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JULY 1996

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BEFORE YOU TAKE THAT PILL...

Drugs are so pervasive in our lives that many of us never stop to think about how cavalierly we consume them: the birth control pill gulped down with our orange juice each morning; the antacids taken after a quick lunch at our desks; the sleeping tablets we turn to at the slightest hint of insomnia.

Often, we take several different drugs at the same time, probably without giving it a thought. Usually, the medicines do their jobs and that's that. But not always. Sometimes, inside the body, certain drugs may deactivate other ones or, worse, combine to form a dangerous—even lethal—brew. "Taking more than one medicine at a time could be like loading a gun and spinning the chamber," point out pharmacologist Joe Graedon and his wife, medical anthropologist Teresa Graedon, in their book *The People's Guide to Deadly Drug Interactions* (St. Martin's Press, 1995). "Do you really want to play Russian roulette?"

And it can fall to women to protect themselves, because doctors may lag in their knowledge of the hundreds of drugs known to interact. Consider this alarming scenario, reported in 1993 in *The Journal of the American Medical Association*: A twenty-nine-year-old woman with nasal congestion had been using the popular antihistamine Seldane regularly when her physician prescribed Nizoral, an antifungal agent, to treat a nail infection. A week later, she fainted and was rushed to an emergency room. Three days later, she died of heart failure.



You may not think about the pills you pop every day, and your doctor and pharmacist may not, either. Here, what you need to know to avoid a lethal interaction

By Kathleen McAuliffe

A rare aberration in medical care? Unfortunately not. The manufacturer of Seldane had sent warning letters to doctors about this interaction three years *before* this incident occurred, yet a study conducted a year later in Oregon uncovered 122 cases in which Seldane and Nizoral were still being prescribed together.

Even scarier, pharmacists—the last line of defense for protecting patients from prescription errors—may not always be knowledgeable. In a letter published recently in *The Journal of the American Medical Association*,

doctors at Georgetown University Medical Center reported that when they took a prescription for Seldane and the antibiotic erythromycin—two drugs whose interaction has been well publicized—to fifty pharmacies in the Washington, D.C., area, 32 percent filled the prescriptions.

In other instances, it's a lack of communication that leads to trouble. "It's not unusual for a woman to get one prescription from her dermatologist, another from a gynecologist and still another from her general practitioner," says James O'Donnell, president of Pharmaconsultant Inc., a pharmacology and pharmacy consulting firm in Inverness, Illinois.

Just how often do serious interactions occur? No one knows for sure. The Food and Drug Administration (FDA) does require pharmaceuticals manufacturers to test for interactions before approval to market a new drug. However, says Philip Hansten, a leading expert on drug interactions and a professor of pharmacy at the University of

Washington, in Seattle, "The number of potentially dangerous combinations is so large that it would be economically prohibitive to test for them all." As a result, a drug may be on the market for months or years before a serious interaction comes to the attention of health professionals. And once an interaction has been documented, doctors and pharmacists may be reluctant to report subsequent cases out of fear of malpractice litigation. In fact, one study found that "only about one percent of serious (continued on page 64)

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[interaction-related] events are reported.”

To help you guard against dangerous combinations, *Ladies' Home Journal* has quizzed the experts on which interactions are of greatest risk to women in their thirties and forties. Here, five important ones to know. (Check with your doctor before taking one of these drug combinations. If you're already doing so, be sure to consult your doctor before stopping; abruptly halting any drug can be dangerous, too. Occasionally, it may be safe to take interacting medicines, but *only* under careful medical supervision. And never mix any medication with alcohol.)

■ **Don't take non-sedating antihistamines** (Seldane and Hismanal) **with antifungal medicines** (such as Nizoral and Sporanox) **or antibiotics** (such as erythromycin and Biaxin).

In recent years, Seldane (terfenadine) and Hismanal (astemizole) have provided relief from allergy symptoms without turning sufferers into zombies. As their popularity has soared, however, there have been mounting reports of dangerous interactions.

Patients have experienced such problems as heart-rhythm disturbances and cardiac arrest from taking both Seldane and Nizoral



TAKING DRUGS WITHOUT DANGER

1. Always inform *all* your health-care providers—your primary-care doctor, dentist and pharmacist—of all the drugs you're taking, including over-the-counter (OTC) remedies.
2. Have all prescriptions filled by the same pharmacy so the pharmacist can monitor your medications. To find a good pharmacist, get recommendations from friends and your doctor.
3. Know both the brand and generic names for each medication you're taking. Drug-interaction warnings on packages may identify medications by either name.
4. Consult your doctor or pharmacist before taking an OTC medicine if you're using a prescription drug.
5. Read nonprescription medication labels carefully: Products with similar names may have very different ingredients.
6. Take as few drugs as possible.
7. Check with your doctor before taking vitamins along with a prescription or OTC drug. Some supplements can interact dangerously with drugs; others can negate a medication's beneficial effects.

(ketoconazole), a drug prescribed for fungal infections of the toenails and fingernails. Combining Hismanal with antifungal drugs is similarly risky, because its chemical makeup

resembles that of Seldane. These antihistamines also interact with antibiotics like erythromycin or Biaxin, commonly prescribed to treat infections of the skin, ear, and respiratory and reproductive tracts.

Why both of these possibly deadly interactions occur is well understood: Before being absorbed into the bloodstream, Seldane and Hismanal are broken down by enzymes in the small intestine and liver. Nizoral and erythromycin interfere with those enzymes, causing the antihistamine to climb to toxic levels, damaging the heart.

Fortunately, not all non-sedating antihistamines carry this risk. A good alternative for people who need to take antifungals or antibiotics is a new antihistamine called Claritin (loratadine), which does not cause cardiac problems—even in high doses.

■ **Don't take monoamine oxidase inhibitor (MAOI) antidepressants** (such as Nardil, Parnate, Marplan) **with selective serotonin reuptake inhibitor (SSRI) antidepressants** (such as Prozac, Paxil, Zoloft), **tricyclic antidepressants** (such as Pamelor, Elavil, Norpramin, Tofranil), **cold and cough medications containing ephedrine, phenylephrine, phenylpropanolamine (PPA), pseudoephedrine or dextromethorphan**

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The Pill: What you need to know if you take it with anticonvulsants (such as Tegretol, Dilantin), antibiotics (such as ampicillin, tetracycline, penicillin-like drugs), barbituates, drugs to treat tuberculosis (TB), or antifungals.

More than ten million women rely on the Pill to prevent unwanted pregnancies, but few realize that its effectiveness can be compromised by other drugs. This is especially true now that many oral contraceptives contain less estrogen and progestin than they did thirty years ago (the lower the hormone dose, the more vulnerable the Pill is to deactivation by another drug). Pill users should be alert to breakthrough bleeding and other menstrual irregularities—signs that they may not be fully protected against pregnancy.

Many antibiotics are suspected to diminish the power of the Pill—perhaps by killing bacteria in the colon that may play a role in maintaining adequate blood levels of Pill hormones (some researchers dispute the theory). However, all experts agree that Pill takers need to use an additional form of birth control when taking antibiotics.

Users of oral contraceptives should be especially wary if they need to take the anticonvulsant drugs Tegretol or Dilantin, often prescribed for epilepsy. These compounds are known to alter Pill metabolism, rendering it less effective. This interaction is particularly worrisome because anticonvulsants can increase the risk of birth defects such as deformities of the face and hands.

Also known or suspected of reducing the Pill's protection against pregnancy are the TB drug rifampin, certain antifungals used to treat infections of the toenails and fingernails, and barbituates, often prescribed as anticonvulsants. Beware: The latter can turn up in unexpected places—notably in the popular prescription tension-headache remedies Fiorinal and Fioricet.

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(Sudafed, NyQuil, Dime-tapp Elixir and many other OTC cold treatments), **painkiller meperidine** (Demerol), **or foods containing tyramine** (including processed meats like salami, aged cheeses and over-ripe fruits).

MAOI antidepressants are prescribed for those who don't respond to the newer antidepressants like Prozac. They are also used to treat eating disorders like bulimia, obsessive-compulsive disorder and panic disturbances.

Doctors have known since the 1960s that MAOIs interact with foods containing the chemical tyramine. But since then, new interactions have surfaced. Especially worrisome is the use of MAOIs along with other types of antidepressants. Because psychiatrists can rarely predict which individuals will benefit from a particular drug, a patient may be switched from one to another. But combining an MAOI with a tricyclic can produce fever, agitation, rapid heart rate and coma; combining an MAOI with an SSRI can produce nausea, shivering, confusion and uncontrollable muscle contractions. In the case of SSRIs, a rapid increase in brain levels of serotonin may cause this reaction.

Surprisingly, the combination may be dangerous even if the drugs are taken *consecutively* rather than simultaneously, because antidepressants have long-lasting effects on brain chemistry. Experts advise waiting at least five weeks after stopping Prozac and two weeks after stopping a tricyclic before starting treatment with an MAOI, and waiting two weeks when switching from an MAOI to another antidepressant.

The painkiller meperidine (Demerol) in conjunction with an MAOI can be just as deadly. The

WHY MELATONIN AND ANTIDEPRESSANTS

DON'T MIX

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any of us, wooed by the promise of a cure for jet lag, insomnia or depression, have been taking regular doses of melatonin, the hormone produced by the brain that is responsible for our wake/sleep cycle.

Because the hormone is regarded as a supplement and not as a drug, many people think of it as harmless. Yet when it is taken with certain antidepressants (the serotonin reuptake inhibitors, or SSRIs, like Prozac; or the monoamine oxidase inhibitors, or MAOIs, like Nardil), a potentially dangerous interaction could occur. Melatonin and these antidepressants stimulate the effects of the chemical serotonin, low levels of which have been associated with depression. Taken together, these substances could cause what's known as serotonin syndrome. This toxic reaction occurs when serotonin is overactive in the body. It can cause a stroke or heart attack. Symptoms of the syndrome include confusion, restlessness, sweating, shivering and tremors, as well as a lack of coordination, increased blood pressure, high fever, diarrhea and convulsions. So before you take melatonin, review the medications you're taking with your doctor.

—Mary Jackson-Leavitt, Pharm.D.

reason is not well understood, but the result is a buildup in levels of the neurotransmitter serotonin, which can culminate in a heart attack or stroke.

Even a seemingly innocuous OTC cold remedy (see list, above left) can be lethal when combined with an MAOI. The MAOI prevents the breakdown of norepinephrine, a neurotransmitter involved in blood vessel constriction. When you take an MAOI, levels of norepinephrine build up in nerve cells throughout the body. Taking a decongestant, too, releases the stored norepinephrine, causing a rapid increase in blood pressure that can lead to a stroke. So check the label of your medication before combining the two. And don't be fooled by products with virtually identical names: One woman taking an MAOI suffered a life-threatening elevation of blood pressure when she took Robitussin PE (which contains a decongestant). In fact, her physician had recommended *regular* Robitussin.

■ **Don't take the asthma drug theophylline** (such as Primatene tablets—not the mist—Slo-bid and

Theo-Dur) **with the ulcer drug Tagamet** (cimetidine) **or antibiotics** (erythromycin and Cipro).

Theophylline, one of the best-selling asthma medications in the world, makes breathing a lot easier for millions of Americans who suffer from chronic asthma. But because the drug's therapeutic dose is only slightly smaller than the dose that will induce side effects, extreme care must be used when taking other medicines.

Theophylline can upset the stomach. But taking the heartburn and ulcer drug Tagamet to treat the problem can lead to life-threatening theophylline toxicity (Tagamet interferes with

the metabolism of theophylline, boosting blood levels of the asthma drug by 33 to 50 percent). Signs of theophylline toxicity include persistent nausea, vomiting, diarrhea, headache, restlessness, heart palpitations and seizure. According to research, a person's risk for theophylline toxicity increases fivefold if she takes Tagamet. Also a potential cause of theophylline toxicity are certain antibiotics that may be prescribed to treat the respiratory infections asthmatics often develop.

Other drugs, notably birth control pills containing estrogen, may alter theophylline metabolism, changing the dose necessary to achieve symptom control. Tell your doctor about every drug you're taking. ●

Kathleen McAuliffe is a former senior editor at U.S. News and World Report.

For More Information

Read *The People's Guide to Deadly Drug Interactions* by Joe Graedon and Teresa Graedon (St. Martin's Press, 1995), and *The Consumer's Guide to Drug Interactions* by Jeffrey R. Schein and Philip Hansten (Collier Books, 1993).