

Antibiotics: Avoiding Interactions

By Amy Ehlers, BS, PharmD, BCPS

According to the Food and Drug Administration (FDA), there were more than 480,000 adverse events associated with drugs and therapeutic biological products reported by consumers, healthcare providers and drug manufacturers in 2007. Of these, nearly half a million adverse events, or more than 270,000, were associated with a serious outcome, such as hospitalization or death. While this number may appear high, it represents only a fraction of the nearly 3.5 billion prescriptions that were filled in retail pharmacies in 2007.

The single, largest group of medications, antibiotics, can have side effects and interactions that can range from mild and inconvenient, to serious and potentially life-threatening. How can patients avoid becoming one of these adverse event statistics?

Use of Antibiotics


Patients should avoid taking antibiotics unless absolutely necessary. This may be much easier said than done for those with an immune deficiency. However, ensuring that patients do not self treat unless directed by a physician is the most important first step. Antibiotics are effective only against infections caused by bacteria and should not be used for viral illness such as influenza, colds and non-bacterial sore throats.

Following directions is also important. There is a misconception that if a little medicine works, a lot must be better. Patients may be tempted to increase the dose or frequency of their medication, because they are "really sick" compared to last time. But, making this decision without consulting a physician can have



serious consequences. It can cause kidney or liver damage or other potentially permanent effects.

With each overuse or misuse of antibiotics, the risk of antibiotic resistance increases. Bacteria are able to quickly mutate in an attempt to survive the hostile environment created by the antibiotic. Over time, the bacteria adapt in



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such a way that they become harder to kill and have the potential to cause more serious infections that are more difficult and costlier to cure. These antibiotic-resistant bacteria then have the ability to be spread to others.

One of these bacteria, *Clostridium difficile* (often referred to as *C. difficile* or *C. diff*), is also a potential risk with antibiotic use. *Clostridium difficile* naturally occurs in the large intestine. With broad-spectrum, high-dose or long-term antibiotic use, especially in older adults, the other normal bacteria in the gut die off, allowing the *C. difficile* to overgrow and produce toxins. These toxins cause swelling and irritation of the large intestine that manifests as watery diarrhea (at least three episodes a day for two consecutive days), fever, loss of appetite, nausea and abdominal pain/tenderness. In more severe cases, *C. difficile* can cause pseudomembranous colitis, a severe inflammation of the colon with blood and pus in stools, which can cause death. This infection can be treated with oral metronidazole or oral vancomycin. However, like other bacteria, resistant strains of the *C. difficile* bacteria have been seen, which have caused conventional treatments to be less effective.

Antibiotics and Drug Interactions

Drug interactions are a concern with antibiotic use. There are several categories of drug interactions: drug-drug, drug-food and drug-nutrient.

Drug-drug interactions are the most likely to cause more serious events. Most of these interactions occur due to a change in one of the drug's levels caused by a change in metabolism of one the drugs. The greater the change in drug concentration or the more narrow the therapeutic window, the more likely or severe a drug interaction will occur.

A well-documented drug interaction is between oral contraceptives and antibiotics. An increase in the clearance of the oral contraceptive estrogen can decrease its effectiveness. Patients should discuss appropriate alternatives with either their physician or pharmacist.

Patients taking the drug warfarin (Coumadin) should also be aware of the potential for a change in their bleeding duration. Warfarin doses may need to be adjusted while on an antibiotic, and then changed again once antibiotic therapy is completed.

The heart medication digoxin (Lanoxin) can be problematic when taken with several antibiotics. Digoxin has a narrow line between effectiveness and toxicity, so when taken with antibiotics such as clarithromycin (Biaxin) or azithromycin (Zithromax), the level of digoxin may increase, causing some of its toxic side effects.

Antibiotics can have interactions not only with other drugs, but food as well. It is important to know if there are any restrictions when taking antibiotics in relation to meals. Most antibiotics can be taken independent of meals and snacks, but that is not always the case. For example, amoxicillin (Amoxil) is best taken on an empty stomach, which is usually defined as one hour before or two hours after a meal. If taken with food, the effectiveness of the antibiotic is reduced and may be the equivalent of throwing the dose in the trash.

The type of foods eaten with antibiotics may also be of concern. For instance, grapefruit juice has been shown to affect the metabolism of a large group of drugs, including some antibiotics. Patients who tend to consume large amounts of whole grapefruit or juice should inform their physician and pharmacist.

Medications in the tetracycline (doxycycline) and fluoro-

Table 1. Antibiotics and Their Common Uses

Antibiotic Class	Generic Name (Brand Name)	Common Uses
Penicillins	Penicillin V (Pen V K) Amoxicillin (Amoxil) Amoxicillin/clavulanic acid (Augmentin)	Skin, urinary tract, dental, ear infections
Cephalosporins	Cephalexin (Keflex) Cefaclor (Ceclor) Cefuroxime (Ceftin)	Pneumonia, upper respiratory, skin, ear, dental infections
Macrolides	Erythromycin (Ery tab) Azithromycin (Zithromax) Clarithromycin (Biaxin)	Respiratory, gastrointestinal, soft tissue, genital infections
Fluoroquinolones	Ciprofloxacin (Cipro) Levofloxacin (Levaquin) Moxifloxacin (Avelox)	Respiratory, skin, urinary tract infections
Sulfas	Sulfamethoxazole/Trimethoprim (Bactrim DS) Sulfisoxazole (Gantrisin)	Urinary tract, skin, ear infections, chronic bronchitis exacerbations
Tetracyclines	Tetracycline (Achromycin) Doxycycline (Vibramycin) Minocycline (Minocin)	Respiratory infections, acne, Lyme disease

quinolone (ciprofloxacin) classes should not be taken with calcium-, magnesium-, iron- or zinc-containing foods or dietary supplements one hour before or two hours after. The drugs will bind with these elements rendering them ineffective. Calcium, magnesium, zinc and iron can be found in foods and dietary supplements, such as multivitamins, as well as over-the-counter medications, such as antacids.

Herbal medications also have the potential to interact with antibiotics. St. John's wort, an herbal product often used for depression, can increase the photosensitivity in fluoroquinolone, tetracycline or sulfa antibiotics. Green tea extracts, when taken with fluoroquinolones, can decrease the clearance of the caffeine and its derivatives found in the green tea. This may cause an increase of classic caffeine symptoms such as nervousness, insomnia and heart palpitations.

It should be noted that the herbal and natural products industry is not regulated by the FDA and, therefore, is not held to the same manufacturing standards and practices as prescription and over-the-counter medications. This is not to say that all herbal and natural products are unsafe and should not be used. What this means is that the review process concerning appropriate doses and dosage forms and the study of side effects and interactions are not required and, therefore, there is no oversight to ensure

the products are safe and effective. As a precautionary measure, patients should read all information contained on a product's label and packaging, and discuss using the product with their physician or pharmacist.

Mixing alcohol and antibiotics can have different effects depending on the drug. Alcohol can cause side effects such as drowsiness, stomach upset and dizziness. When alcohol is consumed with antibiotics, the same outcomes can occur and the effect can be intensified. When the drug metronidazole (Flagyl) is taken with alcohol, a severe reaction, called a disulfiram reaction, can occur. This reaction will cause nausea, vomiting, flushing, headache, rapid heart rate and shortness of breath. Patients should be aware that there may be alcohol in over-the-counter cold and cough medications, as well as mouthwash.

As a rule of thumb, patients should always protect themselves when out in the sun. This is especially important when taking fluoroquinolones, tetracycline or sulfa antibiotics, as these types of antibiotics can cause photosensitivity, which can cause sunburns despite the use of sunscreen.

Antibiotics and Drug Allergies

Drug allergies are another common challenge with medications, but especially with antibiotics. An allergic response is defined as a hypersensitive immune reaction to

a substance that normally is harmless or would not cause an immune response in most people. There are two main types of allergic reactions: IgE mediated and T cell mediated. Reactions that are IgE mediated typically occur within one to two hours of exposure and may include anaphylaxis and/or anaphylaxis-related symptoms, such as bronchospasm (difficulty breathing), angioedema (swelling of the face, mouth and throat) and urticaria (hives). These reactions are serious and potentially life-threatening, and require immediate medical attention. T cell mediated reactions are usually delayed reactions occurring anywhere from six hours to weeks following exposure, and they are commonly expressed as skin symptoms, such as a rash. These reactions can be resolved on their own or with antihistamine or steroid treatment.

If a patient suspects an allergic reaction to a medication, they should contact their physician to determine the next steps to take, and provide them the opportunity to see the reaction firsthand. Once an allergic reaction is confirmed, the drug and reaction should be noted in the patient's medical record and consistently noted when seeing any healthcare provider.

It is not uncommon for patients to report allergies to medications that are actually sensitivities to, or known side effects of, the medications. Many side effects of antibiotics are not life-threatening, but they can make life miserable. Patients may report a sensitivity or side effect as an allergy based on their level of tolerance to the specific side effect.

For example, diarrhea is fairly common with the oral antibiotic Augmentin, which is in the penicillin family. Patient A may describe the event as a less-than-pleasant experience, but tolerable, and will be able to complete the entire course of therapy. If Patient A were to be prescribed Augmentin again, they may ask for an alternative if possible, but would not describe themselves as being allergic to either Augmentin or penicillin. Patient B may describe the same event as the worst experience ever and stop taking the medication after the first few days.

If Patient B were prescribed Augmentin again, they will state that they are allergic to it and can never take it again. Their physician marks the medical record as allergic to Augmentin.

This may never be an issue. But, what happens if Patient B is hospitalized with a serious staph infection and the treating physician wants to use nafcillin, a penicillin derivative? If Patient B merely states that they are allergic to penicillin and does not or is unable to disclose that the reaction was diarrhea, the physician will be forced to pick another class of antibiotics. The alternate choice of antibiotic may require a longer duration of therapy, have an increased potential for side effects or be more expensive than the original antibiotic preferred by the physician.

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Taking Control of Antibiotic Use

The best advice when it comes to safely using not only antibiotics, but any medications, is to have open, constant and thorough communication with all members of your healthcare team. Patients should keep lists of all prescriptions, over-the-counter, vitamins and herbal products taken regularly,

including the date started, strength, dose and frequency of administration. This list should be updated regularly and given to any provider who is not aware of the changes to help avoid problems before they occur. Medications should always be taken as prescribed by the physician, and patient counseling information provided by the pharmacist should always be followed. If something is unclear, patients should not be afraid to ask questions or to ask for something to be repeated or further clarified. Ultimately, patients are responsible for their own health and well-being and should take an active role in trying to achieve that goal. ■

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