

# Letters to the Editor

## Potential Drug Interactions in Patients Taking Oral Contraceptive Pills

**Original Article:** Clinically Relevant Drug-Drug Interactions in Primary Care

**Issue Date:** May 1, 2019

**See additional reader comments at:** <https://www.aafp.org/afp/2019/0501/p558.html>

**To the Editor:** This is a useful article, but I find it curious that it does not mention potential interactions with oral contraceptive pills (OCPs). Antiepileptics such as carbamazepine (Tegretol), topiramate (Topamax), and phenytoin (Dilantin) are fairly well known for decreasing contraceptive effectiveness of OCPs, whereas the use of lamotrigine (Lamictal) and an OCP increases metabolism of lamotrigine. These interactions are most likely to arise in women of childbearing age with a seizure diagnosis. However, antiepileptic drugs may be prescribed to women for other conditions, such as migraines and mood disorders. I expect that the absolute number of patients who are taking these drugs while taking OCPs is probably a lot less than the number who might be prescribed an antibiotic while taking warfarin (Coumadin), for example. Still, a drug interaction that could increase the risk of an unintended pregnancy is certainly clinically relevant.

In addition, a discussion of possible interactions of OCPs with antibiotics would be very helpful. I know of a handful of cases of unintended pregnancies that seemed to be related to antibiotic use while taking OCPs. However, I have not seen a guideline recommending the use

of backup contraception if a patient taking OCPs is also taking a course of antibiotics.

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**In Reply:** Thank you for your interest in our article. Your points are well taken. Regarding interactions with OCPs and antiepileptics, a recent study showed the drug interactions between ethinyl estradiol/estradiol and valproate (Depacon), oxcarbazepine (Trileptal), and carbamazepine to be among the most prevalent interactions in a group of 395 women with epilepsy seen in a tertiary outpatient clinic.<sup>1</sup>

Antimicrobials may reduce the effectiveness of OCPs when taken concurrently; however, there have been few well-documented reports of women using OCPs who became pregnant after taking antimicrobials. It is not well understood whether more common or broad-spectrum antibiotics increase the risk of OCP failure. Three mechanisms have been proposed: the effect of antimicrobials on hepatic enzyme induction, which increases metabolism of hormones; reduction of gut bacteria with broad-spectrum antibiotics, which alters enterohepatic circulation and reduced plasma hormone concentrations; and an increase in gastrointestinal motility with antibiotics, which decreases absorption (and reabsorption) of OCPs.

Antibiotics more likely to reduce OCP effectiveness include azithromycin (Zithromax), erythromycin, ketoconazole, penicillin (and derivatives), rifampin, rifabutin (Mycobutin), and tetracycline antibiotics.<sup>2</sup> Rifampin, an inducer of enzymes that metabolizes estrogens, decreases the effectiveness of OCPs. A systematic review concluded that pharmacokinetic and ovulation outcomes support a clinically relevant drug interaction between OCPs and rifampin and, to a lesser extent, rifabutin, but data are limited for other rifamycins.<sup>3</sup> Ketoconazole's interaction is less well documented, but combining that agent with low-estrogen (low-dose) OCPs warrants caution. Erythromycin and azithromycin may interact with OCPs, but the clinical significance of this interaction is unknown. Tetracyclines and penicillin were the antibiotics most frequently involved in case reports of pregnancy from the United Kingdom.<sup>2</sup>

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Antibiotics less likely to reduce OCP effectiveness include ciprofloxacin<sup>4</sup> and trimethoprim/sulfamethoxazole. Another systematic review concluded that current evidence does not support the existence of drug interactions between OCPs and nonrifamycin antibiotics.<sup>5</sup>

Because the degree of variability between patients is unknown and obesity rates are increasing, concern that the effectiveness of low-dose OCPs may be reduced when combined with antibiotics may be warranted.<sup>6</sup> Whereas the absolute risk of unintended pregnancy seems small, the most conservative approach is to advise patients to use a backup method of contraception during times of antibiotic use.

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**Dr. Carpenter** would like to acknowledge Dr. Allen Pelletier for his contribution to the original article and the letter to the editor response. Dr. Pelletier passed away on September 7, 2019, prior to this publication. His passion for collaboration, both scholarly and clinically, will be forever remembered. She would like to dedicate this article in memory of Dr. Pelletier and his contributions to the practice of family medicine.

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## Electronic Cigarettes: More Questions Than Answers

**Original Article:** Electronic Cigarettes: Common Questions and Answers

**Issue Date:** August 15, 2019

**See additional reader comments at:** <https://www.aafp.org/afp/2019/0815/p227.html>

**To the Editor:** Because we provide care to thousands of adults and youth with nicotine dependence annually, we appreciate the excellent overview article on electronic cigarettes (e-cigarettes). The article contains excellent

references for helpful terms when screening for and talking about e-cigarette use. Although there are likely benefits of e-cigarettes in assisting patients with quitting regular cigarettes, it is increasingly certain that vaping can be harmful.

Millions of e-cigarette users face potential exposure to toxins. For instance, as of October 15, 2019, there were 1,479 cases of severe pulmonary disease associated with vaping reported in adolescents and young adults in 49 states (all except Alaska), the District of Columbia, and one U.S. territory (USVI), and 33 deaths.<sup>1</sup> In response to these cases, Michigan has enacted policy to prohibit the sale of flavored e-cigarette products and Massachusetts banned all e-cigarettes for a four-month period. Symptoms have included dyspnea, fatigue, chest pain, cough, and weight loss that worsened days or weeks before hospitalization. Imaging studies demonstrated bilateral opacities on chest radiography and diffuse ground-glass opacities on computed tomography. Recent case studies have highlighted eosinophilic pneumonia in e-cigarette users,<sup>2,3</sup> and an observational study found increased rates of bronchitis in adolescent e-cigarette users.<sup>4</sup> These cases have involved traditional e-cigarette use and vaping of multiple substances, including nicotine, tetrahydrocannabinol (THC), synthetic cannabinoids, and combinations of these substances.<sup>5</sup>

Clinicians need to ask patients about their use of traditional e-cigarettes, but also about their use of emerging vaping products, devices, liquids, refill pods, and cartridges. Clinicians should also report cases of significant respiratory illness of uncertain etiology in patients with a history of vaping to state and local health departments.

Although e-cigarettes are marketed as a healthier alternative to cigarettes, far more longitudinal research is needed to examine e-cigarettes and their ingredients, including high nicotine content and flavoring; exposure to metals; combination use with other substances; and chronic use influence pulmonary toxicity.<sup>6</sup> In the meantime, clinicians should discuss adverse pulmonary toxicity with both traditional cigarette users and e-cigarette users.

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**Author disclosure:** Dr. Goldstein disclosed that in 2018 he was paid by Pfizer to attend a one-day meeting on tobacco cessation treatments. Drs. Baca-Atlas and Mounsey have no relevant financial affiliations.

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## Spinosad: A Low-Risk, Effective Treatment for Lice

**Original Article:** Lice and Scabies: Treatment Update

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**Available online at:** <https://www.aafp.org/afp/2019/0515/p635.html>

**To the Editor:** I enjoyed this article regarding treatment of lice, which is a common problem in young school-aged children and causes great stress for parents because of school policies and social stigma. The authors list permethrin 1% lotion (Nix) as first-line treatment based on its low cost and over-the-counter availability. However, resistance is a problem in some areas, as noted in the article. Many effective treatments are limited by high cost (spinosad [Natroba], malathion [Ovide]); limited effectiveness because of not being ovicidal (dimethicone [Nix Ultra, Lice MD], isopropyl myristate [Resultz], pyrethrins, permethrin); or toxicity/safety concerns, such as for pregnant women (oral ivermectin [Stromectol]).

Of these, spinosad has an extremely low risk of toxicity, is highly effective, and requires only a single treatment because it is ovicidal.<sup>1,2</sup> In one trial, a single application of spinosad without the use of combing was more effective than permethrin.<sup>1</sup> Unfortunately, it is limited by the high cost per treatment and the need for a prescription.

Yet spinosad is available without a prescription, and at 1/20th of the cost, if it is purchased at any gardening store. Permethrin has long been available as an organic pesticide at 0.5% concentration that has been deemed safe with low environmental and toxicity risks.<sup>3</sup> This is compared with the

0.9% concentration of the prescription product. The additional product in the pesticide formulations tends to be propylene glycol, which is substantially less toxic (not known to be toxic at all, except in incredibly high exposures) than benzyl alcohol, which itself is known to be safe in terms of potential exposure to infants or mucosal linings.<sup>4,5</sup>

It remains to me a wonder why topical spinosad is not available inexpensively over the counter but instead is a very high-cost prescription drug, particularly when almost the exact same formulation is profitably sold at gardening centers around the world for a substantially lower price.

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**Editor's Note:** In publishing Dr. Wright's letter, we wanted to clarify that *AFP* does not recommend that patients with lice self-treat with an unregulated product purchased at a garden store, regardless of cost savings. Rather, this scenario serves as an example of the disconnect between a pharmaceutical company's pricing of a drug for a common medical condition and the actual cost required to profit from its sale. Further information on what family physicians can do to help patients manage excessively high medication costs is available in a previous *AFP* editorial.<sup>1</sup>—Kenny Lin, MD, MPH, deputy editor

<sup>1</sup> Shaughnessy AF. Problematic jumps in drug prices and what you can do. *Am Fam Physician*. 2017;96(1):16-18. <https://www.aafp.org/afp/2017/0701/p16.html>

**This letter** was sent to the authors of "Lice and Scabies: Treatment Update" who declined to reply. ■