Drug interactions in a pill-popping age

Mixed medications swallowed by pill-happy Americans are causing unforeseen and sometimes dangerous complications

Quietly, unobtrusively it's happening all over. Physicians' best-laid drug prescribing plans are going astray. Hospital out-patients show bizarre side effects from drugs. Surgery for in-patients must be delayed because of unexpected drug complications. The problem, perhaps not a sleeper in this pill-popping age, is drug-drug interactions. Or as one doctor puts it, "Some drugs, although innocuous in solo, can be lethal in concert."

Most patients diagnosed as suffering from drug interactions aren't intentionally after a drug trip. Not a few of them, though, are guilty of the ominous drug habits of the times—resorting to medications to relieve a plethora of psychological and physiological problems; stockpiling medicine cabinets like there is no tomorrow; keeping old prescriptions around; pill-swapping with spouse and friends; having various physicians prescribe drugs without alerting them to the drugs one is already taking, and filling these prescriptions in various pharmacies around town. Even if drug interactions could always be predicted—and this is by no means the case—physicians and pharmacists are rarely in a position to catch them.

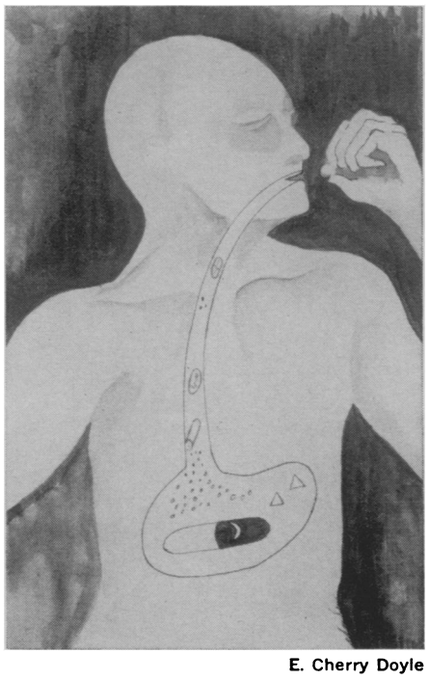
The urgency of this state of affairs, however, was brought home last week at a pharmacology and toxicology symposium in Washington. It was sponsored by the National Institute of General Medical Sciences, one of the 10 National Institutes of Health, and attending scientists, NIGMS grantees, had come to make progress reports and hash out larger medical issues.

Having seen a lot of unexpected, and undesirable, drug interactions in hospital out-patients, Ronald B. Stewart of the University of Florida College of Pharmacy recapped the results of a study he and colleagues Drs. Kenneth Finger and Leighten Cluff had made of 75 patients' drug habits over a month, and how these habits might have led to interactions. They found one patient was spending $70 a month for drugs prescribed by three physicians. Another was taking seven prescription drugs prescribed by four physicians. Forty-three percent of the patients got their prescription drugs from more than one physician. "For the seven patients taking drugs from more than two prescribers," Stewart stated, "we were able to identify the possibility of drug interactions within their therapeutic agents."

The average number of prescription drugs being taken by patients was 3.2. Although 60 percent of the patients couldn't identify the drugs they were taking, they were able to identify the products' purposes. One man, though, had been taking a medication for over a year with a mistaken idea about its purpose. Twelve percent of the patients had borrowed some of their prescription medications. More women than men were taking prescription drugs, particularly sedatives, diuretics and hormones.

The average number of nonprescription (over-the-counter) drugs taken per patient was 2.9. However, the average patient was exposed to some 10 different chemicals in both his prescription and nonprescription drugs. One patient was exposed to more than 28 chemicals monthly.

The kinds of drug interactions experienced by patients in the Florida study included therapeutic duplication, as with depressants like cough syrup and alcohol; therapeutic antagonists, such as an antihypertensive agent, like methyl dopa, being used with vasopressor agents in cough preparations; therapeutic contraindications, such as taking aspirin, when one has a severe ulcer; synergistic effects, such as alcohol, a sleeping pill and a tranquilizer producing effects in combination that they could not produce if taken singly.



E. Cherry Doyle

Yet even if a patient doesn't bring a history of drug over-dosing and drug interactions to the hospital, he still stands to get over-dosed and drug-interacted when esconced in a hospital bed. Dr. Richard Crout, professor of pharmacology and medicine at the Michigan State University School of Medicine, told NIGMS conferees: "I rarely see a hospital chart with less than 10 to 15 drugs listed on it; 20 to 25 drugs is more the average. I recall one chart listing 43 drugs."

Not unexpectedly, such epidemiological tinder has sent other pharmacologists and toxicologists to their labs to see if they can find out exactly how certain drugs might interact in the nether regions of stomach or small intestine. Dr. Aryeh Hurwitz, assistant professor of medicine and pharmacology at the University of Kansas Medical Center, detailed for fellow NIGMS'ers how he painstakingly has come up with a pretty solid case—contrary to clinical literature—that a simple antacid ("which people don't usually think of as a drug") can alter the pH of the gastrointestinal tract, and hence throw off the action of a sleeping medication like pentobarbital (e.g. Nembutal, or the "yellow submarine"). He doggedly pursued the question of pentobarbital-antacid interaction when he found that laboratory rats on antacid and pentobarbital had more trouble getting to sleep than rats on the sleeping pill alone. In fact, many of the former crew failed to sleep at all. "For others drugs," Dr. Hurwitz reported, "antacids may depress and increase absorption sufficiently to eliminate drug effects or cause toxicity."

Although studies of drug interactions, such as Dr. Hurwitz's, have only gotten under way in the past three years or so, the compendium of known or suspected drug interactions is growing. Several books on the subject for pharmacists and physicians were published last year; several more are in press. Traditionally pharmacists have been more aware of drug interactions. Pharmacologists have become aware of them only in the past several years. And the clinician is just starting to take note of them. Drug interactions received attention at the Southern Medical Association 1970 Convention in

Science Service, Inc. is collaborating with JSTOR to digitize, preserve, and extend access to *Science News*. www.jstor.org

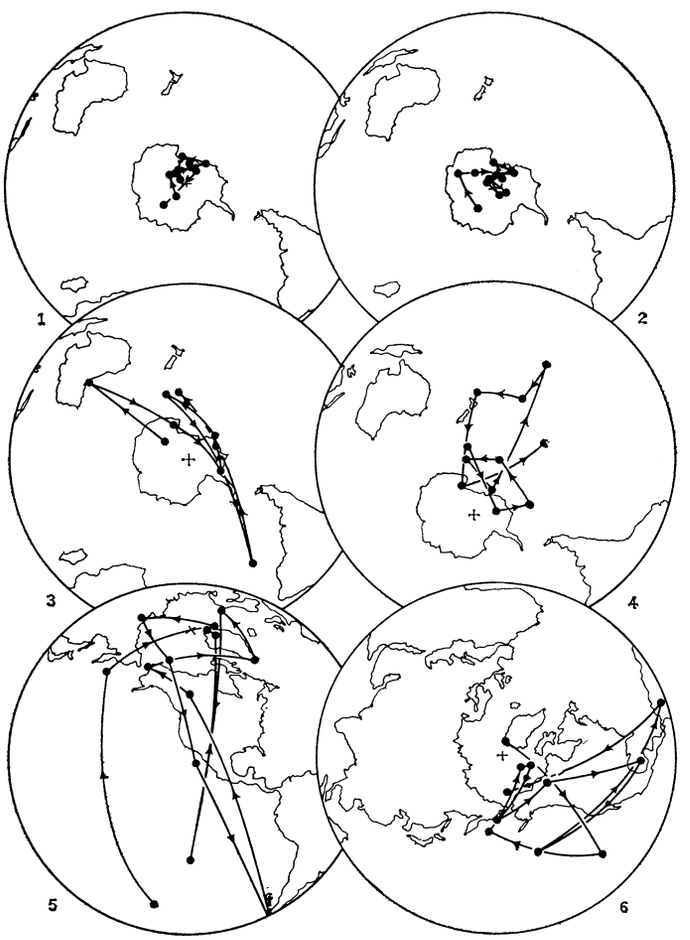
November. Clinical literature is showing more drug interaction studies. Physicians are worrying over interactions in medical journals. And when it comes to interactions triggered by combination drugs, the U.S. Food and Drug Administration is really getting fired up.

On Feb. 17 the FDA proposed that fixed drug combinations be removed from the market unless their manufacturers prove each ingredient contributes to a medication's therapeutic effectiveness, usage or the prevention of drug abuse, or diminishes side effects by being in combination. Briefly, what the FDA wanted is better-defined required tests for effectiveness of both prescription and nonprescription combination drugs. The agency has been deluged with letters from physicians about the proposed tighter stringencies on combination drugs. One American Medical Association faction holds that prescription combination drugs have a place in medical practice. Another AMA faction is for chucking all prescription drug combinations that don't have a rational purpose.

What an FDA crackdown on prescription or nonprescription drugs would mean to the over-all drug interaction problem remains to be seen. What is certain, though, is that with increasing drug production, drug consumption and medical specialization, drug interactions will be commanding attention on many fronts. □

THOUSAND-YEAR JOURNEY

Following the trail of a magnetic reversal



Science

As the earth's magnetic field reversed 14.7 million years ago, the magnetic south pole followed a meandering path to its new northern position.

Reversals of the earth's magnetic field have been shown to be related to an increasing number of other phenomena (SN: 4/10/71, p. 251). A thorough understanding of the processes and time scales involved in reversals could be useful in the study of sea-floor spreading, continental drift, ocean core stratigraphy and even evolution. It is also essential to understanding of the field itself.

It is known that a reversal takes several thousand years and that during the reversal the intensity of the field diminishes. But a high-resolution continuous record of a reversal has just now been obtained for the first time.

J. R. Dunn and Drs. Michael D. Fuller, Haro Ito and V. A. Schmidt of the University of Pittsburgh have studied reversals recorded by the natural remanent magnetization—the direction of polarity recorded—in rocks at about a dozen locations in the Pacific Northwest. They obtained records of two reversals. The first, recorded in rocks near Mount Hood in Oregon, occurred about 8.2 million years ago, and was from reverse to normal polarity (normal polarity is defined as that existing today). The record of this reversal, however, was somewhat confused, they report in the May 21 SCIENCE.

The second reversal was recorded in rocks in Mount Rainier National Park in Washington. The age of the rocks is about 14.7 million years. This reversal was also from reverse to normal. A section about half a mile from the main outcrop in which they studied the reversal was investigated for evidence of variations in the field prior to reversal. They found that the intensity of the remanent magnetization decreased. During the major part of this intensity decrease, the direction of magnetization did not change significantly.

The earth scientists then traced the path of the magnetic south pole during a reversal by determining the virtual geomagnetic poles (VGP) of progressively older rock samples. As certain molten rocks cool, they become magnetized in the direction of the prevailing magnetic field. The VGP is thus the spot on the globe where the magnetic fields in rocks of a certain age point—the magnetic pole.

As the field intensity diminished, the magnetic south pole began to move around the Antarctic Continent. During the final stages of the decrease in intensity, it began to swing back and forth like a pendulum, describing arcs of a great circle. While still swinging back and forth, the pole then moved northward, tracing a complex path through the Pacific to the opposite side of the earth. There it eventually settled down to its final position as the magnetic north pole. During the latter part of this process, the researchers report, the path traced by the pole was very similar to variations in the magnetic north pole that have been observed in the recent past. Soon after the magnetic field achieved its new polarity, its intensity increased.

Assuming that the VGP is a true measure of the movements of the magnetic poles and that the cyclic motions of the pole that are recorded in the rocks at Mount Rainier took about the same amount of time as similar motions observed in the recent past, the researchers speculated on the duration of the reversal. The transition in direction from reversed to normal took about 1,000 to 4,000 years, they estimate. This is in general agreement with earlier paleomagnetic results. The time scale of the intensity changes was longer—about 10,000 years. □