

Do antibiotics interfere with the efficacy of oral contraceptives?

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EVIDENCE-BASED ANSWER

Among antibiotics, only rifampin has been demonstrated to interfere with the effectiveness of oral contraceptives (OCs) (strength of recommendation [SOR]: **C**, limited case series).¹⁻⁴ There is little convincing evidence to show a systematic interaction between other antibiotics and oral contraceptive steroids (SOR: **B**, based on systematic reviews, case reports, and pharmacologic studies).

However, current studies may not have separately evaluated the minority of women whose metabolism of contraceptive steroids makes them more vulnerable to OC failure.^{1-3,5,6} Given the significant consequences of unintended pregnancy, some experts recommend a conservative approach, including patient education and backup forms of birth control^{1,7} (SOR: **C**, expert opinion).

CLINICAL COMMENTARIES

Discussing drug interactions improves patient awareness and may prevent unplanned pregnancies

Identifying the patient at risk of OC failure is difficult. Add to that the unknown impact of antibiotics, and risk assessment becomes virtually impossible. Although rifampin is the only antibiotic shown at this time to interfere with the effectiveness of OCs, others may have the same effect. Thus, in my judgment, a conservative approach is best. Before prescribing oral contraception and antibiotics, I advise my patients that there may be a risk of contraceptive failure. As a result, many choose to use an additional nonhormonal method while taking antibiotics.

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Discussing the risk may not be the most beneficial use of your time

If antibiotics interact with OCs in a clinically significant way, the effect is uncommon and unpredictable. Discussing this with the patient may lead to undue anxiety, avoidance of needed antibiotics, nonadherence with the antibiotic or OCs or both, and, because of the time this discussion might take, neglect of other beneficial discussions (eg, smoking cessation). On both sides, risks and benefits are small. I don't bring it up if I'm prescribing a short course of an antibiotic. I might if I'm starting a long-term antibiotic (eg, for acne), knowing the patient will read the patient information from the pharmacy, which raises the concern.

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■ Evidence summary

Oral contraceptives (OC) are taken by approximately 70 million women worldwide.² Studies suggest there is extreme variation in plasma concentrations of active hormone between individuals, even without

any significant drug interactions.^{2,7} Current preparations contain lower doses of estrogen; a drug interaction causing decreased efficacy of OCs may be more likely.^{1,2,4,5}

More than 200 occurrences have been reported anecdotally, in adverse-event

monitoring systems, and in retrospective surveys of OC failure for women treated with various antibiotics. But no prospective RCTs have been done, and most of the retrospective case series have not used control groups.¹ All the pharmacokinetic and retrospective studies have a small sample size, which may conceal an interaction within the normal OC failure rate.^{1,2} Given this, 4 retrospective surveys on women taking OCs who were treated with antibiotics (erythromycin, tetracycline, minocycline, penicillin, ampicillin, sulfa, cephalosporins) found OC failure rates of 1.2% to 1.6%, within the range for typical populations.¹ These data are subject to recall bias and underreporting of poor compliance.

Multiple studies have looked at OC serum levels with and without antibiotic treatment.¹ These studies show that the coadministration of antibiotics (ampicillin, tetracycline, doxycycline, metronidazole, erythromycin, clarithromycin, temafloxacin, fluconazole, ciprofloxacin, or ofloxacin) did not reduce serum levels of either the estrogen or progestin components of the oral contraceptives.^{1,2} Rifampin is a potent inducer of the cytochrome P450 system, capable of reducing serum estrogen and progestin levels, and a small-scale study has suggested breakthrough ovulation among 2 of 9 women taking oral contraceptives and rifampin.^{2,8}

It is possible, however, that a true interaction between antibiotics and OCs may only manifest itself in the very small subset of women who have unusually low steroid hormone levels.¹⁻³ The women most likely to have pill failure are those with low rates of ethinyl estradiol hydroxylation, high rates of hepatic conjugation, low plasma concentrations of ethinyl estradiol, extensive intestinal hydrolysis of estrogen conjugates, or gut flora particularly susceptible to the antibiotic.^{1,3} These women may be identified by symptoms of breakthrough bleeding, cramping, nausea, vomiting or diarrhea, or by unwanted pregnancy.^{2,3} Unfortunately, they cannot be identified by any routine diagnostic tests. The most conservative approach emphasizes patient

education and additional forms of non-hormonal contraception for any woman on OCs during any antibiotic therapy and for at least 1 week after treatment.^{1,3}

Recommendations from others

Williams Obstetrics (2001) states that some antibiotics still have in their labeling that they may reduce the effectiveness of OCs, but that this is likely not true.⁹ They do not have a recommendation on how to handle this. The *MMWR Recommendations and Reports* (2003) recommend that women of reproductive potential on OCs who are also taking rifampin should add a barrier method of contraception.¹⁰ The World Health Organization (WHO) states that there have been suspicions that broad-spectrum antibiotics may lower OC effectiveness based on case reports, but that pregnancy rates are similar among women on OCs and women on both OCs and antibiotics.¹¹ According to the WHO 2003 Expert Working Group, broad-spectrum antibiotics are in Medical Eligibility Criteria category 1, which allows use in any circumstances.¹¹

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FAST TRACK

It is possible that a true interaction between OCs and antibiotics may occur in a small subset of women with low steroid hormone levels