Danger at the Drugstore

Too many pharmacists fail to protect consumers against potentially hazardous interactions of prescription drugs

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A Philadelphia CVS store makes the point with a gum machine filled with colorful prescription drugs: "This is not," the sign says, "how it works." Far from just pill dispensers, the message reminds customers, pharmacists deserve respect as important partners with other healthcare providers in the field of disease management. They are getting it, too. In 11 states, pharmacists have been granted the limited right to prescribe certain medications—a privilege traditionally reserved for doctors. More generally, pharmacists are regarded as among the nation's most admired professionals. In several recent Gallup polls, for instance, Americans ranked pharmacists above doctors, teachers, even clergymen.

That's the perception. The reality, according to an exclusive new study by U.S. News in cooperation with Georgetown University School of Medicine, is that many of the nation's pharmacists are falling down on the job. In particular, they are failing to protect consumers against dangerous interactions of prescription drugs, an exploding health-care problem that sends hundreds of thousands of Americans to the hospital every year.

The U.S. News investigation, which tested 245 pharmacies in seven cities, found that well over half of all pharmacists failed to warn consumers when presented with prescriptions for drugs that, when taken separately, are safe but when taken together can be at best risky and at worst deadly. So dangerous was one interaction that medical experts said the prescriptions should never have been filled at all. Yet a disturbing one third of pharmacists dispensed both medications with no comment beyond, "Thank you, have a nice day." The results, says Dr. Marcus Reidenberg, a pharmacologist at New York Hospital–Cornell Medical Center, "prove that systems to correct prescription errors in this country are of very limited reliability." Says Dr. Thorir Bjornsson of Jefferson Medical College in Philadelphia: "The disappointing results of this study should serve as a wake-up call to the entire industry."

The magazine's investigation expands on a study earlier this year of pharmacists in Washington, D.C., by researchers at the Georgetown University Medical Center's Division of Clinical Pharmacology. That study found that more than 30 percent of Washington pharmacists did not challenge doctors who simultaneously prescribed the potentially deadly mix of Seldane, the popular non-sedating antihistamine, and erythromycin, a common antibiotic. Working with Georgetown's Dr. Raymond Woosley, who conducted the study with colleagues Dr. Nicholas Cavuto and Dr. Mark Sale, U.S. News asked seven physician-pharmacologists to write prescriptions for
three other drug combinations with reactions of varying degrees of familiarity and severity. A pharmacist was considered to have warned the patient if he counseled him, offered to call the doctor or refused to fill the prescriptions. The findings:

About one third of pharmacists did not alert consumers to the potentially severe and widely publicized interaction between Hismanal, a common antihistamine, and Nizoral, an often-prescribed antifungal drug. Like Seldane and erythromycin, the Hismanal-Nizoral mix can cause irregular heartbeat, cardiac arrest and sudden death. Clearly contraindicated, the prescriptions prompted such stunned druggist reactions as "What was your doctor thinking?" and "Don't even try to fill this prescription anywhere else." But 32 percent of the pharmacists dispensed the potentially lethal combination with no verbal warning, and half of those filled it with only a vague written caution. Some pharmacists went so far as to counsel consumers to take Hismanal on an empty stomach and Nizoral with food but were silent on the fact that taking them together could kill the patient.

Only four out of 17 pharmacists warned of the acute interaction between oral contraceptives and Rimactane, an antibiotic used to treat tuberculosis. Like some other antibiotics, Rimactane diminishes the effect of birth-control drugs and can render them ineffective. "Heck, yeah, an unintended pregnancy when you're on birth control deserves a verbal warning," says Reidenberg, echoing widespread medical opinion. But 77 percent of those surveyed didn't issue verbal warnings; fewer than half included a written suggestion to use a backup contraceptive.

Only three out of 61 pharmacists issued any verbal warnings about the interaction between Vasotec and Dyazide, both drugs used to control high blood pressure. Used together, these drugs can trigger a condition called hyperkalemia, an abnormally high level of potassium that can cause dizziness, heart failure and death. The risk of heart attack is low, and the condition rare, but, says Dr. Bjornsson, "the public needs to know that, especially if they are just starting out taking the two drugs." Of the 61 pharmacists asked to fill prescriptions for the two, only one declined to do so.

Consumers' chances of being alerted to potentially dangerous drug interactions varied widely among the cities surveyed. In Denver, more than half the pharmacists tested dispensed Hismanal–Nizoral without verbal warnings. In suburban New York, 40 percent did. But Indianapolis pharmacists were a far more cautious lot: All but three of 20 pharmacists surveyed refused to fill the prescriptions, and the three who did fill them issued strong warnings against taking the two drugs together.

Fewer than half the pharmacies surveyed included written warnings with the drugs after filling the prescriptions, and what warnings there were varied considerably in usefulness and reliability. A minority offered detailed information about interactions; more often, the warnings counseled patients simply to "talk with your physician if you are taking other medications." Thorough or not, written alerts are no substitute for verbal warnings: "Even my wife throws them away," says Columbus, Ohio, pharmacist Martin Ruehle.

Although independent drugstores represented half the total pharmacies tested, they accounted for nearly two thirds of the pharmacies that failed to warn consumers of the most dangerous of the three drug interactions. And while pharmacies in low- and lower-middle-income neighborhoods represented less than half the total survey sample, they accounted for nearly two thirds of the pharmacies that failed to warn consumers of the most dangerous interactions.

The magazine's findings come at a time of unprecedented prescription drug use in the United States—and growing concern about side effects. Filling more than 2 billion prescriptions a year, pharmacists are widely regarded as the last line of defense in
catching doctors' prescribing errors and preventing drug mishaps that, according to
the U.S. General Accounting Office, cost an estimated $20 billion a year. It's a
responsibility they willingly shoulder. Pharmacists are quick to point out that six
years of rigorous training in such specialized disciplines as toxicology,
pharmacokinetics (the study of how drugs move through the body) and
pharmacology make them far more expert in matters pharmaceutical than their
colleagues with the medical degrees.

At the same time, however, increasing financial turmoil in the retail drug business
has pharmacists working under greater stress. According to the National Association
of Retail Druggists, 3,000 independent pharmacies have gone out of business in the
past two years—victims of competition from big drug-, grocery- and department-store
chains. Even more threatening are pressures from health maintenance organizations,
which now cover many pharmacy customers. HMOs have slashed reimbursement
rates to the point where pharmacies often get reimbursed at rates well below what
the drugs cost them. "Pharmacy is no longer a pleasant profession," says William
Sullivan, former owner of a San Francisco-area pharmacy. "I wouldn't recommend it
to anyone."

Dangerous Mix

Like the mixture of certain drugs in dangerous combinations, the dual pressures of
rising costs and greater competition are a prescription for trouble. Many pharmacists
surveyed conceded that their failure to catch dangerous drug interactions was
impossible to justify ("Whoever filled this prescription shouldn't even be a
pharmacist," said a shaken Denver druggist on learning his assistant dispensed
Hismanal–Nizoral without warning). But most also seized the opportunity to blast
insurers for the financial pressures that cause them to work 12 hours a day with
hardly a break to build higher volume and make up for lower prices. Meantime,
pharmacists are supervising greater numbers of lesser-trained technicians. "This
place is a sweatshop," says a pharmacist at a Denver area Kmart, still counting pills
while talking with a reporter. Too often, druggists say, time arguing with insurers
eats into the time pharmacists should be taking to counsel customers about their
prescriptions.

Doctors tend to sympathize with the pharmacists' plight. But they argue—and many
pharmacists agree—that druggists are professionally obligated to catch and prevent
prescription errors even when they are not legally liable. And increasingly they are
legally liable. A 1990 federal law requires pharmacists to offer counseling to all
Medicaid patients, and more than 40 states have since elected to expand that
protection to all patients. Pharmacists who advertise these services may be even
more vulnerable. In an opinion apt to affect the entire retail drug industry, a
Michigan State Court of Appeals ruled recently that pharmacists had assumed a legal
duty to warn consumers when they implemented and advertised a computer system
that checked for adverse drug interactions before filling a prescription. In the 1996
case, Baker v. Arbor Drugs, it was claimed a Wyandotte, Mich., pharmacist failed to
warn a customer of the adverse effects of taking Parnate, an antidepressant, and the
decongestant Tavist-D in combination. The patient suffered a stroke as a result of
the interaction and later killed himself.

In light of the Michigan ruling, the actions of a suburban Philadelphia pharmacy
tested by U.S. News take on particular significance. In every bag containing
prescription drugs sold to customers, the pharmacy included a flier stating, "Every
prescription filled for you is entered in our Patient Profile System so we can check for
drug interactions and allergies. . . . We will warn you of any expected side effects."
Despite these assurances, the pharmacy dispensed the potentially lethal
Hismanal-Nizoral combination without a word of warning to a reporter.

That was not an exception either. Indeed, many actions of pharmacists tested by 
U.S. News ranged from the mystifying to the downright reckless. Asked why his 
drugstore filled prescriptions for Hismanal–Nizoral, a Philadelphia pharmacist replied 
that he was on vacation at the time and that the prescriptions were filled by his 
assistant—a lawyer. In Denver, a pharmacist explained that she was well aware of 
the dangerous Hismanal–Nizoral interaction, but because it didn't pop up on her 
computer, she didn't mention it. Another independent pharmacist in Philadelphia said 
he didn't report the birth-control pill–Rimactane interaction because Rimactane didn't 
render the contraceptive completely ineffective, only partially ineffective. In 
Columbus, a young pharmacist explained her failure to warn of the danger of taking 
Hismanal and Nizoral in combination this way: "I'm new," she said. "I've never 
dispensed a drug in my life."

In several cases, pharmacists who touted personal service and pledged to counsel 
patients seemed to violate their own policies. "We always have time to talk to 
customers," asserted an independent pharmacist in suburban Philadelphia. But he 
was at a loss to explain why he didn't warn a reporter of the dangers of taking 
Rimactane and a birth-control drug when he filled the prescriptions for the two 
medications. In Denver, a Safeway pharmacist attached warnings to bottles of 
Hismanal and Nizoral, then covered them by slapping "thank you" stickers on top of 
them. One Houston Walgreen store filled the Hismanal-Nizoral combination without 
comment; another in the same city wouldn't let the drugs out the door. Similar 
inconsistencies occurred among pharmacies operated by other big chains, including 
Safeway, Wal-Mart and Kroger.

Computerized Database

Virtually all pharmacies today use computer programs that display the levels of 
severity of a drug interaction, from moderate to severe. But whether their databases 
are outdated, inaccurate or simply unheeded is not clear. The Hismanal-Nizoral 
combination shows up on databases as a Level 1 interaction, the most serious. Under 
the entry for Hismanal (generically known as astemizole) in the Physician's Desk 
Reference, an unmistakable boxed warning in boldface type clearly states: 
"Concomitant administration of astemizole with ketoconozole [Nizoral] is 
contraindicated." That means the two drugs should never be taken together. Yet 
several pharmacists, without consulting the prescribing physician, addressed the 
problem of filling the two drugs in combination by directing the customer to start 
taking one drug after finishing the other. A Columbus pharmacist, noting that a 
doctor had neglected to include a specific dosage, added his own instructions to 
"take as directed." In both cases, says Georgetown's Woosley, the pharmacist 
exceeded his authority. In fact, Woosley and other experts say, no pharmacist should 
have filled the Hismanal-Nizoral prescriptions in the first place.

Pharmacists apparently applied a different standard to the Vasotec-Dyazide 
combination tested by U.S. News, since there are no prohibitions against the two 
drugs being prescribed together. While most pharmacies included literature about 
the individual drugs, only two mentioned the specific interaction between them. Most 
pharmacists who responded to the survey results, including those who warned 
customers against taking the other drugs in combination, said they wouldn't warn 
about the Vasotec-Dyazide interaction since doctors often experiment with different 
combinations of heart medications and monitor patients carefully. Further, 
Vasotec-Dyazide is classified as a Level 2 interaction, not as risky as, say, 
Hismanal-Nizoral. The pharmacists' actions, says Woosley, seem to suggest that 
many are now too busy to discuss anything but Level 1 interactions. That may be
understandable in today's cost-conscious climate, he says, but it still is troubling. Dr. David Kessler, the commissioner of the federal Food and Drug Administration, views the results of the *U.S. News* survey in a harsher light: "It is simply untenable in 1996 to walk into a pharmacy and receive a bottle of pills and no other information. It is not good patient care."

**Misplaced Trust**

As important as they are to customers seeking to cure or manage illness, pharmacists are just one link in a chain of safeguards intended to prevent prescription errors. The most crucial link is the doctor. Thus, many pharmacists told *U.S. News* that when the same doctor prescribes two interacting drugs, they are less likely to question his judgment. "If the prescriptions came from two different doctors, that would warrant a call," says pharmacist Gordon Tom of San Francisco. "But if it's the same doctor, we assume he's aware of the interaction." Recent studies show that such trust is often misplaced. The Seldane-erythromycin interaction is a case in point: Despite widely disseminated warnings by the drugs' manufacturers and the federal Food and Drug Administration, 3 to 10 percent of doctors last April still were prescribing the two drugs together.

Such mistakes, pharmacologists say, point to serious gaps in physicians' education in pharmacology—as well as to limitations in basic, clinical research on the actions of prescription drugs. Not surprisingly, the pharmaceutical industry focuses its clinical studies on finding the positive impact of drugs. Far fewer resources are devoted to the study of adverse drug effects and drug interactions. Academic medical centers have proposed a federally authorized network of researchers who would study the causes of drug interactions and educate doctors, nurses and pharmacists on prescriptive drugs.

Given the potential severity of the drug-interaction problem, reformers like the FDA's Kessler have been frustrated by the efforts of pharmacies and pharmaceutical manufacturers to block other federal solutions. It took more than 15 years for the FDA to secure passage of a law this summer that will require pharmacists to distribute uniform and easy-to-understand information with every new prescription or refill by the year 2006. Manufacturers, fearing that too many warnings will only confuse customers, say voluntary efforts will suffice.

In any event, many pharmacists say their business cannot continue on its current course if it is to meet the two competing goals of educating patients and making a profit from prescription drugs in an atmosphere of managed care. "We find ourselves significantly challenged," says Dr. John Gans, executive vice president of the American Pharmaceutical Association. "We are looking at a re-engineering of the whole profession."

As is already the practice in doctors' offices, pharmacists want to concentrate on their clinical tasks and delegate financial matters to clerks. But it may be a while before that transformation occurs. Managed-care companies would have to change their pricing structures to give pharmacists more incentive to judge and report the clinical significance of the interactions and side effects that accompany nearly every prescribed drug. They also would have to boost compensation to allow for more clerks to ring up sales and handle questions of reimbursement. Since that is unlikely to happen anytime soon, says Gans, patients have little choice but to look out for themselves. Simply put, he says, "You have to manage your own care."