

## > THE PATIENT

56-year-old woman

## > SIGNS & SYMPTOMS

- Hot flushes, night sweats
- Concern about estradiol effects on pet
- Nipple, vulvar enlargement in pet

## > THE CASE

A 56-year-old postmenopausal woman with a history of anxiety, depression, alcohol abuse, fatigue, insomnia, and mental foginess presented to the family medicine clinic with concerns about her companion animal because of symptoms possibly associated with the patient's medication. Of note, the patient's physical exam was unremarkable.

The patient noticed that her 5-year-old, 4.5-lb spayed female Chihuahua dog was exhibiting peculiar behaviors, including excessive licking of the abdomen, nipples, and vulvar areas and straining with urination. The dog's symptoms had started 1 week after the patient began using estradiol transdermal spray (Evamist) for her menopause symptoms. The patient's menopause symptoms included hot flushes, insomnia, and mental foginess.

The patient had been applying the estradiol transdermal spray on her inner forearm twice daily, in the morning and at bedtime. She would let the applied medication dry for approximately 2 hours before allowing her arm to come in contact with other items. She worried that some of the hormone may have wiped off onto her couch, pillows, blankets, and other surfaces. In addition, she often cradled the dog in her arms, which allowed the canine's back to come in contact with her inner forearms. To her knowledge, the dog did not lick or ingest the medication.

The patient had taken the dog to her veterinarian. On physical exam, the veterinarian noted that the dog had nipple and vulvar enlargement but no vaginal discharge, vaginal bleeding, skin changes, or urine abnormalities.

## THE (PET'S) DIAGNOSIS, THE PATIENT'S Rx

The veterinarian diagnosed the Chihuahua with vaginal hyperplasia and vulvar enlargement secondary to hyperestrogenism. The animal's symptoms were likely caused by exposure to the owner's hormone replacement therapy (HRT) medication—the estradiol spray. The veterinarian advised the woman to return to her family physician to discuss her use of the topical estrogen.

The patient asked her physician (SS) to change her HRT formulation. She was given a prescription for an estradiol 0.05 mg/24-hour transdermal patch to be placed on her abdomen twice weekly. After 2 weeks of using the patch therapy, the patient's menopausal symptoms were reported to be well controlled. In addition, the companion animal's breast and vulvar changes resolved, as did the dog's licking behavior.

## DISCUSSION

Estrogen therapy, with or without progesterone, is the most effective treatment for postmenopausal vasomotor symptoms.<sup>1</sup> Given the concerns raised in the Women's Health Initiative (WHI) and other clinical trials regarding hormone therapy and cardiovascular and

**Shannon Scott, DO,**  
**FACOPF; Erin Raney,**  
**PharmD, BCPS, BC-ADM;**  
**Heather Weber, DO,**  
**PGY-1**

Arizona College of  
Osteopathic Medicine,  
Glendale, AZ (Dr. Scott);  
Midwestern University  
College of Pharmacy,  
Glendale, AZ (Dr. Raney);  
St. Francis Hospital and  
Medical Center, Hartford,  
CT (Dr. Weber)

✉ [sscott1@midwestern.edu](mailto:sscott1@midwestern.edu)

*The authors reported no  
potential conflict of interest  
relevant to this article.*

breast cancer findings, many clinicians look to alternative, nonoral dosage forms to improve the safety profile.

### ■ Safety of nonoral estrogen therapy.

Administration of nonoral estrogen is associated with avoidance of hepatic first-pass metabolism and a resulting lower impact on hepatic proteins. Thus, data indicate a potentially lower risk for venous thromboembolic events with transdermal estrogen compared to oral estrogen.<sup>1</sup> Since the publication of the results of the WHI trials, prescribing patterns in the United States indicate a general decline in the proportion of oral hormones, while transdermal prescription volume has remained steady, and the use of vaginal formulations has increased.<sup>2</sup>

■ **Topical estrogen formulations.** Transdermal or topical delivery of estrogen can be achieved through various formulations, including patches, gels, and a spray. While patches are simple to use, some women display hypersensitivity to the adhesive. Use of gel and spray formulations avoids exposure to adhesives, but these pose a risk of transfer of hormonal ingredients that are not covered by a patch. This risk is amplified by the relative accessibility of the product-specific application sites, which include the arms or thighs. Each manufacturer recommends careful handwashing after handling the product, a specific drying time before the user covers the site with clothing, and avoidance of contact with the application site for a prescribed period of time, usually at least 1 to 2 hours.<sup>3-6</sup>

■ **Our patient.** This case illustrates the importance of discussing the risk of medication transfer to both humans and animals when prescribing individualized hormone therapy. While the Evamist prescribing information specifically addresses the risk of

unintentional medication transfer to children, it does not discuss other contact risks.<sup>6</sup> In the literature, there have been a limited number of reports on the adverse effects from transdermal or topical human medication transfer to pets. Notably, the American Pet Products Association estimates that in the United States, approximately 90 million dogs and 94 million cats are owned as a pet in 67% of households.<sup>7</sup>

## THE TAKEAWAY

Use of HRT, including transdermal or topical estrogen formulations, is common. Given the large number of companion animals in the United States, physicians should consider that all members of a patient's household—including pets—may be subject to unintentional secondary exposure to topical estrogen formulations and that they may experience adverse effects. This presents an opportunity for patient education, which can have a larger impact on *all* occupants of the home. **JFP**

### CORRESPONDENCE

Shannon Scott, DO, FACOPF, Clinical Associate Professor, Arizona College of Osteopathic Medicine, 19389 North 59th Avenue, Glendale, AZ 85308; sscott1@midwestern.edu.

### References

1. The NAMS 2017 Hormone Therapy Position Statement Advisory Panel. The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2017;24:728-753.
2. Steinkellner AR, Denison SE, Eldridge SL, et al. A decade of postmenopausal hormone therapy prescribing in the United States: long-term effects of the Women's Health Initiative. *Menopause*. 2012;19:616-621.
3. Divigel [package insert]. Bridgewater, NJ: Vertical Pharmaceuticals, LLC; 2014.
4. Elestrin [package insert]. Somerset, NJ: Meda Pharmaceuticals; 2014.
5. Estrogel [package insert]. Herndon, VA: Ascend Therapeutics; 2018.
6. Evamist [package insert]. Minneapolis, MN: Perrigo; 2017.
7. American Pet Products Association. Pet Industry Market Size & Ownership Statistics. [www.americanpetproducts.org/press\\_industrytrends.asp](http://www.americanpetproducts.org/press_industrytrends.asp). Accessed November 1, 2019.

3. The American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 200. Early pregnancy loss. *Obstet Gynecol*. 2018;132:e197-e207.
4. National Institute for Health and Clinical Excellence. Ectopic pregnancy and miscarriage: diagnosis and initial management. Clinical guideline 154. [www.nice.org.uk/guidance/cg154/resources/guidance-ectopic-pregnancy-and-miscarriage-pdf](http://www.nice.org.uk/guidance/cg154/resources/guidance-ectopic-pregnancy-and-miscarriage-pdf). Published December 2012. Accessed December 5, 2019.
5. Neilson JP, Hickey M, Vazquez JC. Medical treatment for early fetal death (less than 24 weeks). *Cochrane Database Syst Rev*. 2006;CD002253.

6. Schreiber CA, Chavez V, Whittaker PG, et al. Treatment decisions at the time of miscarriage diagnosis. *Obstet Gynecol*. 2016;128:1347-1356.
7. Ngoc NT, Blum J, Westheimer E, et al. Medical treatment of missed abortion using misoprostol. *Int J Gynaecol Obstet*. 2004;87:138-142.
8. US Food and Drug Administration. Mifeprex (mifepristone) information. [www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/mifeprex-mifepristone-information](http://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/mifeprex-mifepristone-information). Updated February 5, 2018. Accessed December 5, 2019.

➤ All members of a patient's household—including pets—may be subject to unintentional secondary exposure to topical estrogen formulations and thus, experience adverse effects.

## PURLs®

CONTINUED FROM PAGE 569