
 - **SERM- selective for vaginal tissue but NOT Endometrium**
 - **Unclear effect on breast (animal models reassuring)**
 - **2 RCTs (n=1431) showed improvement in**
 - **Objective findings of GSM**
 - Severity of dyspareunia decreased by 2 to 3 points in 53 %vs 39% placebo (60 mg dose)
 - Either 30 or 60 mg found to significantly decrease vaginal dryness but only 60mg treats dyspareunia

Bachmann et al *Menopause* 2010

Portman et al *Menopause* 2013

Off label/Investigational HT

- **Testosterone data lacking**

- 4-week pilot trial of 20 postmenopausal women with breast cancer found that vaginal testosterone (150 µg and 300 µg) improved dyspareunia, vaginal dryness, and vaginal maturation index without increasing estradiol

Witherby Oncologist 2011

- **Intravaginal DHEA**

- thought to exert an effect through the androgen and estrogen receptors
- Several studies showed improvements in VMI and vaginal pH at 2 doses—3.25 mg and 13 mg, once daily. It also significantly improved the most bothersome symptoms

Labrie et al Menopause 2009

Labrie et al Gynecolog Endo 2010

- Most recent data shows 6.5 mg dose sig improves FSFI scores 41.3 % over placebo (2.59 units), positively affecting all domains of FSFI

Labrie et al JSM 2015

More Experimental HT

- **Lasofoxifene: SERM to tx osteoporosis**

- RCT with raloxifene, produced significant improvements in vaginal pH and VMI at 6 months compared with placebo
- A separate RCT (n=387) reported reduced symptoms associated with sexual intercourse

Portman et al *Menopause* 2004

Bachmann et al *Menopause* 2005

- **Bazedoxifene (BZA) / CEE –systemic HRT**

- Largest RCT (n=664)
- Is BZA 20 mg/CE (0.45 mg or 0.625 mg) demonstrated significantly improved measures of VVA and sexual pain
- Rates of endometrial hyperplasia similar to placebo.

Kagan R et al *Menopause* 2010

Bottom Line

- **GSM very real and bothersome condition**
- **Many patients do not ask and providers to not address**
- **Physical exam is key to making dx**
- **Treatment options are ideally topical**
- **Many options to choose from**
- **Hormones are known to have best effects**
- **New experimental treatments on horizon!**

Thank You!!!

