Mistakes That Can Kill

Medical errors occur with a frequency that is causing growing concern. Although little is known about the extent of the problem, some physicians are offering innovative solutions.

BY JOEL GREENBERG

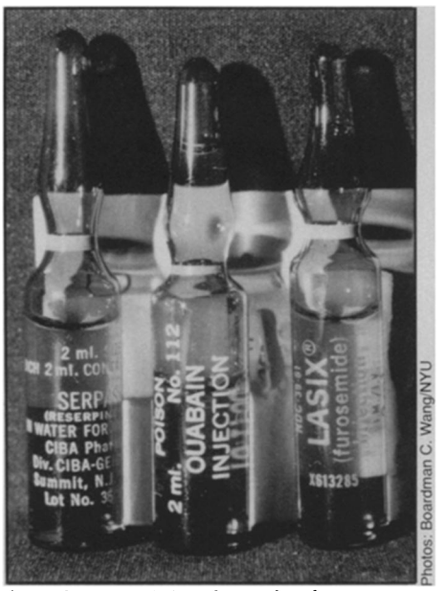
"Take a Buffalo."
— Advice from a Chinese woman, shortly after her first exposure to language in the United States, to her headache-suffering daughter.

The woman in the above example, of course, meant to say "Bufferin"; in this case, the mistake is a product of cultural and language differences. But medical errors, often with serious consequences, occur thousands of times each year among doctors, nurses, drug manufacturers and others—most not only of the same tongue, but products of sophisticated medical training — as well as among patients. "Unquestionably, more people are killed by human errors in hospitals than by all nuclear areas, with the exception of the [two atomic] bombs dropped," says the University of Toronto's John W. Senders, a psychologist and engineer who specializes in the human factors of nuclear power plant operation.

Despite such dour observations, there appears to be no widespread movement to publicize or combat medical errors; indeed, data in this area are almost nonexistent.

"It is difficult to do a study — lots of cases are not reported," says Boardman C. Wang of the department of anesthesiology at New York University's School of Medicine. Wang has been a crusader against medical error since an early 1970s incident that occurred just before a prostate resectioning operation. As he was about to give the patient anesthesia, Wang asked a nurse to bring him two ampules of a certain medication. She returned to the operating room with two similar-looking ampules, but at the last moment Wang noticed that one contained Neo-Synephrine, which "would have raised the [patient's] blood pressure to above 300," according to Wang. "I said, 'Honey, do you realize what you're trying to do to me?'"

After the surgery, Wang visited the hospital pharmacy and "found that a lot of meds [medications] looked alike." Thus, Wang had encountered, firsthand, what he now identifies as a major type of error: mistaking one type of medication for another. "Manufacturers want to maintain their own identity, across all their drugs,"



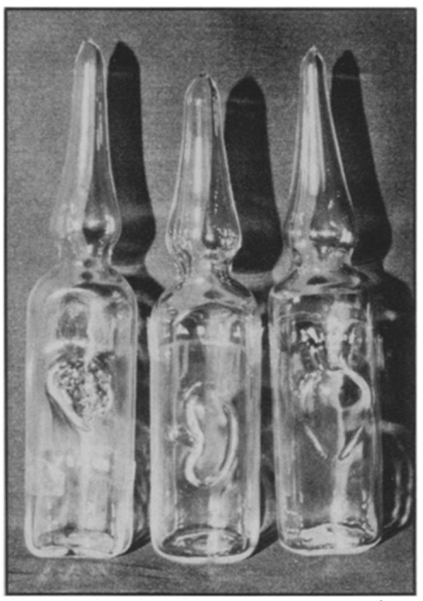
Photos: Boardman C. Wang/NYU

Ampules containing drugs that lower blood pressure (left), regulate heart rhythm (center) and promote urine secretion are similar enough to be mistaken for one another.

he says. Therefore, a substance that has one effect on one aspect of the body may come in a container almost identical to that of a substance with a quite different action, perhaps on another part of the body. The medical literature, and Wang, are loaded with examples: A patient who was supposed to receive a topical anesthetic for the eye was instead given a blood-testing solution made of 95 percent alcohol and 5 percent hydrogen peroxide; a drug that lowers blood pressure was mixed up with a drug that raises it; an antileukemic drug, which is not supposed to be injected into the spine, was mistaken for another drug and injected into a boy's spine, causing paralysis.

In a letter in the May 9 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, Duke University eye specialists point out a potentially dangerous problem in the naming of a new drug. The compound, Isosorbide, is used for "the short-term reduction of intraocular pressure," write Edward G. Buckley and M. Bruce Shields of Duke's Eye Center. "Another compound, isosorbide dinitrate, has been used in this country for many years for the treatment of angina pectoris [chest pain]. The similarity between generic names of the two compounds presents a potential for confusion." And in a related problem reported in the May 9 JAMA, two patients recently swallowed pill bottle dessicants — cylindrical, nonsoluble containers of activated carbon or silicon gel used to keep the capsules dry. In both cases, which resulted in obstruction of the gastrointestinal tract,

Bottles containing Benadryl, which counteracts allergies, and Adrenalin Chloride, which, among other things, raises blood pressure, are almost identical.


Wang had a glass blower create raised shapes of (from left) brain, kidney and heart for appropriate drugs. Such ampules could be used primarily by elderly patients and others with sight problems.

the patients were relatively old and could not visually distinguish the dessicant from the pill.

"In the last decade, lots of progress has been made in medicine, but one area where very little progress has been made is human error," Wang said recently in Columbia Falls, Maine, at a conference on human error. In the past few years, Wang has journeyed to medical conferences, exhibiting examples of confusing medication packaging. (The Pharmaceutical Manufacturers Association, however, has refused to permit his exhibit at their meeting, he says.)

. . . Mistakes

In addition to having hospital personnel pay closer attention to the medications they choose, Wang also proposes innovations in bottling, including distinct sizes, shapes and colors for specific drugs. But perhaps his most intriguing idea is to incorporate a sort of organic relief map on the ampule itself. Each such bottle would be embossed, Wang says, with "the principal site of action of the drug" — i.e., the shape of a kidney, heart, brain, etc. — primarily to aid persons who might have trouble reading the print on the label. "God has given us five senses — we can utilize touch on the outside of containers," says Wang, who also advocates using different colored intravenous lines for different substances.

Confusing medication labeling, however, constitutes just one aspect of medical errors. A Johns Hopkins Hospital survey of 178 medication errors divided the incidents into seven categories, in order of frequency (a, b and c occurred with equal frequency):

a. The wrong patient received or almost received a medicine.

b. A patient received or almost received the wrong dose.

c. A patient received or almost received an extra, unordered, dose of medicine.

d. A patient's medicine was omitted or almost omitted.

e. A patient received or almost received the wrong drug.

f. A patient received or almost received a medication at the wrong time.

g. A patient received or almost received a medicine through an improper route.

Researchers Alphonse Chapanis and Miriam Aronstein Safren found that such incidents often happened not only during "stress periods" such as shift-changes and meal times but, somewhat surprisingly, when a nurse had to administer medication to just a single patient, rather than to several. Single dose administrations, they note, are almost always unscheduled and tend to break up the nurse's routine — apparently contributing to the error.

The researchers recommend that:

- The pharmaceutical industry should set up clear standards for drug nomenclature. Errors often occurred because certain drug names — generic, brand or both — resemble others of different function.
- The decimal point labeling of dosages — where .1 cc can be misread as 1 cc or 2.5 mg as 25, etc. — should be improved, or changed, possibly by writing the dose as a fraction to avoid perceptual errors.
- Confusing medical abbreviations pertaining to dosages should be changed. Terms such as q.n. (every night) were confused with q.h. (every hour), and q.o.d. (every other day) with q.d. (every day).
- Drug labels should be improved. Small print, poor area lighting and ambiguous wording all contribute to label problems.
- Arrangement of drugs in ward medication cabinets should be standardized. Such arrangements can vary greatly within a hospital as well as among hospitals. It is often difficult to see or reach a drug; drugs with similar names are frequently placed next to each other or in the same section of the cabinet.

Finally, the researchers suggest a more efficient cross-checking system regulating the flow of medication orders between doctors and other hospital personnel.

The fact that the Hopkins study was performed in the 1960s and still remains among the most "recent" formal studies cited by current human error investigators testifies to what Wang and others say is a neglect of the medical errors problem. And though Chapanis says the situation has "improved at this hospital [Johns Hopkins]," he adds, "I don't know about other places."

Wang suggests that in many hospitals, most of the medication problems identified some two decades ago still exist. "This is why I go around to these meetings, exhibiting," he says. Although it may be impossible to determine exactly how often mistakes are made in hospitals, one study in Little Rock, Ark., estimated the error-incidence rate at 15 percent. Says Wang: "I would say it's maybe even more." □

. . . Calmodulin

Means and colleagues Bill Brinkley and John Dedman have used antibodies that bind to it. Antibodies to those antibodies are labeled with a fluorescent dye, and striking patterns of calmodulin distribution can been seen. For instance, during cell division the fluorescence is associated with the mitotic spindle, the cell's apparatus for organizing and distributing chromosomes. The fluorescence is most intense at the poles of the spindle and projects toward the chromosomes lined up across the center of the cell. A variety of experiments indicate that calmodulin bound to calcium disassembles, and thus shortens, microtubules of the mitotic apparatus. The chromosomes therefore are drawn toward opposite sides of the dividing cell under calcium-calmodulin direction.

Calmodulin's many roles make it, and related compounds, key candidates for diagnostic and therapeutic use. For example, calmodulin, which has been found in both the head and the tail of sperm, may provide a new approach to contraception. Proportionally more calmodulin is measured in sperm (and curiously in the electric organ of eels) than in any other cells. In sperm 7 percent of the total cellular protein is calmodulin.

Several important reactions in sperm, including motility, are inhibited by calmodulin-binding drugs, such as phenothiazines. Milton Cormier and co-workers at the University of Georgia have made progress toward a calmodulin-directed contraceptive.

Calmodulin may also play a role in development of new antipsychotic tranquilizers. The ability of individual phenothiazines to bind calmodulin, in a calcium-dependent fashion, correlates to the drug's activity as an antipsychotic agent.

Calmodulin also may provide a tool for diagnosing cancer, Means says. It is present in elevated levels in a wide variety of tumor cells, including those made cancerous by virus, hormone and chemical carcinogens. The boost in calmodulin in tumor cells seems to be due to a general acceleration in protein synthesis. The rate of degradation of most proteins in the tumor cells increases to compensate, but the rate of calmodulin degradation remains fixed.

The role of hormones in calmodulin's actions is not yet clear. Means says it has long been known that hormones influence calcium ion's distribution. And now it looks as if hormones also affect the distribution of calmodulin within each cell. Speaking at the recent Endocrine Society meeting in Washington, Means emphasized the potential importance of calmodulin's role in the endocrine system. "It opens an entirely new field of endocrinology and of cell biology," he says.

One speculation about how calcium carries out its many roles is that it acts as a messenger inside a cell. When specific events raise the level of free calcium in a cell, those additional ions bind to calmodulin, which acts as an intracellular calcium receptor. That protein then interacts with a distinct set of proteins in each tissue, amplifying the calcium-calmodulin impact.

The more traditional example of a "second messenger" is the cyclic nucleotide cAMP, which stimulates enzymes that add phosphate groups to proteins. Because the calmodulin-calcium complex regulates cyclic nucleotide metabolism, the two messenger systems in cells seem to be coupled. Moreover, many of the enzymes regulated by the calmodulin-calcium complex are also the substrates for enzymes activated by cAMP.

"At the moment most of the data concerning calmodulin regulation must be considered as phenomenological," Means and Dedman say in a review article in the May 8 NATURE. "What is now required is a concerted effort to understand the chemical basis for each of calmodulin's actions."

Claude B. Klee, Tom H. Crouch and Paul G. Richman of the National Cancer Institute conclude in the 1980 ANNUAL REVIEW OF BIOCHEMISTRY, "It may soon become more interesting to ask which cellular processes are not under calmodulin control than which are, since it is already clear that a large part of cellular metabolism and function is under the direct or indirect control of this small but precisely designed protein." □