



Antibiotics and Oral Contraceptive Failure

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Over the past 3 decades, published reports have described hundreds of women taking oral contraceptives who have become pregnant after a course of oral antibiotic therapy. Accordingly, many pharmacists warn patients on oral contraceptives to take additional precautions to avoid pregnancy when antibiotics are used concomitantly. Yet, there are many misconceptions about this purported interaction. Primary among these misconceptions is the belief that adequate data are available to prove or disprove the existence of the interaction.

A Bogus Interaction?

This interaction has not been disproved, despite frequent proclamations that it is a “myth.” Some people have erroneously concluded that—because there are substantial flaws in the data supporting the existence of the interaction—the interaction has been shown *not* to exist. In making this claim, however, they have failed to understand the saying “absence of proof is not proof of absence.”

Inadequacies in the Positive Studies and Reports

The reports of oral contraceptive failure during antibiotic therapy are numerous, but they are essentially anecdotal. Specific details of the cases are rarely

reported, and it is not possible to determine whether the unintended pregnancy resulted from the antibiotic or simply represents the “background” failure rate normally seen with oral contraceptives. Although some of the pregnancies occurred in women who had been taking oral contraceptives correctly and successfully for years, there is still no certainty that the antibiotic caused the contraceptive failure in any given case.

Inadequacies in the Negative Studies and Reports

There are also serious flaws in the studies that *failed* to find an increase in oral contraceptive failure rates with concurrent antibiotics. Virtually all of the studies had 1 or more of the following flaws: retrospective design, dependence on patients’ memory of events, long-term antibiotic use, or combining data for antibiotics that might reduce estrogen levels (eg, amoxicillin) with those for antibiotics that may *increase* estrogen levels (eg, erythromycin, clarithromycin).

Pharmacokinetic studies also have been performed, looking at the effect of various antibiotics on ethinyl estradiol pharmacokinetics, and in general they have found little effect. Some of the antibiotics used in these studies, however (eg, clarithromycin, ciprofloxacin, metronidazole) would not be expected to reduce estrogen levels. Moreover, if only a small fraction of women (eg, less than 5%) develop this interaction, as some people believe, a statistically significant change in estrogen pharmacokinetics would not be expected.

Other variables also have been disre-

garded in these studies. For example, women taking an antibiotic for an acute infection might be less likely to have sexual intercourse because they are not feeling well, either due to the infection or because of side effects of the antibiotic (eg, nausea, vomiting, diarrhea). This could result in an underestimation of the ability of antibiotics to reduce the efficacy of oral contraceptives. Another flaw in most negative studies is the failure to consider how many of the patients received information on how to avoid the interaction.

Proposed Mechanism of the Interaction

The mechanism, if any, is not clear. Theoretically, antibiotics such as penicillin and tetracycline can reduce bacteria in the intestine that are involved in the enterohepatic circulation of estrogens, leading to a reduction in estrogen serum concentrations. Other mechanisms include





enzyme induction following rifampin, griseofulvin, nafcillin, and dicloxacillin, or malabsorption of contraceptive hormones due to antibiotic-induced diarrhea and vomiting.

Pharmacists' Role

Women on oral contraceptives still should be warned about the possibility of contraceptive failure if they receive a prescription for an oral antibiotic. To comply with oral contraceptive product information, the patient should be advised to add alternative non-hormonal contraception during the time and for 7 days after the antibiotic is taken. No one knows, however, whether 7 days is enough. The pharmacist should recommend backup contraception for 2 weeks after discontinuation of the antibiotic or through the end of the current cycle—whichever is longer. Advising the patient to report any menstrual irregularities may be prudent, but there is no evidence that their absence ensures adequate contraception.

Conclusion

The available data produce this conclusion: In any given patient, antibiotics are unlikely to impair the efficacy of oral contraceptives. The data emphatically, however, do *not* establish that any antibiotic can be used in any woman on any oral contraceptive without increasing the risk of unintended pregnancy. Thus, only 2 possibilities are left: (1) antibiotics cause contraceptive failure in a very small percentage of patients, or (2) antibiotics have no effect on oral contraceptive efficacy. With the available data, it is simply not possible to choose which of these 2 possibilities is correct, so pharmacists must continue to warn patients accordingly. 

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