



Microscopic images courtesy of Jamie Shutter, MD.

# ATROPHIC VAGINITIS

## Diagnosis and Treatment Options

Catherine M. Lynch, MD

Atrophic vaginitis is prevalent among postmenopausal women; however, it is often underreported and underdiagnosed. The estrogen-related changes to the vaginal epithelium can adversely affect a woman's quality of life. Although systemic therapy can be of benefit in the treatment of atrophic vaginitis, vaginal estrogen preparations are often recommended. Postmenopausal women may find relief of symptoms of atrophic vaginitis with vaginal estrogen therapies.

*A 68-year-old female presents with symptoms of frequency, urgency, and incontinence worsening over the past year. She has had 3 episodes of urinary tract infections (UTIs) in the past year. Her medical history is significant for a myocardial infarction 3 years ago and breast cancer 10 years ago. She had a hysterectomy in her 40s for fibroids. She has never taken hormones. She is a widow and does not have a sexual partner. Her vaginal exam demonstrates flat, pale vaginal mucosa with petechiae. Her friend with similar issues recently had improvement with vaginal estrogen therapy, so she is wondering if she is a candidate.*

**A**trophic vaginitis symptoms are due to estrogen deficiency and result in involution of the vaginal tissue. These changes lead to itching, burning, dryness, irritation, and dyspareunia.<sup>1</sup> Estrogen stimulation maintains thick vaginal epithelium and production of glycogen. Lactobacilli depend upon glycogen for lactic acid production to maintain vaginal pH.<sup>1,2</sup> As estrogen levels drop after menopause, vaginal secretions decline, making sexual activity painful, and sometimes resulting in vaginal discharge. Urinary tract epithelia are also estrogen dependent. Therefore, urinary tract symptoms, such as dysuria, UTI, and stress incontinence, may develop following estrogen depletion.<sup>1,2</sup>

Urogenital atrophy is estimated to occur in 10% to 40% of postmenopausal women, including 10% to 25% of women on systemic hormone therapy.<sup>3</sup> Although common in postmenopausal women, only 20% to 25% seek medical treatment for their symptoms.<sup>4,5</sup> Pastore et al described a self-reported survey of postmenopausal women ages 50 to 79 endorsing a variety of symptoms associated with atrophic vaginitis.<sup>6</sup> They found the frequency of these symptoms was as follows: dryness (27%), vaginal irritation (18.6%), discharge (11.1%), and dysuria (5.2%). In addition to hypoestrogenism, cigarette smoking, lack of sexual activity, lower levels of androgens, and nulliparity are all associated with a greater risk of atrophic vaginitis symptoms.<sup>7,8</sup>

## DIAGNOSIS

The diagnosis of atrophic vaginitis should be based on a complete medical history and physical exam. Findings of smooth, pale mucosa that may have petechiae and friability are consistent with atrophy. External changes consistent with atrophy include sparse pubic hair, vulvar dermatoses, vulvar lesions, and labial fusion.<sup>1</sup> If diagnosis is uncertain following history and physical examination, testing may include hormone analysis, as well as cytology, which may show an increase in parabasal cells as reflected by the vaginal maturation. A pH greater than 5.0 may also indicate atrophic vaginitis.<sup>1</sup> A vaginal maturation index may also be used, as it is an indirect measure of the estrogen status. As estrogen levels decrease, the parabasal and intermediate cells in-

crease. The maturation index is calculated from the total numbers of parabasal, intermediate, and superficial epithelial cells per 100 cells.<sup>7</sup>

## THERAPY

Therapy for atrophic vaginitis includes vaginal estrogen therapy as well as moisturizers, lubricants, and sexual activity. Estrogen has been shown to be effective in restoring vaginal anatomy and symptom relief. Cardozo et al found in a meta-analysis of 10 clinical trials of estrogen therapy that vaginal estrogen therapy provided the greatest symptom relief and improvement in atrophic changes.<sup>4</sup> In women with vasomotor symptoms as well as atrophic vaginitis, systemic therapy may be warranted, but additional vaginal therapy may still be necessary.<sup>9,10</sup>

Vaginal estrogen products for the treatment of atrophic vaginitis include creams, tablets, suppositories, and rings. Initial trials of a 25- $\mu$ g estradiol tablet for 52 weeks comparing once- versus twice-weekly therapy, after a 2-week induction period, found that there was better symptom relief with the twice-weekly therapy, and safety was comparable, with only weakly proliferative endometrium in some subjects at a year.<sup>11</sup> More recently, a comparative trial of estradiol 25 or 10  $\mu$ g or placebo found improvement in symptoms at both doses, although greater with the 25  $\mu$ g compared to the 10  $\mu$ g. Endometrial histology was normal in all groups.<sup>12</sup> Bachmann and colleagues compared conjugated equine estrogen (CEE) cream (0.3 mg), 21 days on with 7 days off, versus twice-weekly CEE (0.3 mg) or placebo for 12 weeks with a 40-week open-label phase.<sup>13,14</sup> They found equivalent improvement in symptoms that were superior to placebo, and there were no reports of endometrial hyperplasia or carcinoma at the end of a year.

There are 2 vaginal rings available today for estrogen therapy: Estring (Pfizer) and Femring (Warner Chilcott). Vaginal rings are worn for 3 months at a time, which many women may find advantageous. When initially inserted, there is a burst increase in hormone release that stabilizes within the first 3 hours after insertion.<sup>11</sup> Estring contains 2 mg of 17 $\beta$ -estradiol (E2), which releases 7.5  $\mu$ g per 24 hours for 90 days.<sup>15</sup> Femring has 2 strengths: 12.4 mg of estradiol

## FOCUSPOINT

**Estrogen-related changes to the vaginal epithelium can affect a postmenopausal woman's quality of life. She may find relief for atrophic vaginitis with vaginal estrogen therapies.**

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**FOCUSPOINT**

**Therapy for atrophic vaginitis includes vaginal estrogen as well as moisturizers, lubricants, and sexual activity.**

acetate, which releases 0.05 mg of estradiol per day for 3 months, and 24.8 mg of estradiol acetate, which releases 0.1 mg of estradiol per day for 3 months.<sup>16</sup>

Estradiol rings have been compared to CEE creams and are found to relieve symptoms of vaginal dryness and dyspareunia to a similar de-

gree. Estradiol rings did relieve symptoms of pruritus better than estradiol creams.<sup>17</sup> Femring has been shown in a 13-week double-blind, placebo-controlled trial of 333 postmenopausal women to effectively relieve systemic vasomotor symptoms as well as improve vaginal symptoms.<sup>16</sup> Therefore, in contrast to Estrin, Femring is indicated for the treatment of both moderate to severe vasomotor symptoms and vulvovaginal atrophy. Since Femring is a vaginal administration of systemic estrogen, progesterone would need to be administered in patients with a uterus.

In the patient with symptoms of recurrent UTIs in our case example, vaginal estrogen therapy has been found to reduce the rate of recurrent infection. Eriksen reported that the es-

tradiol-containing 2-mg ring was found to reduce the risk of recurrent infection, as well as statistically significantly reduce symptoms of overactive bladder, stress incontinence, dyspareunia, and pelvic pain.<sup>18</sup>

Several studies have evaluated the systemic absorption of vaginal estrogen tablets and creams. Mettler and Olsen followed 51 women for 1 year and found 3 patients with weak endometrial proliferation after a year.<sup>11</sup> Nine women continued the study for 2 years, and no endometrial proliferation was found. Additionally, levels of E2, follicle-stimulating hormone, and luteinizing hormone were all maintained in the postmenopausal range.<sup>11</sup> Akrivis et al evaluated estradiol 25- $\mu$ g tablets daily for 2 weeks, then 2 times per week, and found that although hormone levels increased, they remained within postmenopausal ranges.<sup>19</sup>

In terms of breast cancer risk, there are limited data specifically looking at long-term use of vaginal estrogen therapy and breast cancer. The Women's Health Initiative (WHI) estrogen/progesterone study arm showed a small but significant increase in the risk for invasive breast cancer with combination therapy.<sup>20</sup> The WHI estrogen-only arm, however, demonstrated no

**Coding for Atrophic Vaginitis**

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As this article proposes, there are various symptoms that would direct the clinician to a diagnosis of atrophic vaginitis. For an established patient, you need document only 2 of 3 components (history, examination, and medical decision making) to code at the 99213 or 99214 level of service. Since the examination might involve only 6 to 11 elements (99213), by reviewing and updating the patient's comprehensive intake history, a clinician could choose either a 99213 or 99214 based on the level of medical decision making. If the patient is new to the practitioner, then the level of service would most likely be 99202 or 99203.

- 627.3** Postmenopausal atrophic vaginitis  
Senile (atrophic) vaginitis
- 624.1** Atrophy of vulva
- 788.1** Dysuria  
Painful urination
- 788.30** Urinary incontinence, unspecified
- 788.41** Urinary frequency
- 788.63** Urgency of urination
- 596.51** Overactive bladder
- 625.0** Dyspareunia
- 625.6** Stress incontinence

- 625.9** Pelvic pain (unspecified symptom associated with genital organs)
- 412** Healed myocardial infarction  
Past myocardial infarction diagnosed on EKG but currently presenting no symptoms
- 599.0** Urinary tract infection
- V10.3** Personal history of breast cancer
- V88.01** Acquired absence of both cervix and uterus  
Status post total hysterectomy
- 698.1** Pruritus of genital organs
- V15.82** History of tobacco use
- 305.1** Tobacco dependence

As you can see, most of these patient encounters are not of low complexity but require a great deal of clinician work to appropriately diagnosis and treat the condition.

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increase in risk for breast cancer with estrogen monotherapy.

Replens and K-Y Jelly may be used as lubricants with or without estrogen. These products provide lubrication and may improve dyspareunia, as well as normalize vaginal pH. Since they do not address the underlying etiology of atrophic vaginitis, the relief is temporary.<sup>1,21</sup> Additionally, there is a positive association between sexual activity, vaginal elasticity, and pliability.<sup>1</sup> Women who have regular sexual activity report fewer symptoms of atrophic vaginitis and interestingly also have higher mean circulating levels of androgens and gonadotropins.<sup>17</sup>

## CONCLUSION

Currently both ACOG and the Society of Obstetricians and Gynaecologists of Canada recommend that women with severe atrophic vaginitis symptoms may be offered vaginal estrogen therapy, after discussion of risks and benefits.<sup>22,23</sup> Very low doses of vaginal estrogen therapy, as low as 0.3 mg of CEE twice weekly and estradiol 10- $\mu$ g twice weekly, may relieve symptoms of moderate to severe atrophic vaginitis.<sup>12,14</sup>

Symptoms of vaginal atrophy have been shown to be effectively treated by vaginal estrogen therapies. Studies comparing estrogen therapy to placebo have demonstrated subjective improvement in vaginal dryness, irritation, pruritus, and dyspareunia. Additionally, vaginal estrogen can decrease the rate of recurrent UTIs in postmenopausal women, as well as alleviate symptoms of stress incontinence and overactive bladder. Objective parameters such as vaginal maturation indices have also been shown to improve. Some women may find relief of symptoms with the use of vaginal lubricants that potentially facilitate sexual activity, which may also improve symptoms.

Atrophic vaginitis need not be an inevitable consequence of aging or hypoestrogenism. Diagnosis and intervention with vaginal estrogen therapy may alleviate patient symptoms and improve quality of life. The many choices of delivery options available today allow for tailoring therapy to an individual patient's needs.

*The author is on the speakers bureau for Glaxo-SmithKline, Pfizer, Warner Chilcott, and Wyeth.*

## REFERENCES

- Bachmann GA, Nevadunsky NS. Diagnosis and treatment of atrophic vaginitis. *Am Fam Physician*. 2000;61(10):3090-3096.
- Carcio H. Urogenital atrophy: a new approach to vaginitis diagnosis. *Adv Nurse Pract*. 2002;10(10):40-48, 51.
- Willhite LA, O'Connell MB. Urogenital atrophy: prevention and treatment. *Pharmacotherapy*. 2001;21:464-480.
- Cardozo L, Bachmann G, McClish D, Fonda D, Birgerson L. Meta-analysis of estrogen therapy in the management of urogenital atrophy in postmenopausal women: second report of the Hormones and Urogenital Therapy Committee. *Obstet Gynecol*. 1998;92(4 Pt 2):722-727.
- Pandit L, Ouslander JG. Postmenopausal vaginal atrophy and atrophic vaginitis. *Am J Med Sci*. 1997;314(4):228-231.
- Pastore LM, Carter RA, Hulka BS, Wells E. Self-reported urogenital symptoms in postmenopausal women: Women's Health Initiative. *Maturitas*. 2004;49(4):292-303.
- Castelo-Branco C, Cancelo MJ, Villero J, Nohales F, Juliá MD. Management of post-menopausal vaginal atrophy and atrophic vaginitis. *Maturitas*. 2005;52(suppl 1):S46-S52.
- Leiblum S, Bachmann G, Kemmann E, Colburn D, Swartzman L. Vaginal atrophy in the postmenopausal woman: the importance of sexual activity and hormones. *JAMA*. 1983;249(16):2195-2198.
- Samsioe G. Urogenital aging—a hidden problem. *Am J Obstet Gynecol*. 1998;178(5):S245-S249.
- Rigg LA. Estrogen replacement therapy for atrophic vaginitis. *Int J Fertil*. 1986;31(3 Suppl [Estrogen]):29-34.
- Mettler L, Olsen PG. Long-term treatment of atrophic vaginitis with low-dose oestradiol vaginal tablets. *Maturitas*. 1991;14(1):23-31.
- Bachmann G, Lobo RA, Gut R, Nachtigall L, Notelovitz M. Efficacy of low-dose estradiol vaginal tablets in the treatment of atrophic vaginitis: a randomized controlled trial. *Obstet Gynecol*. 2008;111(1):67-76.
- Bachmann G, Bouchard C, Hoppe D, et al. Endometrial safety of two low-dose regimens of conjugated estrogens vaginal cream in postmenopausal women with atrophic vaginitis. Poster presented at: 19th Annual Meeting of the North American Menopause Society; September 24-27, 2008; Orlando, FL.
- Bachmann G, Bouchard C, Hoppe D, Hauck B, Helzner E, Ranganath R. Efficacy of two low-dose regimens of conjugated estrogen vaginal cream in postmenopausal women with atrophic vaginitis. *Fertil Steril*. 2007;88:S243.
- Crandall C. Vaginal estrogen preparations: a review of safety and efficacy for vaginal atrophy. *J Womens Health (Larchmt)*. 2002;11(10):857-877.
- Estring estradiol vaginal ring 2 mg [package insert]. New York, NY: Pharmacia & Upjohn Company, Division of Pfizer Inc; 2007.
- Femring (estradiol acetate vaginal ring) [package insert]. Rockaway, NJ: Warner Chilcott, Inc; 2008.
- Eriksen B. A randomized, open, parallel-group study on the preventive effect of an estradiol-releasing vaginal ring (Estring) on recurrent urinary tract infections in postmenopausal women. *Am J Obstet Gynecol*. 1999;180(5):1072-1079.
- Akrivis Ch, Varras M, Thodos A, Hadjopoulos G, Bellou A, Antoniou N. Action of 25 microg 17beta-oestradiol vaginal tablets in the treatment of vaginal atrophy in Greek postmenopausal women; clinical study. *Clin Exp Obstet Gynecol*. 2003;30(4):229-234.
- Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA*. 2004;291(14):1701-1712.
- Nachtigall LE. Comparative study: Replens versus local estrogen in menopausal women. *Fertil Steril*. 1994;61(1):178-180.
- American College of Obstetricians and Gynecologists Women's Health Care Physicians. Genitourinary tract changes. *Obstet Gynecol*. 2004;104(4 suppl):56S-61S.
- Society of Obstetricians and Gynaecologists of Canada. SOGC clinical practice guidelines. The detection and management of vaginal atrophy. Number 145, May 2004. *Int J Gynaecol Obstet*. 2005;88(2):222-228.