Thousands a Year Killed By Faulty Prescriptions

By BOYCE RENSBERGER

Every year perhaps 30,000 Americans accept the drugs their doctors prescribe for them and die as a direct result. Perhaps 10 times as many patients suffer life-threatening and sometimes permanent side effects, such as kidney failure, mental depression, internal bleeding and loss of hearing or vision.

These figures are among the more conservative to be found in studies of the prescription drug problem by the medical profession itself. Although most medical authorities agree that some of these deaths and near-deaths could have been prevented if the doctors involved had exercised better judgment in prescribing drugs for their patients, no one knows how

This is the third of five articles on the problem of incompetent doctors. Subsequent articles will discuss the reluctance of doctors to criticize colleagues and give guidelines for choosing a reliable doctor.

Dr. John C. Ballin, director of the American Medical Association's Department of Drugs. "The literature abounds with references to the prescription of the wrong drug or dose, to unforeseen drug reactions, or simply to the administration of a drug when none was indicated."

"You have to realize," adds a New York doctor who requested anonymity "that the whole idea of studying adverse

Continued on Page 17, Column 1

300,00 Are Hospitalized

The international study, called the Boston Collaborative Drug Surveillance Program, is directed by Dr. Herschel Jick of the Boston University Medical Center. Dr. Jick has estimated that about 300,000 people are hospitalized in the United States annually because of a drug reaction, making this one of the 10 leading causes of hospitalization.

Dr. Jick's study found that for every 18 prescriptions written in a hospital, one adverse reaction occurs. Ten percent of the reactions are major and 1.2 percent are fatal.

Part of the adverse drug reaction problem can be traced to the bewildering variety of drugs available to doctors. About 1,200 different drugs are on the market, many more than any doctor can possibly know well. No drug is completely safe: all have potential side effects, some minor and some major. Each drug is intended for a specific use and many are not supposed to be given except under very carefully controlled conditions.

Yet any licensed doctor is free to use any drug in any way he cares to, regardless of how well or how long ago he has been trained or how diligently or poorly he keeps his knowledge up to date.

Majority Are Helped

In the vast majority of cases, patients are helped by the drugs prescribed for them. Prescription drugs are undeniably responsible for many millions of lives saved, pains relieved and miseries banished. But experts contend that in a small and possibly growing share of cases, something goes wrong.

Not long ago, for example, a 50-year-old New York woman went to her doctor, complaining of a sore throat. He gave her an injection of penicillin and within minutes she lay dead in his office, the victim of penicillin sensitivity that triggers a shutdown of breathing and circulation.

The city's Medical Examiner's Office found that the doctor had failed to make a standard test for such sensitivity, which afflicts one in every hundred persons. The doctor had not even asked whether she had a history of sensitivity.

Warning Not Heeded

In another case, a 48-year-old New Jersey man was hospitalized by his doctor because of a kidney infection. The doctor chose to combat the infection with neomycin despite the manufacturer's warning that the antibiotic was to be avoided in kidney disease cases.

If neomycin builds up to high levels in the blood, it can permanently damage hearing nerves. Because the kidneys are needed to remove foreign chemicals from the blood, any disease reducing their efficiency could allow a dangerous build-up of neomycin.

The New Jersey doctor did not know this, and his patient gradually lost his hearing and became totally deaf. His condition is permanent.

"Although the occasional horror story becomes known, usually through a sensational malpractice trial, there are literally thousands of others that the public doesn't hear about," said a New York doctor who sought anonymity. "Some adverse reactions send people into the hospital and they're treated as medical problems like any other. But a lot of them never go beyond the private physician's office.

"Look," the doctor continued, "some of these guys who practice all by themselves don't keep up with the scientific literature and don't even recognize an adverse reaction. They treat it like just another symptom and prescribe another drug for it."

Efforts to determine the total number of deaths caused by adverse reactions have been few. One of the most widely cited studies was made in 1971 by Dr. Samuel Shapiro and his associates at the Lemuel Shattuck Hospital and the Tufts University Medical School, both in Boston.

Dr. Shapiro studied 6,199 consecutive drug cases in several hospitals and found 27 fatal reactions, 22 of which killed patients not already terminally ill.

Dr. Wolfe has projected this rate to the 10 million patients admitted to hospital medical wards and calculated that about 30,000 hospital patients are killed annually by prescribed drugs. No one knows how many patients die from prescription drugs taken outside hospitals.

Antibiotics Misused

Other studies have suggested there may be as many as 160,000 deaths due to drug reactions. Such studies are hotly disputed by the drug industry, which generally contends that many of the deaths were among patients already seriously ill or that national projections are invalid, or both.

The single most widely prescribed class of drugs and the one that causes the major share of adverse reactions is antibiotics. The American Medical Association's Department of Drugs concluded that "this group of agents may be the most improperly used class of drugs in all medicine."

From 1967 to 1971 the population in the United States grew by about 5 percent. Over the

same interval the number of antibiotic prescriptions filled in drugstores grew six times faster, according to drug-industry marketing surveys. In 1967 Americans were put on antibiotics once every two years, on the average. By 1971 the rate had climbed to nearly once a year. By 1972 antibiotic factories were turning out eight billion doses a year, of which two billion were exported.

Experts on infectious diseases say there has been no appreciable change during the same period in the incidences of diseases warranting antibiotic therapy or in the types of antibiotics available. This rate, they say, suggests the average adult has a bacterial infection requiring antibiotics only once every five years.

Increase in Prescriptions

The rise in antibiotic prescribing is often attributed by practioners to growing patient demand. Whenever a patient goes to a doctor with an infection, they say, the patient expects and sometimes demands an antibiotic. Many private practitioners have remarked that it is easier to accede to such demands and keep patients satisfied than to withhold the drug and risk alienating them.

"The gap between the actual antibiotic prescribing practices and the ideal practices recommended by infectious-disease specialists appears to be widening," said Dr. Henry E. Simmons, then United States deputy assistant secretary for health, and Dr. Paul D. Stolley of the Johns Hopkins School of Hygiene and Health in a 1974 article in the Journal of the American Medical Association.

One suggestion that doctors may not know as much as they should about antibiotics is the generally poor showing of physicians participating in the National Antibiotic Therapy Test, a voluntary exercise devised by the private Network for Continuing Medical Education. Of the first 4,513 doctors to take the 50-question, multiple-choice test, half scored 68 percent or worse.

Dr. Harold C. Neu, head of the division of infectious diseases at Columbia University's medical school, who devised the test, said the results "brought home to me that many physicians are not as conversant with antibiotics as they ought to be."

Superinfection a Hazard

The test was designed to be difficult enough to challenge the best doctors. Thus, even university-affiliated physicians, who are presumed to be the most up-to-date practitioners, averaged only 80 percent correct. Of the private practitioners, the family doctors for most Americans, only 17.2 percent scored 80 percent or better.

In addition to adverse reactions, one of the most feared hazards of antibiotic therapy is superinfection. The effect of combating an infection can be to encourage a worse infection by a microorganism resistant to the antibiotic. Superinfections, once started, are fatal in 30 to 50 percent of cases.

Ordinarily, many species of bacteria live in the human gut and various other parts of the body. Some can be harmful, but because they compete and keep one another in low numbers, none becomes a threat to health. When a broad-spectrum antibiotic is given for some infection, it may kill not only the target bacteria, but also many others in the body's normal flora, leaving one or two resistant species to proliferate without competition.

Thus, a bacterial species may suddenly explode in numbers and toxicity, overwhelming the body. Experts agree that some risk of superinfection occurs every time any patient is put on broad-spectrum or medium-spectrum antibiotics, those capable of killing a wide range of organisms.

Upsurge in Patients

In recent years doctors have noticed an upsurge in the number of patients developing infections from the body's normal bacteria, known as Gram negative, and some have linked this rise to the growing use of antibiotics. Other doctors contend, however, that the rise in Gram negative infections is due to the larger proportions of elderly and severely debilitated patients in hospitals today.

Dr. William R. McCabe, an infectious-disease expert at the Boston University medical school, reported in the New England Journal of Medicine, that the incidence of such infections may now be as high as 1 percent of all patients admitted to hospitals. Thus, given the 30-million annual hospital admissions, there may be as many as 300,000 cases of superinfection. If a third are fatal, Dr. McCabe said, superinfection alone may account each year for 100,000 deaths.

"We are dealing not with a scattering of local institutional problems, but with a full-blown national epidemic," said an editorial in the Journal of Infectious Diseases, which independently calculated "a minimum of some 50,000 deaths" related to superinfection.

Various medical experts have estimated that betwen one-fifth and one-half the antibiotics given are not really necessary and that, therefore, the same proportion of deaths due to Gram-negative superinfection could have been prevented by more intelligent prescribing of antibiotics.

Antibiotics also account for another potential hazard—an adverse reaction to the drug itself. One study conducted at the University of Florida of 7,765 hospitalized patients found that 341 suffered adverse side effects of the drugs they had received. Most victims recovered soon, but 48 patients died or almost died. If the same proportion holds nationally, then 55,000 people a year die or almost die from antibiotic reactions.

Because most of those people needed an antibiotic in the first place, the risk of an adverse reaction had to be taken. But, if 20 percent of the antibiotics given in hospitals are unnecessary, as experts such as Dr. Wolfe of the Health Research Group estimate, then perhaps 20 percent of those potentially fatal reactions need never have happened.

"Prudent non-use of antibiotics could have prevented over 10,000 life-threatening adverse drug reactions," Dr. Wolfe told a 1974 Congressional hearing on overprescribed drugs.

One of the most controversial uses of antibiotics is in treating viral infections because, with rare exceptions, known antibiotics do not affect viruses.

In 1973, for example, about 7.5 million Americans suffering from runny noses and coughs went to their doctors and were diagnosed as suffering nothing more than the common cold. About 95 percent came away with a prescription, more than half for antibiotics that cannot kill cold viruses. Some of the antibiotics were among the more hazardous available.

These figures are from confidential market-research studies conducted for the drug industry by International Marketing Services in Ambler, Pa. The numbers are projected from a sample of about 10,000 doctors who are paid to report all their diagnoses and drug prescriptions. Annual compilations of the statistics are printed and sold chiefly to drug manufacturers. The New York Times has obtained copies of the statistics pertaining to certain diseases and drugs.

Drug-industry figures show that about 277,000 patients were given the closely related and potent antibiotics Lincocin and Cleocin, both of which are known to have a high rate (up to 33 percent) of harmful side effects such as colitis, an intestinal ailment that can be fatal. The drugs are intended for serious infections of "strep" and "staph" bacteria that are resistant to safer antibiotics.

Perhaps the antibiotic best known for causing serious side effects is chloramphenicol, commonly prescribed for typhoid, Rocky Mountain spotted fever and other uncommon infections. A potential side effect of the antibiotic, however, is a fatal anemia.

Chloramphenicol's lethal properties have been well known and publicized for over a decade. Yet Dr. Wolfe estimates from the drug-industry surveys that one in every four prescriptions for the drug are for diseases in which it is known to be useless or for which there are safer alternatives.

For example, if the drug industry's own figures are correct, doctors prescribed chloramphenicol for the common cold 12,000 times in 1972. Another 24,000 prescriptions of the drug were written for "acute upper respiratory infections," which, like colds, are almost invariably viral. In all, 161,000 prescriptions for chloramphenicol were written for, in Dr. Wolfe's words, "diseases for which no competent physician could reasonably argue chloramphenicol is indicated."

Although some physicians argue that no antibiotics should ever be given for a common cold, others maintain that if a "cold" is bad enough to send a person to a doctor, more serious bacterial complications may well have set in. In such cases, antibiotics could be useful.

In any event, the appropriate antibiotic, most experts would agree, would be something other than chloramphenicol. Similar reasoning applies to several other diseases for which the drug was used. Yet 161,000 times a year physicians apparently choose one of the most dangerous antibiotics known when a safer drug was available or no drug at all should have been used.

Parke, Davis and Company, the drug's developer and largest supplier, has long recognized chloramphenicol's hazards and now routinely includes in its labeling the warning, "Chloramphenicol must not be used when less potentially dangerous agents will be effective. It must not be used in the treatment of trivial infections or where it is not indicated, as in colds, influenza, infections of the throat, or as a prophylactic agent to prevent bacterial infections."

Because doctors are legally free to prescribe drugs as they see fit, however, such warnings are only advisory.

While the vast majority of ailments treated by doctors receive appropriate medication, if any is necessary, at least one ailment may be receiving the wrong medication in the vast majority of cases.

Of the 2.4 million women who went to their doctors for nausea and vomiting due to pregnancy, 98 percent, according to the drug-industry survey, were put on a drug. Of these, three-quarters were given Bendectin, a brand name for a combination of three drugs in one pill.

This drug, which accounts for $27-million a year in sales, was evaluated by the National Academy of Sciences and found to lack substantial evidence of effectiveness. The American Medical Association's Council on Drugs studied the product

because of its overwhelming popularity and called it an "irrational mixture" with "no evidence that [the ingredients] are effective either alone or in combination." The council's verdict on Bendectin was, "Not recommended." If a drug is needed to reduce vomiting, it said, another class of drugs, which cost about one-fourth as much, would be a better choice.

In addition to high price and low efficiency, doctors who incorrectly prescribe Bendectin can expose their patients to the risk of a variety of adverse reactions. According to information supplied by the manufacturer, Merrell-National Laboratories, the following may occur: Dry mouth, dizziness, blurring of vision, thirst, drowsiness, vertigo, nervousness, epigastric pain, headache, palpitation, diarrhea, disorientation and irritability.

Merrell-National says that additional reactions may occur on rare occasions, including fatigue, sedation, rash, constipation, loss of appetite, painful urination and, ironically, nausea and vomiting.

Dr. John Chewning, a spokesman for Merrell-National, said in an interview that the drug company still considers Bendectin to be an effective drug and is conducting studies that it expects will demonstrate the drug's efficacy.

When these studies are completed they will be submitted to the Food and Drug Administration. If the new evidence is not sufficiently persuasive, the Federal agency says it will ban the drug from the market.

Side Effects Listed

The list of Bendectin's side effects is not an unusually long one for a prescription drug. Similar lists are issued by the manufacturers of most of the drugs on the market today.

They are all given on a piece of paper, called the package insert, which Federal law requires manufacturers to include with every package of a prescription drug sold to a pharmacist. The insert must also include chemical descriptions of the drug, its proper uses and types of patients for whom the drug could be especially hazardous.

Because doctors seldom see the package insert, the same information is available to them in a book called the Physicians' Desk Reference. Because much of the information is written in technical language beyond the vocabulary of most laymen, pharmacists have traditionally removed the insert before selling the drug to the patient.

Patients who wish to see the information can consult the Physicians' Desk Reference in a library or request the insert from the druggist. Contrary to what some pharmacists have told patients, there is no law prohibiting the patient from having the insert.

Ads Promote Drugs

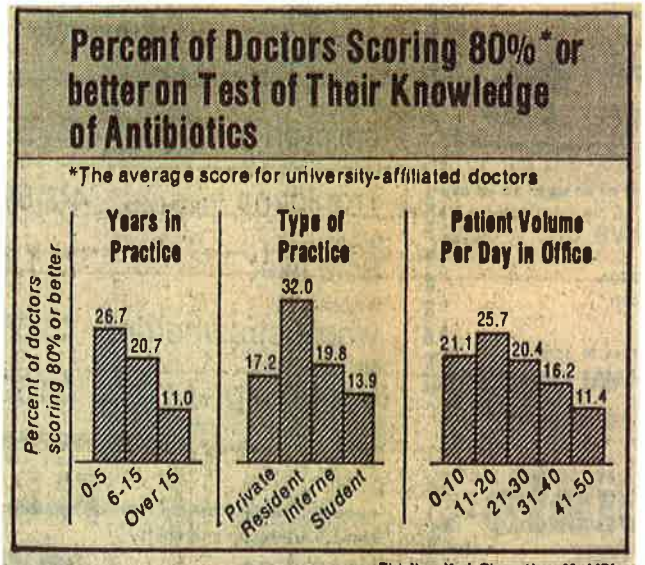
How does the average doctor learn what drugs are good for the treatment of a disease or what hazards the drug poses?

For many doctors, who left medical school before most of the current drugs were developed, their knowledge is gained in about the same way that ordinary consumers learn of a new detergent or of the nicotine content of a cigarette brand.

Advertisements in medical journals, free samples, door-to-door salesmen and direct-mail promotions are widely used by drug manufacturers to build brand recognition and acceptance by doctors.

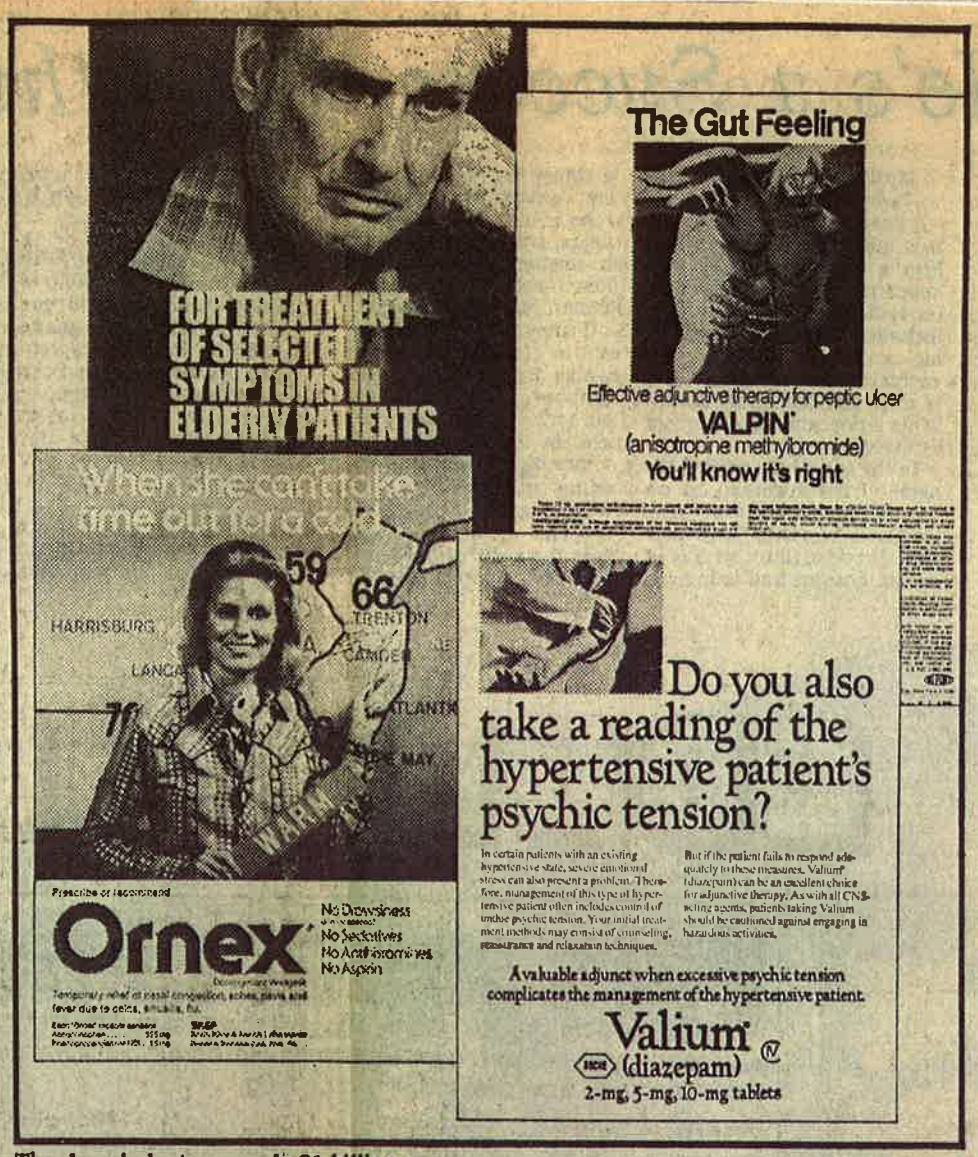
Some medical experts say that doctors are not swayed, that most regard drug companies as biased sources of information and, instead, read scientific articles in journals and go to scientific meetings to keep up.

Drug companies, on the other hand, say most doctors do rely on their advertising and they spend more than a billion dollars a year to maintain their efforts.



The New York Times/Jan. 28, 1976

The doctors who are most up-to-date on how to prescribe antibiotics are those most recently graduated from medical school and those who see only a modest number of patients a day, according to a study of 4,513 doctors. The study, a 50-question test, was given by the Network for Continuing Medical Education. Results were in the New England Journal of Medicine.



The drug industry spends $1 billion a year to encourage doctors to prescribe one brand over another. Much of this money goes for advertisements, such as these randomly chosen from medical journals. The drug makers try to influence the doctor's decision by using many of the same techniques used to sell consumer products.