This clinical e-newsletter from The North American Menopause Society (NAMS) presents questions and cases commonly seen in a menopause specialist’s practice. Recognized experts in the field provide their opinions and practical advice. Kathryn M. Macaulay, MD, NCMP, the Editor of Menopause e-Consult, encourages your suggestions for future topics. Note that the opinions expressed in the commentaries are those of the authors and are not necessarily endorsed by NAMS or by Dr. Macaulay.

**Question**

We often see patients start to complain about vasomotor symptoms even though they are still having menses, albeit irregularly. What is the ideal hormone regimen for these patients? If their menses remain irregular, should we be concerned? What regimen would best regulate their cycles? Do we need to more aggressively evaluate the patient for other medical issues that may cause hot flashes?

**Commentary by**

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Irregular menses and vasomotor symptoms (VMS) represent the hallmark of the perimenopause transition, a time in a woman’s life some have described as “hormonal chaos.”

Vasomotor symptoms are most prevalent during the later stages of perimenopause; the Study of Women’s Health Across the Nation indicated that as many as 70% of perimenopausal women report these symptoms.²

In a woman in her late 40s or early 50s who reports characteristic VMS and has had normal thyroid-stimulating hormone levels in the last year or so, additional medical/endocrine evaluation is not recommended.

If bleeding is heavy or prolonged, endometrial evaluation is appropriate. However, if menses are simply less regular (or the patient reports a skipped/oligomenorrheic menstrual pattern), endometrial evaluation is not indicated.

If the VMS are bothersome and disrupting normal activities, including sleep, treatment is appropriate.

Whether birth control is needed, combination (estrogen-progestin) hormone contraceptives (CHCs, including combination oral contraceptives [COCs]), suppress VMS, cause regular withdrawal bleeding, and reduce the amount of bleeding, as well as dysmenorrhea.

In addition, these agents carry additional health benefits, including prevention of ovarian and endometrial cancer and (when used in women during the late perimenopause transition) increased bone mass.
On what appears to be a dose-related basis, use of CHCs increases risk of venous thromboembolic events (VTEs). Although their use has not been extensively studied in older reproductive-aged women, use of CHCs does not appear to affect risk of breast cancer.

Almost all CHCs are formulated with the potent, synthetic estrogen ethinyl estradiol (EE)—5 μg of EE is approximately equivalent to 0.625 mg of conjugated estrogens; therefore, a 20-μg COC delivers about 4-fold more estrogen than standard-dose hormone therapy (HT).

A COC containing 10 μg of EE and 1 mg norethindrone is available in the United States (but not in Canada). In addition, an oral contraceptive formulation with estradiol valerate (most pills contain 2 mg) and the progestin dienogest is available in the United States and Canada. The estrogen dose of these COC formulations is in the range of use in HT.

Other CHCs include a monthly vaginal ring (available in the United States and Canada) and a weekly patch (generic in the United States; Evra in Canada), both worn for 3 of 4 weeks.

In women who seek treatment for perimenopause symptoms and also need contraception and who are appropriate candidates for combination contraceptives, these agents can be continued until they are in their mid-50s. At that time, the likelihood of menopause is high (meaning that future ovulation is unlikely), and patients can discontinue combination contraceptives and transition to conventional HT, if desired.3,4

Women using CHCs strictly for noncontraceptive indications may consider stopping these methods in their early 50s.

As women age, the prevalence of comorbidities, including obesity, hypertension, and VTEs, which increase the cardiovascular risks associated with CHC use, grows. In addition, CHC use is not appropriate for older reproductive-aged women who smoke or have migraine headaches.

Combination hormone formulations indicated for use as HT have estrogen doses lower than those used in CHCs and can be used off-label to treat VMS in perimenopausal women who are not candidates for CHCs. A prior history of VTE would contraindicate both CHC and HT use.

Optimal symptom management in perimenopausal women likely requires consistent ovulation suppression, because the occurrence of sporadic ovulation in such women can aggravate irregular uterine bleeding.5

Accordingly, it is important that HT formulations used to suppress perimenopause symptoms are formulated with contraceptive doses of progestins. Continuous oral HT formulations with norethindrone acetate 0.5 mg (combined with 1.0 mg estradiol) or norethindrone acetate 1.0 mg (combined with 5 μg EE) likely suppress ovulation and can be used off-label to effectively treat VMS and suppress menstruation in perimenopausal women. Both formulations are available in Canada as well as in the United States.

References

**Disclosures:** Dr. Kaunitz reports consultant/advisory board for Allergan, Bayer, Merck, Pfizer; grant/research support for Bayer, Merck, TherapeuticsMD; and royalties/patents for UpToDate.

**Case**
A woman who is 3 years postmenopausal comes in to your office with a chief complaint of severe vaginal dryness. There are no visible signs of infection or lichen sclerosis. She is severely atrophic and frustrated. She has tried Estrace vaginal cream, Vagifem, and Estring. Do you have any suggestions to help her severe dryness?

**Commentary by**

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Studies have shown that vaginal atrophy may significantly interfere with a woman’s quality of life, especially in regard to vaginal dryness and pain with vaginal penetration.1,2 Remarkably, 20% to 45% of women experience either decreased lubrication or pain with penetration sometime during midlife3; therefore, clinicians who care for women during midlife will likely be asked to address these concerns. An understanding of vaginal atrophy as well as modalities to educate and counsel women is necessary when caring for this population.

Vaginal atrophy describes changes that occur to the vagina after estrogen levels decrease after or during the menopause transition, either naturally or because of cancer therapies. Anatomic changes include thinning of the vaginal tissues, reduction in the size of the labia minora, and retraction of the vaginal introitus.4 Physiologically, vaginal pH may increase, vaginal epithelium may become altered, and vaginal blood flow may be reduced.

According to the 2013 North American Menopause Society vulvovaginal atrophy position statement, first-line treatment should include the use of vaginal moisturizers and lubricants.5 Vaginal moisturizers should be used on a regular basis every 3 days to provide a moisture barrier within the vagina and reduce the symptoms of vaginal atrophy.

Vaginal moisturizers typically do not cure vaginal atrophy; however, vaginal moisturizers containing hyaluronic acid have been found to improve vaginal lubrication and symptoms of vaginal atrophy, including reducing pain with vaginal penetration.6 Vaginal lubricants are to be used at the time of vaginal penetration to reduce pain with penetration. Clinicians counseling women about vaginal lubricants should include a discussion that reviews the difference between water-based and silicone-based products.

Oil- and petroleum-based lubricants should be avoided because they can damage condoms and cause vaginal irritation. Water-based lubricants are safe for use with condoms but may dry out quickly and cause more discomfort. Silicone-based lubricants are safe with all condoms, do not absorb into
the skin, and may provide longer-lasting comfort because of reduction in friction.

In addition to vaginal moisturizers and lubricants, clinicians should discuss vaginal stretching with their patients. Vaginal stretching has been noted to reduce symptoms of vaginal atrophy, including pain with penetration. Clinicians may counsel women about vaginal stretching and use of vaginal dilators, including teaching women how to use vaginal dilators.

The literature also has shown that the use of vaginal stimulation may reduce pain with penetration. Vaginal stimulation was shown to increase blood flow to the vagina and improve arousal, which overall reduced the symptoms of vaginal atrophy.

Vaginal estrogen in the form of a vaginal tablet, cream, or ring is considered a second-line therapy for the treatment of vaginal dryness. However, if vaginal estrogen has failed, other prescriptive treatment options may be discussed with the patient.

Ospemifene, a selective estrogen receptor modulator, has been approved by the US Food and Drug Administration (FDA) for the treatment of pain with intercourse. Ospemifene was shown to improve the symptoms of vaginal atrophy, including improving vaginal epithelial tissue and decreasing vaginal pain with penetration. Patients should be counseled that the risks associated with ospemifene include venous thrombus and stroke. Ospemifene was not studied in a breast cancer population.

Intravaginal dehydroepiandrosterone (DHEA) has been found to reduce vaginal atrophy and significantly improve symptoms. Intravaginal DHEA used nightly (0.5% or 1%) as an intravaginal ovule was shown to improve vaginal lubrication and arousal and reverse the physiologic signs of vaginal atrophy, including normalizing vaginal pH. Patients should be counseled that intravaginal DHEA has been studied in phase 3 clinical trials but is not yet FDA approved.

Caring for women with vaginal atrophy and associated symptoms requires clinicians to carefully counsel women regarding all treatment options. Nonprescriptive modalities, such as educating women about types of vaginal moisturizers and lubricants, the importance of vaginal stretching, and the benefits of vaginal stimulation, should also be reviewed.

If vaginal estrogen fails to adequately treat the symptoms of vaginal atrophy, women may be advised regarding various other prescriptive treatments such as ospemifene and intravaginal DHEA. A careful review of adverse effects and indications should be included.

References

6. Jokar A, Davari T, Asadi N, Ahmadi F, Foruhari S. Comparison of the hyaluronic acid vaginal cream and conjugated estrogen used in treatment of vaginal atrophy of menopause women: a randomized


**Disclosures:** Dr. Chism reports consultant/advisory board for Hologic and JDS Therapeutics and speakers' bureau for JDS Therapeutics.

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What is your preferred treatment for women experiencing severe vaginal dryness even after trying several remedies? Have you discovered any treatments that work especially well? Visit our [Member Forum](#) to discuss the April *Menopause e-Consult*.

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