

# Dialogues in Menopause Management: Facilitating Counseling about Hormone Therapy

Healthcare providers and patients alike receive confusing, and seemingly conflicting, data about the benefit-risk ratio associated with hormone therapy (HT) use for postmenopausal women. To avoid misperception about risk, healthcare providers must have a clear and accurate understanding of risk concepts. With a fuller understanding of these concepts, healthcare providers will then be able to explain the most accurate information to their patients. The series “Dialogues in Menopause Management: Facilitating Counseling About Hormone Therapy” attempts to present case-based activities about counseling women on the benefits and risks of HT in live venues (Primary Care Network), Web-based programs (Medscape.com), and the written word (*Menopause Management*).

## Case #1: Counseling Women about Vaginal Atrophy

Holly L. Thacker, MD, FACP

### Teaching Point

To demonstrate to a woman the potential benefits and risks of using vaginal estrogen therapy (ET) for treatment of vaginal atrophy.

### Case History

The first case in our counseling series centers on a 61-year-old postmenopausal woman who presents to her clinician suffering from extreme vaginal dryness, itching and pain during intercourse — symptoms that were not as severe during her last checkup

1 year ago and, at that time, caused no distress.

The patient’s chart reveals that she reached menopause spontaneously at age 50 and has experienced no menopause-related symptoms, including hot flashes. She does not have a personal or family history of cardiovascular disease, breast cancer or uterine cancer. As of 4 years ago, her bone density was within normal ranges for her age. Her last Pap smear and mammogram were normal. The patient never smoked nor used HT in any form.

Her physical examination reveals that she weighs 135 lb and is 5'8" tall. Her blood pressure is 125/80 mm Hg. Her gynecological exam confirms an intact uterus and both ovaries. Clinical breast examination is normal. Pelvic examination is unremarkable

except for fragile vaginal mucosa characterized by pallor, decreased elasticity, disappearance of rugae and petechiae. Vaginal secretions are scant and odorless. She has no complaints or signs that would indicate a vaginal infection.

Following a thorough history and careful physical examination, the patient is diagnosed as having severe vaginal atrophy associated with loss of estrogen at menopause. The clinician explains that as a woman reaches menopause her ovaries stop making eggs, thus producing much less estrogen, and it can take a few years before the lack of estrogen results in this thinning of the vaginal walls. The timing of onset of symptoms in relation to menopause varies from one woman to another. The patient is concerned about adverse effects of treatment.

### Vaginal Atrophy

The decrease in circulating estrogen during perimenopause, or after induced menopause, causes the vagina to shorten and narrow. Petechiae may appear on the vaginal walls, which become thinner, less elastic and progressively smoother as rugal folds decrease. Vaginal blood flow diminishes, as do secretions from sebaceous glands. As a result, lubrication during sexual stimulation is delayed.<sup>1</sup>

Postmenopausal women often complain about vaginal atrophy symptoms

*\*This article is a brief synopsis of two cases presented as part of several live and Web-based activities from The North American Menopause Society (NAMS) and Medscape on counseling women about hormone therapy. This article and the entire series are supported by an unrestricted educational grant to Medscape from Wyeth. The material presented here does not necessarily reflect the views of NAMS, Medscape, or Wyeth.*

(an estimated 10%–40%), which, left untreated, can result in years of vulvovaginal discomfort that greatly affects sexual health and quality of life. Vaginal symptoms—vaginal dryness, vulvovaginal irritation and itching and dyspareunia—are usually progressive and do not resolve spontaneously.

Vaginal pH in vaginal atrophy increases to 5.0 or greater from the premenopausal range of 3.5 to 4.5.<sup>2</sup> This shift from healthy pH to alkalinity is caused by a lack of estrogenic stimulation and a decrease in lactobacilli.<sup>3</sup> A higher pH allows colonization of the vagina by fecal flora and other pathogens. Clinicians can see, via wet-mount microscopy, more than one white blood cell per epithelial cell, immature vaginal epithelial cells with relatively large nuclei (parabasal cells), and reduced or absent lactobacilli. Repopulation with diverse flora, including enteric organisms, occurs and is commonly associated with urinary tract infections.<sup>4</sup> Because the wet mount of atrophy is identical to that of desquamative inflammatory vaginitis or vaginal lichen planus, the clinician must consider a trial of vaginal ET to differentiate between the two conditions.

### Management Options

The primary goals of vaginal atrophy management are to alleviate symptoms and to reverse atrophic anatomic changes. First-line therapies for women with mild vaginal atrophy include non-hormonal vaginal lubricants and moisturizers, as well as continued sexual activity. For severe vaginal atrophy or symptomatic vaginal atrophy that does not respond to these options, prescription ET may be required. The basic premise of treating a condition caused by a lack of adequate hormonal stimulation is to supplement that hormone. The same premise applies to pharmacologic treatment of hypoestrogenic vaginal atrophy. Unlike age-

related changes in the urogenital tissues, most vaginal effects of diminished estrogen levels can be reversed. Exogenous estrogen, delivered either systemically or locally in the vagina, is the therapeutic standard for prescription therapies.<sup>5</sup>

Even though systemic ET (ie, oral, transdermal) is an effective treatment for a variety of postmenopausal symptoms associated with estrogen deprivation, including vaginal atrophy, it may be contraindicated in some women or unacceptable to some because of its potential for systemic adverse effects, especially with long-term use.<sup>6</sup>

Vaginally administered local therapy can provide sufficient estrogen to reverse atrophic changes in the vaginal tissues and relieve associated symptoms while limiting systemic absorption. With limited systemic absorption, enterohepatic metabolism does not occur; thus, lower doses of vaginal ET achieve a tissue effect similar to that achieved by oral or transdermal systemic dosing. However, low-dose local ET has no effect on either reducing vasomotor symptoms or lowering the risk of osteoporotic fracture.

### Low-dose vaginal ET

All of the low-dose vaginal ET products approved in the United States for treatment of vaginal atrophy are equally effective at the doses recommended in labeling.

Localized doses of ET are available in several regimens: an estradiol cream (Estrace Vaginal Cream, available in the US but not Canada), a conjugated estrogens vaginal cream (Premarin Vaginal Cream), and a cream with esterified estrogens (Neo-Estrone Vaginal Cream, available in Canada but not the US). Two other options are available in the US but not Canada: a sustained-release Silastic ring that delivers estradiol (Estring) and a micronized estradiol hemihy-

drate vaginal tablet (Vagifem). The regimens used clinically reflect the treatment protocols used in studies, commercial product availability and government-approved labeling.

Premarin Vaginal Cream is also indicated for treatment of moderate to severe dyspareunia due to menopause.

*Adverse Effects.* All low-dose, local vaginal ET products that are government approved in the United States and Canada differ slightly in their adverse-event profiles. Vaginal bleeding, breast pain and possibly nausea and perineal pain can occur with these products. There are no significant differences among the delivery systems.

Progestogen is usually not indicated when low-dose ET is administered locally for vaginal atrophy, nor is endometrial surveillance indicated in asymptomatic women using vaginal ET. For women with a history of hormone-dependent cancer, management is dependent upon the individual woman's preference in consultation with her oncologist.

### Counseling the Patient

The clinician suggests a local vaginal estrogen as treatment, but the patient is still concerned about reports of risk. Her clinician assures her that most of these risks are associated with systemic—not local—ET administered either orally or through the skin.

When might she see improvement? Typically, improvement is seen within a few weeks of starting treatment, but some women may need as much as 4 to 6 weeks to get the desired relief. Overall improvement occurs in over 80% to 90% of women treated with local ET. Then, treatment is continued for as long as a woman needs it.

The patient is scheduled for a follow-up visit in 6 weeks, at which time she will be assessed for any improvement of her vaginal atrophy and other

complaints, and for her comfort level with the treatment she has chosen.

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## Case #2: Counseling Women about Severe Vasomotor Symptoms

**Cynthia A. Stuenkel, MD**

#### Teaching Point

To ensure that the use of HT is consistent with the treatment goals, benefits and risks for the individual woman.

#### Case History

The second case concerns a 52-year-old woman with severe vasomotor

symptoms, drenching night sweats and poor sleep. Her last menstrual period was at age 50. She has had no vaginal bleeding since that time. She has not required contraception since her husband had a vasectomy after their third child was born. Their sex life seems adequate; vaginal dryness is not a problem. She denies a history of heart attack, stroke or venous thromboembolic events. She also denies a history of estrogen-sensitive cancers (breast or endometrium) or liver disease. She is taking no medications (she does take calcium and vitamin D). Her physical exam was essentially normal. Laboratory evaluation, including a mammogram and Pap smear, was normal.

The patient's primary concern at the visit is how to manage her menopausal symptoms. She is determined not to start HT after the controversy surrounding its risks and benefits. She has tried alternative strategies that did not relieve her symptoms, but she would like to review her options again.

#### Options for Relief

Although the gold standard for treatment of vasomotor symptoms is HT, some alternatives have been tried.

#### Alternative Strategies

Appropriate for all women, suggest trying to lower ambient temperature, dressing in layers, using a fan, increasing regular exercise and avoiding hot flash triggers (hot drinks, spicy foods, alcohol, etc.). Another strategy is paced respiration. Among nonprescription remedies studied for relief of vasomotor symptoms are soy foods and isoflavones, black cohosh and vitamin E. Although the results of clinical trials with these preparations are inconsistent, some women obtain relief from these agents.

Among nonhormonal prescription remedies used off-label for hot flash relief are antidepressants, such as se-

lective serotonin-reuptake inhibitors (eg, paroxetine, fluoxetine) and serotonin- and norepinephrine-reuptake inhibitors (eg, venlafaxine, desvenlafaxine). Others are anticonvulsants (eg, gabapentin) and antihypertensives (eg, oral or transdermal clonidine).<sup>1,2</sup>

#### Hormone Therapy

After discussing the options above, our patient decides she would like to learn more about HT—risks, benefits and how it is administered.

*Approved Indications.* The Women's Health Initiative (WHI)—the only large, relatively long-term randomized controlled trial to date of postmenopausal women using HT—was halted in 2002 because the risks of HT, when given for prevention of chronic diseases of aging (not menopause symptom relief), exceeded the benefits.

Government-approved indications for HT (which reflect the findings of the WHI) include treatment of moderate to severe vasomotor symptoms associated with menopause, with the caveat that HT should be prescribed at the lowest dose and for the shortest duration for the individual woman.<sup>3</sup> HT is also approved for treatment of moderate to severe symptoms of vulvar and vaginal atrophy (dryness and irritation) associated with menopause. When prescribed solely for the treatment of symptoms of vulvar and vaginal atrophy, consider topical vaginal products. The third approved indication for HT is prevention of postmenopausal osteoporosis. If HT is to be prescribed for osteoporosis prevention, women should be at significant risk for osteoporosis and unable to use nonestrogen medications.

*Contraindications.* HT should not be prescribed if there is any possibility of pregnancy. Other conditions to look for during a patient evaluation are undiagnosed vaginal bleeding, estrogen-sensitive cancers, history of

stroke or myocardial infarction in the past year, history of blood clots and active liver disease. Any of these conditions would be a contraindication for HT.<sup>4</sup>

**Prescribing HT.** For relief of hot flashes and night sweats, systemic HT is the most effective option. Possible side effects include breast tenderness, vaginal/genital discharge, vaginal/genital irritation, headaches, uterine bleeding and increased gynecologic surgeries (eg, total abdominal hysterectomy, dilatation and curettage).

Since the WHI, HT is prescribed for symptomatic relief at lower (hopefully, safer) doses. In the WHI, participants were taking 0.625 mg oral conjugated estrogens (CE) per day, and women with a uterus also took 2.5 mg daily progestin (medroxyprogesterone acetate [MPA]). Lower daily doses now include 0.3 mg CE, 0.5 mg oral micronized 17 $\beta$ -estradiol and a 0.014-mg to 0.025-mg transdermal 17 $\beta$ -estradiol patch. Typical lowest doses of progestogen for women with a uterus are 1.5 mg oral MPA, 0.1 mg oral norethindrone acetate, 0.5 mg oral drospirenone or 50 mg to 100 mg of oral micronized progesterone.

The good news about lower-dose therapy is that side effects are also reduced. With a standard dose (0.625 mg CE; 0.050-mg transdermal patch), women might expect an 85% reduction in vasomotor symptoms, but there might be a 30% increase in breast tenderness and a 50% increase in vaginal bleeding. With currently recommended low-dose HT (0.30 mg CE; 0.025-mg transdermal patch), a 75% reduction in vasomotor symptoms is expected, but with a 15% increase in breast tenderness and a 25% increase in vaginal bleeding. And, with ultra-low-dose HT (0.15 mg CE; 0.014-mg transdermal patch), studies have shown a 55% reduction in vasomotor symptoms, with an increase in breast

tenderness of only 5%, and a 12% increase in vaginal bleeding.<sup>5</sup>

Current data support minimizing progestogen exposure to reduce breast effects and possible vascular consequences; cyclical therapy might be a better choice for providing endometrial protection. While new regimens are under investigation, there is currently insufficient evidence regarding endometrial safety to recommend off-label use of long-cycle regimens, vaginal administration of progesterone, a levonorgestrel-releasing intrauterine system or low-dose estrogen without progestogen.<sup>6</sup> In women intolerant of progestogen, annual endometrial monitoring with ultrasound or tissue biopsy is recommended.

### Counseling the Patient

It is essential that healthcare providers be able to explain the concept of risk in a clear and tailored manner. Providing figures for absolute risk is a better method than presenting the patient with relative risk. Using absolute numbers puts the risk in perspective. Explain that “rare” means that less than 10 per 10,000 women per year will experience an event from HT, such as stroke or blood clot. “Very rare” means that 1 per 10,000 women per year will experience an event. Based upon the findings in the WHI, it is reasonable to tell your patient that for a healthy woman with a uterus who is age 50 to 54, the risk of an HT-related event with combination HT (estrogen and progestogen) is estimated to be about 15 events per 10,000 women who take HT for a year.<sup>2</sup> The risks are less for women considering ET alone. Transdermal therapy is associated with fewer untoward effects on blood pressure, triglycerides, C-reactive protein and blood clots than oral therapies. A woman’s individual health status and menopause experience must be considered in the discussion: baseline

disease risks, current age, age at menopause, cause of menopause and duration since menopause.

Individualize, individualize, individualize. Get to know your patient: women in their 50s and 60s were born in an era of information. A good quote to use with patients is: “Because baby-boom women are so health conscious, they will be highly aware of menopause symptoms and will demand relief—probably a lot more than their mothers did. Besides, many of their clinicians are women, going through the same damn thing.”<sup>5</sup> Remind your patient that she will be reassessed periodically to decide about continuing or discontinuing HT. Finally, remind her that we are always learning more, and to stay tuned for the latest information at her next visit. ■

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