

# **Clinical Pharmacy and Therapeutics**

**Third Edition**

**ERIC T. HERFINDAL  
JOSEPH L. HIRSCHMAN**

# Clinical Pharmacy and Therapeutics

Third Edition

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# Foreword

When the first edition of this text appeared in 1975, its title and contents served abrupt notice to the nation that a different kind of pharmacist had arrived on the health care scene. It was entitled *Clinical Pharmacy and Therapeutics*, and what a strange and alien combination of words these were. Never before had “pharmacy” and “therapeutics” appeared together on the cover of a textbook because prior to the late 1960s, few persons within the profession saw any connection between them. Until that time, the majority of practicing pharmacists would have firmly declared that their primary professional task was the filling of a prescription “exactly as ordered by the physician.” They would have argued that therapeutics—the act of selecting the right drug for the right patient at the right time—was the sole responsibility of the physician and others who were authorized to prescribe. The pharmacist was not a member of this select group, ergo he or she had no place in therapeutics.

But this changed, albeit somewhat slowly in the beginning. By the early 1970s, pharmacists had already begun to assume the responsibility of assuring that patients received optimum drug therapy. This, in turn, led to changes in the curricula of pharmacy schools, including therapeutics courses and clinical clerkships that enabled students to apply these principles to patient care. These newer concepts of practice came to be known as clinical pharmacy, and the text you now hold in your hand was the very first attempt by a team of editors and authors—all of them clinical pharmacists—to meet the information needs of pharmacy students wishing to assume these new roles.

Yet, even when the book first appeared, there were still many within the profession of pharmacy who felt that clinical pharmacy was simply a shooting star on a wishful horizon, destined to blaze gloriously for the briefest of moments, but destined also to destroy itself in

the process. There is and can be no future role beyond the distribution of drugs, they said, because physicians will never allow pharmacists to assume important roles in drug therapy.

That was nearly 10 years ago, and as I write these words, history has rather resolutely proven the doomsayers wrong. In the interim, clinical pharmacy has traded in its starburst for an eternal flame which it effectively uses to burn down the barricades of resistance. Today, pharmacists are assuming roles totally unheard of or unthought of as few as 5 years ago. Furthermore, the clinical pharmacy faculties of the nation have become as productive as their counterparts in other health professions, and they have had a marked impact on the practice of drug therapy in the United States.

As shall always be the case, however, the sages of doom are with us still. They speak now of computers and cost containment. There is no future, they say, because that which the pharmacist does can be captured on a piece of plastic or metal: a computer disk. Furthermore, they add, the advent of prospective payment schemes and other cost-control measures will result in serious cutbacks in the number of pharmacists, thereby minimizing or totally eliminating their impact on drug therapy.

But I disagree, as do the many dedicated practitioners who have been responsible for the several editions of this book. The future will challenge us, yes, but its winds will bear no doom unless we pay undue heed to the words of the doomsayers and cower before them. Winston Churchill once said that “frightfulness is not a remedy known to the *British Pharmacopeia*.” Nor is it a remedy that has a place in our profession.

Jere E. Goyan  
April, 1984

# Preface

In the dozen years since the original concept for this book was developed, pharmacy has continued to evolve toward a clinical profession. Pharmacists are assuming larger roles as disseminators of drug information, patient educators, therapeutic consultants and direct providers of care. Concomitantly, technology has introduced many new drug entities and dosage forms, and the volume of biomedical information has greatly increased. We realize that the mastery of the knowledge necessary to fully function as an effective health care provider cannot be achieved through a book. However, a book can serve as a starting point. Combined with access to skilled teachers, clinical facilities and recent biomedical literature, the properly motivated student can master the field of clinical pharmacy.

This edition of *Clinical Pharmacy and Therapeutics*, like earlier editions, is based on the concept that pharmacists must be able to make therapeutic judgments as a matter of course.

Indeed, many patients and other health professionals now expect it. The success of the earlier editions of this book indicates that our approach is effective in helping prepare the pharmacist and pharmacy student for this responsibility.

Some chapters contained in previous editions have been dropped, and several new chapters have been included. There has also been an attempt to include more pharmacokinetic information where it is relevant. The selection of contributors continues to be based upon the same criteria used for previous editions, i.e., clinically experienced in the subject discussed.

We cannot mention here everyone who assisted us but we are, nevertheless, grateful to all of them. Our particular thanks, however, go to the participating authors who have put out an extraordinary effort.

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# SECTION 1

## General

# Clinical Toxicology

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## INTRODUCTION

Clinical toxicology deals with the assessment and medical management of persons exposed acutely or chronically to a potentially harmful agent. Because of the diverse nature of the substances involved in poisonings as well as the wide range of clinical manifestations and their treatment, optimal management of the poisoned patient is achieved through an interdisciplinary approach to patient care. Expertise provided by physicians, nurses, pharmacists, social workers and paraprofessionals contributes greatly to the care of these patients.

In order to function effectively as a contributor to the clinical toxicology team, pharmacists must be trained in the retrieval of poison information and be familiar with the basic principles of the treatment of poisoning. Poisoning calls are frequently received by poison centers, community pharmacies and hospital pharmacies. A poisoning call from another health professional, or a frantic parent, can be traumatic, but rewarding, to the pharmacist equipped to handle such a medical emergency. Many pharmacists who receive these calls, however, are not prepared to handle them. It is the purpose of this chapter to provide pharmacy students and pharmacists with the basic knowledge necessary to deal with these poisoning calls.

## GENERAL INFORMATION

Poisoning, be it accidental or intentional, is a serious problem in the United States today. The National Clearinghouse for Poison Control Centers processes approximately 150,000 reports of ingestions per year (1). This figure in no way reflects the actual number reported to poison centers since reporting to the National Clearinghouse is voluntary and most large centers do not report. Since there are no legal reporting requirements for poisoning, it is dif-

ficult to be certain of the true magnitude of the problem. It is estimated, however, that each year 3.5 million poison exposure cases occur nationally (1), with accidental poisoning from liquids, solids and gases accounting for 4,900 deaths in 1979 (2).

Poisoning is the most common pediatric medical emergency. Eighty percent of acute poisonings occur in children, with approximately 75% of these poisonings occurring in children less than 5 years of age. Most childhood poisonings are accidental and occur via the oral route. Children's natural curiosity can at times have disastrous consequences. They are exposed to thousands of drugs and hundreds of thousands of chemicals and household products. Although some children learn by their past poisoning experiences, a significant number of children are "repeaters," i.e., they ingest more than once. The most common substances involved in poison exposures in children less than 5 years of age are drugs, household products, personal care products and plants. In our experience the drugs most commonly involved are analgesics and antipyretics, antihistamines/cough and cold products, vitamins and topical preparations.

For years, aspirin was the leading cause of accidental poisoning and poisoning deaths in children under 5 years of age. This is no longer the case, as there has been a progressive decline in both ingestions and deaths since the mid-1960s (3). The percentage of ingestions due to aspirin in those under 5 years of age has decreased steadily from around 25% in 1966 to 3.9% in 1979 (4). Many factors are responsible for this decrease, and among them are an increased awareness on the part of the general public of the dangers of aspirin. The safety closure requirement for all products containing aspirin, and all liquid preparations containing methyl salicylate, is largely responsible for the decline. Hopefully, safety packaging will further decrease the number of in-

toxications from other products on which these closures are now required. The limit of 36 tablets (each 81 mg) per bottle of children's aspirin has helped reduce the severity of the ingestions which still occur. Working toward preventing poisoning is the most logical approach to this problem. The old cliché "an ounce of prevention is worth a pound of cure" obviously applies here.

Approximately 20% of poisonings occur in adults and are often the result of an intentional exposure (suicide or drug abuse) but may also be accidental (e.g., industrial exposure). While poison prevention activities may decrease the number of pediatric exposures and minimize the severity of childhood intoxications, these efforts have almost no impact on adult poisoning. In fact, many clinical toxicologists feel that poisonings in adults are responsible for more significant morbidity and mortality today.

## ROLE AND STATUS OF POISON CENTERS

Since the first poison center was established in Chicago in 1953, the number of poison centers in the United States has increased dramatically. According to the National Clearinghouse for Poison Control Centers the number of official centers peaked at approximately 590 centers in 1970 and has decline to 466 in 1980 (5).

Official centers exist in most major U.S. metropolitan areas and are most commonly staffed by physicians, nurses and pharmacists. The 1980 survey of poison control centers conducted by the National Clearinghouse for Poison Control Centers found that, of the 275 operating centers that responded, 81% are poison information and treatment centers, 13% are poison information centers, and 4% are treatment centers only. While 88% of the centers are located in hospitals, 10% are found in educational institutions. Sixty-four percent of the poison centers are affiliated with the emergency department, 13% are located in the pharmacy and 13% are affiliated with both the emergency department and other departments. Ninety-five percent of the respondent centers are open 24 hours per day, 365 days per year and 96% of them answer calls from the general public and health professionals. These figures indicate an increase in the percentage of centers that respond to both types of callers since in a 1970 survey this number was only 78%. In 1979 30% of the centers

received less than 500 calls, 43% received over 1000 calls, 15% received over 10,000 calls and 6% received over 25,000 calls annually. Toll-free numbers exist for 17% of these centers and 21% of the centers are linked to 911 emergency systems.

Even today many centers listed in the National Clearinghouse directory are small centers located in hospital emergency rooms whose primary function is to treat poisoned patients who come in. Recently, however, the concept of regionalization of poison centers has developed in an attempt to more efficiently and effectively meet the needs of the poisoned patient. Many large centers serve as regional centers and provide information to a large population or geographic area. This may involve a major metropolitan area, a portion of a large state, an entire state, or several states. The distribution depends primarily upon population and geography. It is not unusual for these regional centers to handle 15,000 to 30,000 or more calls per year. It is the current feeling that development of 50 to 100 top notch regional poison centers could adequately serve the entire United States. In this way one avoids duplication of information sources and staff. In addition, this allows regional poison center staff to handle large numbers of cases and develop expertise in this area.

The American Association of Poison Control Centers has developed standards for regional poison centers and is presently an organization that certifies regional centers. According to their criteria regional programs should provide the following services (6):

1. A regional poison information service including 24-hour a day availability, toll-free telephone access, comprehensive information sources, management protocols and access to regional treatment facilities for patient referral and transport.
2. A regional system for providing poisoning care, with at least one comprehensive poisoning treatment center.
3. An outreach health profession education program.
4. An outreach public education program.
5. A regional data collection and reporting system.

Ideally, the medical director of the center should be a board certified medical toxicologist. As the number of these individuals is limited, however, the medical director is often selected on the basis of interest, training and

experience. Clinical pharmacists or nurses are often administratively responsible for the day to day operation of the center as well as providing professional input into the management of the poisoned patient. Poison information specialists, usually pharmacists or nurses, are responsible for providing primary telephone consultations.

Poison information is also provided by "unofficial" poison centers. Most drug information centers also provide some poisoning information. It is important to note, however, that these two types of centers (drug information versus poison) differ. Poison centers usually provide services both to professionals and to the general public, whereas drug information centers usually provide information only to health professionals. In addition, poison centers specialize in providing poison information, whereas with drug information centers this is usually a sideline. At present several combined poison information-drug information centers exist. Since there is an overlap in both staffing and information sources, more of these combined centers may be expected in the future. It is essential that the pharmacist be acquainted with available centers in the local area so as to be able to refer those problems that are either beyond his or her ability or reference sources. A list of poison centers is included in the *Physicians Desk Reference* and the *Drug Topics Red Book*.

## ROLE OF THE PHARMACIST

Pharmacists, because of their extensive background in biopharmaceutics and pharmacokinetics, drugs interactions, chemistry, pharmacognosy, pharmacy, and therapeutics, can become valuable resources in poison centers. In addition, pharmacists have as much, or more, didactic pharmacology training than any other health discipline. Many pharmacy schools provide specific toxicology coursework.

The community pharmacist may be the first professional contacted after ingestion of a toxic compound, especially when a drug is involved. Pharmacists must be able to determine whether home treatment is advisable or whether the person should be referred to an emergency room. Hospital pharmacists may be involved in the selection, stocking and supplying of drugs used to manage poisoned patients.

Kinnard (7) suggests that pharmacists could be involved in an acute poisoning case in many

ways, including: (a) being the initial patient contact in a poison center, or a pharmacy; (b) serving as a clinical pharmacist in an emergency room or poison center to provide therapeutic consultation; (c) being involved in the identification of the ingested materials both via gross examination and chemical analysis of the agent and body fluids; (d) preparing intravenous fluids the patient may require; (e) serving as a member of the cardiac arrest team that may treat a poisoned patient; (f) in some cases being the individual who directly administers drugs; and (g) providing poison information as a staff member, or director, of a drug information center.

Pharmacists can be involved in providing information on toxicokinetics as well as in researching the kinetics of drugs in overdose situations. Toxicokinetics is the study of the absorption, distribution, metabolism and elimination of drugs from the body in the overdose situation. Each of these parameters may be altered following the ingestion of a large dose of some drugs. Absorption may be delayed and various transport and metabolic processes may be saturated. An awareness of the toxicokinetics of specific drugs allows for an educated prediction of the time course of the intoxication in an individual patient.

Pharmacists already serve in many of these roles. Knowledgeable pharmacists in any setting may perform many of these roles with little additional training.

## POISON PREVENTION

According to the 1980 National Clearinghouse survey, 78% of the respondent poison centers conduct poison prevention education activities. The types of educational activities include distribution of pamphlets, newspaper articles, radio and TV spots, videotapes, slide shows, special school programs, speakers' bureaus, and poison warning labels. The two most common activities are distribution of pamphlets and newspaper and magazine articles. Most centers produce and/or distribute their own materials.

Pharmacists can also play an important role in poison prevention. This should be a year round project with an increase in activity during National Poison Prevention Week.

The FDA approves the nonprescription sale of appropriately labeled 1-oz quantities of ipecac syrup. Pharmacists should stock syrup of ipecac and be familiar with its use for the



management of acute poisoning including indications and dosing.

Pharmacists can be influential in promoting the distribution of syrup of ipecac. Local pharmaceutical organizations have provided ipecac free of charge to families with young children through community pharmacies. If this service is not available, pharmacists can display ipecac, provide information, and urge that families with young children purchase a 1-oz container. Parents should be cautioned to contact their physician, pharmacist or poison center before giving the ipecac. In this way a health professional can evaluate the situation and determine the appropriateness of administering an emetic and if necessary call an ambulance, physician or an emergency room. If syrup of ipecac is indicated, the health professional can review dosing with the caller, follow-up on the call to determine if the person has vomited and provide additional instructions regarding the side effects of ipecac and/or symptoms to watch for which might indicate the need for additional evaluation and treatment. If ipecac is not indicated the health professional can discourage its administration and recommend modalities of treatment if necessary.

Many other poison prevention activities are possible. An important first step is to see that the pharmacy is poison proof. Since children can ingest products stored on low shelves in pharmacies, these shelves should be stocked with articles with a low potential for toxicity. All prescription drugs required to be dispensed in safety containers should be so dispensed. In those few instances where a patient requires a nonsafety container, be certain to warn the patient to store the container properly to avoid an accidental poisoning. Elderly patients who require nonsafety containers may not have young children of their own, but many have young grandchildren who come to visit. Poison prevention posters that make customers aware of the danger of poisoning should be displayed. Fliers discussing poison dangers may be distributed. Pharmacists can act as speakers to discuss poisoning dangers with parents of young children. Points to be stressed include: (a) keeping harmful substances out of reach of children, (b) not calling medicine candy or taking medicine in front of children, (c) using safety closures, (d) keeping medicines and household products in their original containers, (e) disposing of unused portions/clean-

ing out the medicine cabinet, (f) reading labels and precautionary statements, (g) keeping syrup of ipecac in the house, and (h) having the phone number of the poison center in a readily accessible place.

Since the most active ingestors are unable to read, a warning on a product label has no effect on the child. Some toxicologists feel that the traditional warning symbol, the skull and crossbones, is not an effective warning symbol. It has been suggested that many young children think of pirates and adventure, and not poison when they see this symbol (8). In addition, the skull and crossbones is required only on the most dangerous products. Many commonly ingested agents that have the potential for producing fatality, automatic dishwasher detergent, petroleum distillates, and drugs for example, do not carry this warning. Poison warning symbols such as Mr. Yuk and Officer Ugg have been developed to warn young children to stay away from dangerous products.

### ANALYSIS OF A POISONING SITUATION—TYPES OF QUESTIONS ASKED

Unfortunately in many poisoning calls, the caller does not volunteer enough information for the pharmacist to adequately answer all pertinent questions. The history is also often incomplete in cases where the patient is discovered in a coma from an unknown cause, a child ingests an unknown amount of tablets or capsules from an unmarked container, or an unidentified plant has been ingested. Generally, the caller is trying to determine the potential toxicity or lethality of the substance. Some examples: A mother calls and say, "My son took four of my birth control pills. Should I make him vomit?" A suicide prevention worker calls and says, "Mr. X took 100 secobarbital, should I call an ambulance for him?" A physician in an emergency room asks: "Mr. Y took 10 pentazocine, is this a dangerous dose in this patient and what treatment is appropriate?" A family physician calls and asks, "Mrs. Smith's 4-year-old son took four or five green and white capsules with Lilly H69 on them. What are they and what should I do?"

Most of the above questions can be answered with relative ease. Examples of questions more difficult to answer include a physician calling and saying, "Mrs. Jones was found comatose at her home with an empty bottle of amitripty-