OBG MANAGEMENT

A guide to lotions and potions for treating vaginal atrophy

Options for relieving the related itching, dryness, burning, and dyspareunia include a variety of hormonal formulations and nonhormonal alternatives

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CASE

New-onset dyspareunia in a menopausal patient

J. B., 53 years old, has been menopausal for 2 years. Several months after her annual examination, she schedules another appointment to discuss a worsening complaint: dyspareunia. She says she never had the problem until she reached menopause, and reports that it has become so severe that she has started avoiding sexual intercourse altogether. Even when she avoids intercourse, however, she is bothered by vaginal itching and burning.

What can you offer to her?

Various hormonal and nonhormonal products are available to relieve the frequent complaint, in menopausal women, of symptoms of vaginal atrophy: vaginal dryness, itching, burning, and dyspareunia.[1–3] The array of products isn't really surprising: As women advance through menopause, their complaints of vaginal dryness increase fivefold.[4]

Systemic and local estrogen therapies reverse some atrophic changes and alleviate symptoms.[5] After menopause, local vaginal estrogen formulations are recommended as first-line treatment for women who experience moderate or severe symptoms of vaginal atrophy.[3] Formulations such as the vaginal ring, vaginal tablet, and transdermal gels and sprays are increasingly popular.

In this article, we describe these and other products, including nonhormonal lubricants and moisturizers, to relieve:

- the range of symptoms of vaginal atrophy in menopausal women

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- isolated vaginal dryness in premenopausal women.

Although it is difficult to review all over-the-counter lubricant products on the market today, it is important for the practicing gynecologist to understand the basic categories and composition of the products to better counsel patients.

Is hormonal therapy always necessary?

When a postmenopausal woman complains of chronic vaginal dryness, and the exam is consistent with vaginal atrophy, the recommended treatment is local vaginal estrogen. If she complains of vaginal dryness during sexual intercourse only, a vaginal lubricant is a suitable option.

When a premenopausal woman complains of vaginal dryness, a vaginal moisturizer is the best long-term treatment option. However, a vaginal lubricant is recommended for intermittent dryness during intercourse or dyspareunia.

FAST TRACK

Local estrogen treatment is recommended over systemic therapy for vaginal atrophy

Local estrogens avoid many risks of systemic therapy

Topical estrogen preparations are available as vaginal creams, tablets, and rings, and as transdermal lotions, gels, and patches (**TABLE 1**, page 32). Local preparations are preferred to systemic therapy for the treatment of atrophy because they bypass the gastrointestinal tract, undergo less conversion in the liver, and improve local tissue with minimal elevation of the serum estradiol level.[1,3]

The vaginal ring (Estring) delivers the lowest systemic estradiol level—approximately 5 to 10 µg of estradiol daily. Femring delivers more estradiol daily and requires the addition of progesterone in women who have an intact uterus.

Studies suggest that patients favor the estradiol-releasing vaginal ring because of its ease of use, comfort, and effectiveness, compared with vaginal estrogen cream.[2,5]

Local estrogen formulations were compared and reviewed in a systematic Cochrane meta-analysis of 19 trials that included 4,162 women.[5] Vaginal cream, tablets, and rings were all equally effective in treating symptoms of atrophy. One trial found that cream (conjugated equine estrogen) increased the risk of uterine bleeding, breast pain, and perineal pain, compared with vaginal tablets.

Newer estrogen formulations include topical and transdermal patches, gels, lotions, and sprays (**TABLE 1**), all of which are systemic. They are effective in the treatment of vasomotor symptoms and vaginal atrophy.

When to add a progestin

A progestin is recommended in addition to a systemic estrogen formulation in women who have a uterus. For low-dose, local vaginal estrogen formulations, a progestin is usually not needed.[3] However, when the treatment is vaginal cream, consider progestin supplementation when the dosage exceeds 0.5 g twice weekly for an extended time (>1 year).

The serum estrogen level with local vaginal treatment is dose-dependent, and the long-term endometrial effects of vaginal estrogens are unknown. If vaginal bleeding develops, a workup is indicated and may necessitate imaging of the endometrial echo or endometrial sampling to rule out hyperplasia, neoplasia, and cancer.

Counsel the patient about any risks

If you prescribe transdermal or oral estrogen for a patient, be sure to counsel her about the risks of systemic therapy described in the Women's Health Initiative.[6]

Consider the patient's preference

Local estrogen treatment is recommended over systemic therapy for vaginal atrophy, but patient preference should also be considered. Some women may prefer the ring or tablet to minimize excess vaginal discharge, while others may prefer a cream because of its soothing effects. Always individualize management!

Lubricants and moisturizers

Insufficient lubrication during intercourse is a common complaint among both premeno-

TABLE 1 Topical estrogen formulations—a rundown of local and systemic options

Product	Dosing	Administration	Source of active ingredient
Absorbed locally			
VAGINAL TABLET			
Vagifem	25 µg of estradiol	One tablet intravaginally daily for 2 weeks; then, twice weekly	Synthesized from soy
VAGINAL CREAM			
Premarin	0.5 g (0.625 mg/g of conjugated estrogen)	Insert 0.5 g daily for 3 weeks; then, twice weekly (Note: Dosage can be increased to 2 g daily but this may require progesterone supplementation)	Urine of pregnant mares
Estrace	0.1 mg of estradiol/g of cream	Insert 0.5 g daily for 1 or 2 weeks; then, twice weekly	Synthesized from soy and yams
VAGINAL RING			
Estring	2 mg (delivers 6–9 µg of estradiol daily)	Insert 1 ring intravaginally for 3 months	Synthesized from Mexican yams
Absorbed systemically			
VAGINAL RING			
Femring	Delivers 0.05 mg – 0.1 mg of estradiol daily	Insert 1 ring intravaginally for 3 months	Synthesized from soy
ESTROGEN PATCH			
Estraderm	Delivers 0.05 mg or 0.1 mg of estradiol daily	Apply patch twice weekly	Synthesized from Mexican yams
Estradiol (generic)	Delivers 0.05 mg or 0.1 mg of estradiol daily		
Esclim	Delivers 0.025 mg, 0.0375 mg, 0.05 mg, 0.075 mg, or 0.1 mg of estradiol daily		
Vivelle, Vivelle-Dot	Delivers 0.025 mg, 0.0375 mg, 0.05 mg, 0.075 mg, or 0.1 mg of estradiol daily		Synthesized from Mexican yams
Climara	Delivers 0.025 mg, 0.0375 mg, 0.05 mg, 0.06 mg, 0.075 mg, or 0.1 mg of estradiol daily		Synthesized from soy
Alora	Delivers 0.025 mg, 0.05 mg, 0.075 mg, or 0.1 mg of estradiol daily		
Menostar	Delivers 0.014 mg of estradiol daily	Apply patch once weekly (Note: Indicated only for prevention of osteoporosis)	
CombiPatch	Delivers 0.05 mg or 0.14 mg daily of estradiol plus 0.05 mg or 0.25 mg daily of norethindrone	Apply patch twice weekly	Synthesized from soy (estradiol) and Mexican yams (norethrindrone)
ESTROGEN LOTION, GEL			
Estrasorb (lotion)	Content of two pouches delivers 0.05 mg daily of estradiol	Apply one packet to each leg daily	Synthesized from soy
EstroGel (gel)	1.25 g (0.75 mg of estradiol)	Apply one pump to arm once daily	
Divigel (gel)	0.25 g, 0.5 g, or 1 g of 0.1% estradiol	Apply one packet to upper thigh daily	
Elestrin (gel)	0.87 g (0.52 mg of estradiol)	Apply one pump to arm once daily	
ESTROGEN SPRAY			
Evamist	1.53 mg of estradiol in each spray	Apply 1–3 sprays to forearm daily	

Source: Cirigliano M. Bioidentical hormone therapy: a review of the evidence. J Womens Health (Larchmt). 2007;16:600–631.

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TABLE 2 Vaginal moisturizers and lubricants are plentiful and diverse

Product (Manufacturer)	Ingredients	Notes
MOISTURIZERS		
Replens (Columbia Laboratories)	Water, carbomer, polycarbophil, paraffin, hydrogenated palm oil, glyceride, sorbic acid, and sodium hydroxide	Should be used 3 times weekly
Moist Again (Lake Consumer Products)	Water, carbomer, aloe, citric acid, chlorhexidine deglutinate, sodium benzoate, potassium sorbate, diazolidinyl urea, and sorbic acid	Safe to use with a latex condom; no data on effects on sperm motility
Vagisil Feminine Moisturizer (Combe)	Water, glycerin, propylene glycol, poloxamer 407, methylparaben, polyquaternium-32, propylparaben, chamomile, and aloe	
Feminease (Parnell Pharmaceuticals)	Water, mineral oil, glycerin, yerba santa, cetyl alcohol, and methyl paraben	Yerba santa (*Eriodictyon* spp), a plant native to the Pacific Northwest, is used as a moisturizer in place of aloe
K-Y Long Lasting Moisturizer (McNeil)	Purified water, glycerin, mineral oil, calcium/sodium PVM/MA copolymer, PVM/MA decadiene crosspolymer, hydrogenated palm glyceride, methylparaben, benzoic acid, tocopherol acetate, and sodium hydroxide	
K-Y Silk-E (McNeil)	Water, propylene glycol, sorbitol, polysorbate 60, hydroxyethylcellulose, benzoic acid, methylparaben, tocopherol, and aloe	
LUBRICANTS		
Water-based		
Slippery Stuff (Wallace-O'Farrell)	Water, polyoxyethylene, methylparaben, propylene glycol, isopropynol	
Astroglide (BioFilm)	Water, glycerin, methylparaben, propylparaben, polypropylene glycol, polyquaternium, hydroxyethylcellulose, and sodium benzoate	Also sold in a glycerin-free and paraben-free formulation
K-Y Jelly (McNeil)	Water, glycerin, hydroxyethylcellulose, parabens, and chlorhexidine	
Summer's Eve Lubricant (C.B. Fleet)	Water, propylene glycol, methylcellulose, xanthan gum, sodium lactate, methylparaben, lactic acid, dextrose, sodium chloride, edatate disodium, pectin, and propylparaben	
FemGlide (WalMed)	Water, polyoxyethylene, methylparaben, and sodium carbomer	
Pre-Seed (INGfertility)	Water, hydroxyethylcellulose, arabinogalactan, paraben, and Pluronic copolymers	Promoted to women and their partners who are trying to conceive
Silicone-based		
ID Millennium (Westridge Laboratories)	Cyclomethicone, dimethicone, and dimethiconol	Less drying than other lubricants
Pjur	Cyclopentasiloxane, dimethicone, and dimethiconol	Compatible with a condom
Pink	Dimethicone, vitamin E, aloe vera, dimethiconol, and cyclomethicone	
K-Y Liquibeads (McNeil)	Dimethicone, gelatin, glycerin, and dimethiconol	Active ingredients are contained in so-called ovules that release lubricant over several days
Oil-based		
Élégance Women's Lubricant	Natural oils	Does not contain alcohol, glycerin, or parabens; is incompatible with a condom; helpful for women who have vulvodynia or vestibulitis

pausal and postmenopausal women: As many as 60% of women report intermittent episodes of insufficient lubrication.[7]

Many women and their partners use a vaginal lubricant to assist with sexual relations and to self-treat for pain. A wide variety of nonhormonal products are available—many of them advertised at pharmacies and in the media—despite little published scientific evaluation. Because gynecologists routinely counsel patients on sensitive matters, including sexual practices, you may find it valuable—with appropriate candidates—to open a line of questioning about difficulties with intercourse and resulting attempts to self-medicate using over-the-counter products.

What are the indications?

A vaginal lubricant is a solution used locally, and as a temporary measure, to moisten the vaginal epithelium to facilitate a medical examination or sexual intercourse.[2] Because it has a short duration, it must be applied at the time of intercourse. Lubricants can be categorized as water-, silicone-, and oil-based. Each formulation may affect the local inflammatory response, viability of sperm, and condom integrity.

A vaginal moisturizer is a gel or cream used regularly to maintain hydration of the vaginal epithelium for long-term relief of vaginal dryness.[2]

Both lubricants and moisturizers have many indications for both medical and personal use. Personal lubricants can be used for assistance during sexual activity, such as intercourse, masturbation, or use of sex toys. These products reduce friction and are thought to enhance pleasure in women who suffer from vaginal dryness. However, we lack sufficient data to confirm that lubricants can improve sexual dysfunction and vaginal atrophy. In general, these products are affordable, readily available, and may be helpful in the treatment of sexual dysfunction and vaginal dryness.

See **TABLE 2** for a list of personal lubricants and vaginal moisturizers.

What to offer when estrogen is not an option

Some women may want to avoid hormonal treatment, or have a contraindication to it,

FAST TRACK

Because a vaginal lubricant has a short duration of action, it must be applied at the time of intercourse

In the pipeline: A new SERM just for vaginal atrophy

The therapeutic options for vaginal atrophy are likely to broaden in the near future. Ospemifene (Ophena), a selective estrogen receptor modulator (SERM) under development for the treatment of vaginal atrophy, has reached the end of Phase-3 clinical study, with positive efficacy results. A long-term safety study of the orally administered SERM has also been completed, reports QuatRx, the drug's manufacturer. The company expects to file a New Drug Application with the US Food and Drug Administration early next year.

Phase-3 trials documented significant improvement in dryness, dyspareunia, and other endpoints

The first Phase-3 study of Ophena was announced by QuatRx in January 2008 and presented at the 90th annual meeting of the Endocrine Society. Women who were treated with 60 mg daily of Ophena experienced statistically significant improvement in vaginal dryness, dyspareunia, and the proportion of parabasal and superficial cells in the epithelium of vaginal walls. The vaginal pH level also declined. The drug did not cause hot flushes among users.

The second Phase-3 study was a randomized, double-blind, placebo-controlled study of 919 women who had vulvovaginal atrophy. It was conducted at 116 sites in the United States. Among the cohort of 605 women who identified dyspareunia as their most bothersome symptom, positive efficacy results were achieved in all four primary endpoints, including:

- a decrease in parabasal cells
- an increase in superficial cells
- a decrease in the vaginal pH level
- improvement in dyspareunia.

The trial demonstrated statistically significant improvement from baseline to week 12 in all four endpoints, compared with placebo ($P < .0001$).

All women were supplied with a nonhormonal vaginal lubricant to be used as needed during the treatment period; the study found efficacy above and beyond usage of this lubricant, according to a press release from QuatRx.

Is the benefit worth the risk?

Some have questioned whether a systemic drug is overkill for a complaint like postmenopausal vaginal atrophy.[14] Because Ophena is a SERM, it is likely to carry a cardiovascular risk profile similar to that of other drugs in its class. For example, in a large randomized trial, raloxifene (Evista) failed to reduce coronary artery disease and significantly increased the incidence of fatal stroke and venous thromboembolism.[15] When local estrogen formulations that do not carry such risks are already available, some experts question the advisability of developing another systemic agent.

Another question: Is it realistic to expect the patient to take a drug every day when her chief complaint is postmenopausal dyspareunia and she is likely to have intercourse only once or twice a week?

These questions probably won't be addressed until the drug enters the market—and physicians and their patients will be the ones providing the answers.

such as estrogen-receptor–positive breast cancer.[8] In premenopausal women, vaginal atrophy can occur with lactation or postpartum hormonal changes, or may result from the use of anti-estrogenic agents for breast cancer. Other candidates for nonhormonal therapy are women who have chronic vulvar pain syndromes. In these women, vaginal lubricants can be especially useful.

Although they are less effective than estrogen, vaginal moisturizers, such as Replens, have been shown to reverse symptoms of vaginal atrophy and decrease discomfort during intercourse.[9]

Specialty lubricants are unproven

In contrast to products designed to treat vaginal dryness and atrophy, some lubricants are marketed specifically for sexual enhancement. Warming lubricants cause a heating sensation on the skin and usually contain menthol, L-arginine, or capsaicin. Natural and artificial flavors are used to manufacture flavored lubricants.

None of these products have been scientifically proven to enhance sexual function.

Oil-based lubricants may impede condom integrity

It is estimated that 40% of couples who use condoms also use a lubricant to assist with intercourse.[10] The integrity of latex condoms has been shown to deteriorate with the use of an oil-based lubricant or petrolatum. One study, in which the mean burst time of condoms was assessed during pressurized air inflation, showed a significant reduction in that time when vaginal lubricants that contained mineral or vegetable oil were used.[11]

Oil-based lubricants also have been shown to increase the slippage rate, with a trend toward increased breakage.[10]

Water-based lubricants may slightly increase slippage, but they reduce breakage.

Women should avoid oil-based lubricants when their partner uses a condom.

Some lubricants affect sperm quality

Choosing a vaginal lubricant can be of particular concern to a woman who is being treated for infertility. Lubricants may affect the integrity and function of sperm, even if they do not contain spermicide. Noncommercial products, such as glycerin, olive oil, vegetable oil, and, even, saliva have been associated with a loss of sperm function.[12]

A recent study found that Replens and Astroglide cause a dramatic decrease in sperm motility. FemGlide causes less of a decrease—but still a significant one.[12] The nonphysiologic osmolality and pH of these products may be the cause of such sperm damage. Pre-Seed, which has a more physiologic pH level and isotonic quality, was found to cause minimal harm to sperm motility and chromatin quality.[12]

Avoid propylene glycol in women who have vulvodynia

Vaginal lubricants and moisturizers are also used in the treatment of vulvodynia or chronic vulvar pain syndromes. According to an ACOG Committee Opinion, topical application of preservative-free solutions, such as vegetable oil or plain petrolatum, is recommended to hold moisture within the tissues and provide a protective barrier.[13] Adequate lubrication is also recommended during intercourse.

Products that contain propylene glycol, or alcohol, may act as an irritant in women who experience local pain and heightened vaginal sensitivity. For that reason, such products should be avoided in this population.

CASE RESOLVED

Careful examination reveals urogenital atrophy with absence of any fungal or bacterial infection of the vulva or vagina. The patient chooses to use a water-based lubricant during sexual relations and begins using intravaginal estradiol tablets (other options include the vaginal ring or cream). Symptoms of dyspareunia disappear almost immediately, and vaginal burning improves after 6 weeks.

FAST TRACK

Lubricants may affect the integrity and function of sperm, even if they do not contain spermicide

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