

Information For Patients: Antibiotic And Oral Contraceptive Interactions

There has been a lot of talk about whether taking antibiotics can interfere with birth control pills and lead to pregnancy. The overall risk is small and applies more to some antibiotics than others. Here is the current thinking of what experts believe is happening:

Will My Antibiotics Interact With My Birth Control Pills?

The actual incidence of pregnancy in women who take antibiotics while on birth control pills is unknown. There have been few reports considering the huge number of women who take birth control pills each year. However, there is a risk. For example, the antibiotic rifampin *will* interact with your pill, and other antibiotics might also interact. Some women may be more susceptible than others to getting pregnant when taking both antibiotics and birth control pills. Unfortunately, it's not possible to predict *which* women are at higher risk.

Why Does An Interaction Sometimes Occur?

Enzymes in the liver metabolize many of the drugs we take, including the hormones in birth control pills. Some antibiotics are metabolized by the same enzyme as the hormones in birth control pills, and can cause the hormones to be metabolized faster. When this happens, the blood levels of the hormones decrease, and the birth control pill becomes less effective. These antibiotics are very likely to make your birth control pill less effective.

Other antibiotics can decrease the bacteria normally found in the intestines of healthy people. These bacteria help break down estrogen compounds and release active hormone which is then reabsorbed. Without these bacteria, there's less active hormone in the bloodstream for the body to use. Lower hormone levels can increase the chance that your birth control pill won't work.

Which Antibiotics?

Some antibiotics are more likely than others to make your birth control pill less effective. Antibiotics that speed up the metabolism of the pill, such as rifampin (*Rifadin*, etc.) and griseofulvin (*Gris-PEG*, etc.), are the most likely to interact. Other antibiotics, such as those in the penicillin and tetracycline classes, also carry a risk of making your birth control pill less effective, although the risk is less than with rifampin. Some antibiotics in the penicillin and tetracycline classes include penicillin (*Pen Vee K*, etc.), ampicillin (*Omnipen*, etc.), amoxicillin (*Amoxil*, *Augmentin*, etc.),

dicloxacillin (*Dynapen*, etc.), tetracycline (*Sumycin*, etc.), doxycycline (*Vibramycin*, etc.), and minocycline (*Minocin*, etc.). Keep in mind that this is *not* a complete list and other antibiotics might also decrease the effectiveness of your birth control pill. Check with your pharmacist or prescriber if you need to take *any* antibiotic and are concerned about the risk of getting pregnant.

What Can I Do To Prevent Pregnancy While On Antibiotics?

Even though the risk of getting pregnant when taking antibiotics while on birth control pills is small, there is still a risk. Remember that it's usually not possible to tell whether or not you are one of the women who are at high risk. This is especially important today because we now have birth control pills with lower doses of hormones to reduce side effects of the pill. If you take a low-dose birth control pill you might be at higher risk of getting pregnant while taking antibiotics. Low-dose birth control pills include: *Alesse*, *Aviane*, *Cyclessa*, *Levlite*, *Loestrin 1/20*, *Loestrin Fe 1/20*, *Mircette*, and others.

If you need to take rifampin or griseofulvin, and want to continue taking birth control pills, you should also use a second method of birth control while on these antibiotics. Another option is to change to a high-dose birth control pill. Check with your prescriber about what is the best choice for you.

If you need to take any other type of antibiotic and are not comfortable with the risk of getting pregnant you should also use a second method of birth control. You should also use a second method of birth control if you develop breakthrough bleeding while on antibiotics or if you've gotten pregnant while on birth control pills in the past. The second method should be a nonhormonal type (condoms, abstinence, etc.). If you will be taking antibiotics SHORT-TERM, you should also use the second method of birth control for the full time you are taking the antibiotics, and for at least 7 days after you finish them or until the end of your cycle. If you will be taking antibiotics LONG-TERM, such as for acne, you should also use the second method of birth control for at least two weeks after starting the antibiotic, until your intestinal bacteria become resistant, and the birth control pill becomes effective again. Check with your pharmacist or prescriber if you have any questions about how to avoid getting pregnant.

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Antibiotic-Oral Contraceptive Drug Interactions

Lead author: Kay Shaver, Pharm.D., Assistant Editor

Frequency Of Occurrence

It is well-known that certain drugs, such as phenobarbital, phenytoin, and carbamazepine, interact with oral contraceptives (OCs) and can increase the risk of contraceptive failure and pregnancy. But evidence supporting antibiotics' role in decreasing the efficacy of OCs is less definitive, and so this drug interaction is somewhat controversial. The information we have generally comes from case reports, adverse-event monitoring systems, and retrospective surveys, rather than controlled clinical trials.^{1,2}

There are relatively few reported cases of oral contraceptive failure in women who also took antibiotics, especially considering the large number of women who use OCs. Surveys have shown failure rates of 1.2% to 1.6% in women taking both OCs and antibiotics. Although these numbers are greater than those ideally predicted with perfect compliance, they are within the 1% to 3% that is seen with typical use. Because of this low rate of OC failure, it is difficult to determine whether such an incidence is due to the antibiotic or is within the expected failure rate.^{1,2}

Mechanism

Ethinyl estradiol is the estrogenic component of most combined oral contraceptives. It is metabolized in the liver by cytochrome P450 3A4, excreted in the bile, broken down by intestinal bacteria, and then reabsorbed as an active drug.^{1,3,4}

Two suggested mechanisms for how antibiotics can affect OC effectiveness involve liver metabolism and enterohepatic circulation. The most significant interactions are those that occur with other drugs metabolized by the same liver enzyme as estrogen. These would include rifampin and griseofulvin. Rifampin is a potent inducer of cytochrome P450 3A4 and accelerates the elimination of ethinyl estradiol and some progestin components, resulting in an increased risk of OC failure. Rifampin also affects sex hormone-binding globulin (SHBG). SHBG has a high affinity for progestins and drugs that increase

SHBG's binding capacity can decrease the levels of free progestin.^{1,2,4,5}

Antibiotics that don't affect liver metabolism can interfere with OC efficacy by another mechanism. Intestinal bacteria break down estrogen conjugates to restore free estrogen for reabsorption via enterohepatic circulation. Some antibiotics may alter intestinal bacteria which interrupts enterohepatic circulation and can lead to a decrease in the amount of circulating estrogen. Interestingly, some antibiotics may actually increase the levels of ethinyl estradiol and some progestins. Macrolides and azole antifungals inhibit the same liver enzyme (CYP450 3A4) that metabolizes ethinyl estradiol.¹⁻⁴

It's possible that certain women are at high risk for an interaction between antibiotics and OCs. The actual incidence of OC failure is not known, and unfortunately, the risk of failure can't be predicted in individual women. There are large variations between women in plasma concentration and clearance of estrogens and progestins. This means that some women might be more susceptible to OC failure while receiving antibiotics, but we are not able to predict *which* women. This is especially important considering the development of new, lower-dose oral contraceptives (*Cyclessa*, *Levlite*, *Mircette*, etc.). Drug interactions that lead to decreased effectiveness of OCs may be more likely when a woman is taking lower-dose contraceptives.¹

The chance of having a significant interaction between OCs and antibiotics depends on several factors, including: 1) the amount of estrogen/progestin in the OC and the amount needed by the woman, 2) dose and duration of use of the antibiotic, 3) individual variation in response to alteration of bacterial flora, and 4) fertility of the couple. Predicting the outcome in specific women is difficult if not impossible.³

Recommendations

Today it is common to counsel women taking broad-spectrum antibiotics that treatment with

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these drugs may reduce the efficacy of their OC. Although the risk of OC failure appears to be very small, the consequences of an unwanted pregnancy should be taken very seriously. In addition, there is not yet enough evidence to support abandoning this practice. It is advisable to be cautious in order to protect those women using OCs who may be at high risk of OC failure if they take antibiotics.^{1,3,5}

Women taking rifampin with OCs have a significant risk of OC failure. A different method of contraception can be suggested if a woman will be taking rifampin or griseofulvin long-term. For women who choose to use OCs while taking these drugs, tell them they should also use a nonhormonal method of contraception, such as condoms or abstinence, during treatment. Another alternative is to switch to a high-dose (50 micrograms of estrogen) pill during treatment. Suspect interference with OC effectiveness if breakthrough bleeding and/or spotting occurs while taking these drugs together with OCs.^{1,3,5}

Switching to a pill containing a high-dose of estrogen is not practical during typical short-term use (less than two weeks) of antibiotics. Instead, counsel women to continue taking their OC, but to also use a back-up method of contraception such as a condom or abstinence. Some sources recommend continuing to use both methods of contraception for the duration of antibiotic treatment and for at least seven days thereafter. Other sources recommend the alternate method of contraception should be continued for the duration of the cycle. A different approach can be used during long courses of antibiotics, for example when tetracycline is used for acne. In this case, some experts recommend using a back-up method of contraception for at least two weeks from the start of antibiotic treatment, until the intestinal flora become resistant, to allow restoration of normal pill efficacy.^{1,2,4,5}

Counsel women who use OCs that there is a

small overall risk of a drug interaction with antibiotics, and that it's not possible to identify in advance who is at high risk for OC failure. Tell women who aren't comfortable with this risk to also use a nonhormonal method of contraception. Women who have had OC failures in the past or who develop breakthrough bleeding while using antibiotics with OCs should use an alternate method of contraception. These women may be part of the group of women at high risk of contraceptive failure.¹

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References

1. Dickinson BD, Altman RD, Nielsen NH, et al. Drug interactions between oral contraceptives and antibiotics. *Obstet Gynecol* 2001;98:853-60.
2. Ament PW, Bertolino JG, Liszewski JL. Clinically significant drug interactions. *Am Fam Physician* 2000;61:1745-54.
3. Ruggiero RJ. Contraception. In: Young LY, Koda-Kimble MA, Kradjan WA, et al. *Applied Therapeutics: The Clinical Use of Drugs*. 6th ed. Vancouver, WA: Applied Therapeutics, Inc., 1995:43.
4. Carmichael JM, Wieland KA. Contraception and infertility. In: Herfindal ET, Gourley DR, eds. *Textbook of Therapeutics: Drug and Disease Management*. 6th ed. Baltimore, MD: Williams & Wilkins, 1996:1752-1753.
5. International Planned Parenthood Federation. Statement on steroidal oral contraception. September 1998. Available at: www.ippf.org. (Accessed 1/14/02)

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