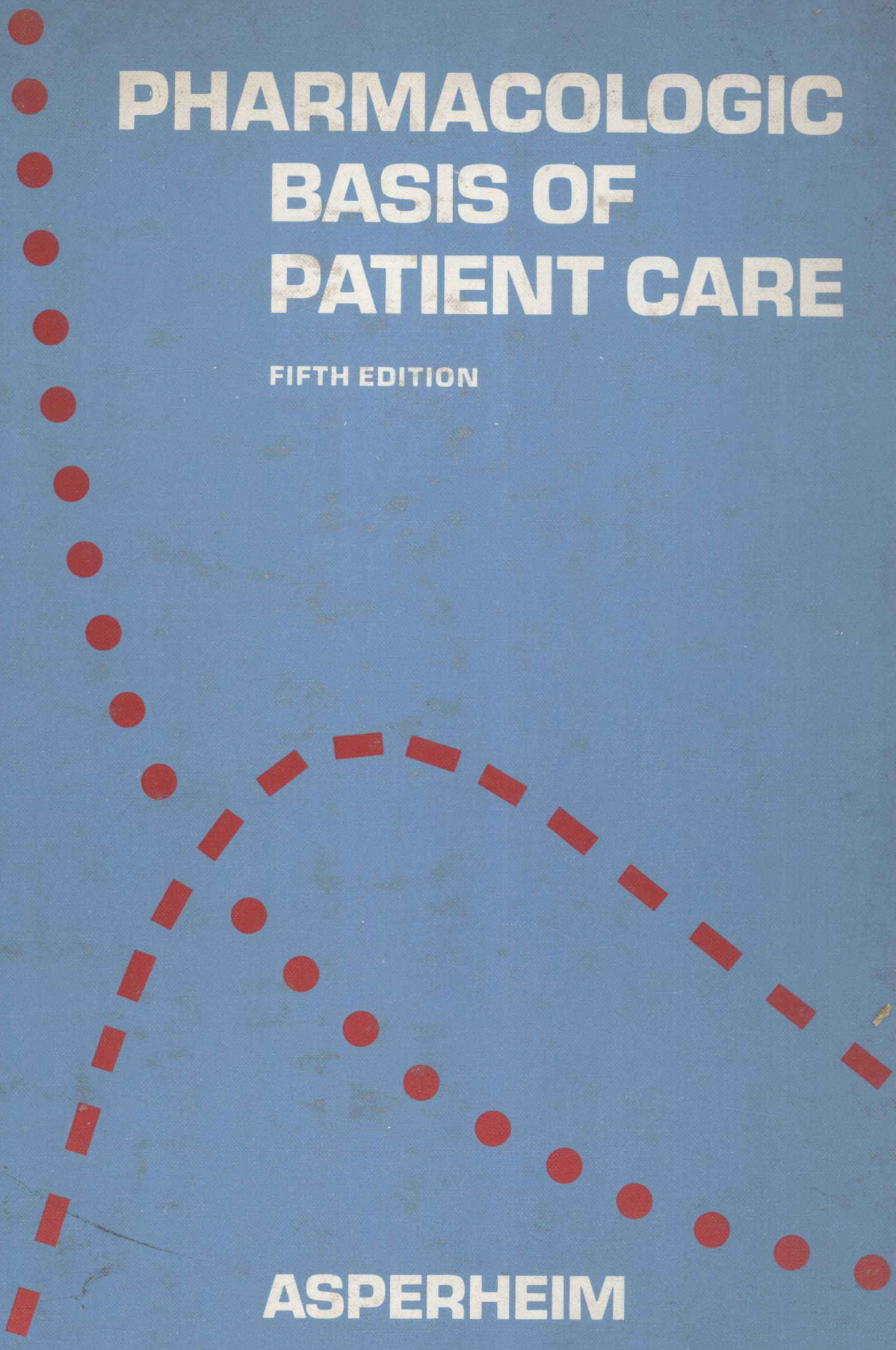
PHARMACOLOGIC BASIS OF PATIENT CARE

FIFTH EDITION



ASPERHEIM

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NOTICE

Extraordinary efforts have been made by the authors and the publisher of this book to insure that dosage recommendations and other drug information are precise and in agreement with standards officially accepted at the time of publication.

It does happen, however, that dosage schedules and other drug data are changed from time to time in the light of accumulating clinical experience and continuing laboratory studies. This is most likely to occur in the case of recently introduced products.

It is urged, therefore, that you check the manufacturer's recommendations (package insert) for dosages and other specifications and recommendations, *especially if the drug to be administered or prescribed is one that you use only infrequently or have not used for some time.*

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FROM THE PREFACE TO THE FIRST EDITION

The field of pharmacology has seen a rapid period of growth in the last few decades as a result of extensive research that has provided knowledge of many new drugs and revealed much additional information about older remedies.

In a text intended for nursing students, it would be impractical—if not impossible—to treat each commercial product and combination in detail. The intent of this book has been, therefore, to set forth the mechanisms of action and the symptoms of toxicity that may be expected with each general class of drugs and to discuss in detail only the more commonly used drugs in each class.

With this sort of background, students can then assimilate information about new products into their general frame of knowledge and more readily understand how each new discovery resembles—or differs from—products already available.

Principles and concepts are emphasized more fully than mere lists of factual information, and a common sense approach to drug usage and administration has been stressed. Nurses should be able to appreciate the correct use of drugs as an invaluable aid in the overall treatment of illness, but at the same time they should retain a healthy regard for the untoward side effects and toxic reactions that are all too frequent with almost every drug in current use.

The chapters of this text are arranged to correspond as much as possible with nursing education in other subject areas. A review of physiology has been included in many chapters when it is necessary to understand the action of drugs.

Each chapter is preceded by a brief outline of the important concepts discussed in that section. The outline is not intended to be all-inclusive but is merely a guide to the study of the chapter.

Questions for discussion and review have been included at the end of each chapter. Some questions may be answered only by resorting to outside sources; thus, students are encouraged to enlarge their field of knowledge in pharmacology and related areas.

MARY KAYE ASPERHEIM

PREFACE TO THE FIFTH EDITION

The field of pharmacology in recent years has presented an almost unprecedented challenge, both to those who have been working in the field for years and to the new student of pharmacology. New advances in cell biology, understanding of disease processes and the pharmacokinetics of drug action at the cell level have necessitated extensive revisions in the teaching of pharmacology. Not only have new, previously unknown drugs been added to the clinical spectrum, but also the mode of action and the clinical uses for old drugs have been extensively upgraded and modified.

In this edition, as in previous editions, there is emphasis on the nurse's role in drug therapy. The use of nursing interventions to enhance a desired drug effect or to detect and minimize side effects has been constantly stressed. Patient teaching as a responsibility of the nurse is also emphasized.

Outlines for nursing implications and patient assessment guides are included, generally following each discussion of the appropriate pharmacologic agents. I wish to express my appreciation to the nurse contributors who have provided additional nursing implications in selected chapters.

Study questions—many upgraded and revised with the new subject material—follow each chapter, and case studies have been added to many chapters. As in previous editions, the Teachers' Manual has been written to enable the pharmacology instructor to stress and clarify subject material.

It is hoped that this edition will fulfill its intent—to enable the student nurse to form a solid base in the pharmacology field on which to continue building for the remainder of his or her professional life.

MARY KAYE ASPERHEIM FAVARO

CONTENTS

1

INTRODUCTION TO PHARMACOLOGY

IMPORTANT CONCEPTS DISCUSSED

- ☐ Drugs are derived from animal, vegetable, mineral and synthetic sources
- ☐ Because of unavoidable variations in drugs derived from natural sources, official standards were established to ensure uniformity in potency
- ☐ The Federal Food, Drug and Cosmetic Act established restrictions governing the purity, labeling, sale and administration of drugs
- ☐ Federal and state laws control all phases of the manufacture, sale and dispensing of narcotics and certain other drugs

Today's nurses are functioning in an environment that differs in many respects from that of their predecessors. Moreover, the nature of nursing responsibilities and the way in which the nurse is educated to meet them have changed. New materials, new methods and new attitudes are continuously presenting exciting challenges, and the mere expansion of knowledge in traditional fields makes its own demands on the conscientious student and the competent practitioner.

Examples of the kinds of changes that come readily to mind are the trends toward automation of some hospital functions and the introduction each year of a staggering number of new drugs or combinations and modifications of older agents. We need to view these innovations in perspective. Unit dose dispensing by the pharmacy certainly eases and modifies some traditional practices of the nurse, but just as certainly it does not reduce the nurse's need for a thorough understanding of how drugs are prepared and administered. Further, nurses must still develop the habitual skills of observing patients to assess effectiveness of the medication and to detect untoward effects and begin corrective action. Indeed, the rapid increase in the number of drug agents—and especially the increase in the number of agents that are truly potent and the interactions among them—makes more necessary than ever the acquisition of real competence in pharmacology.

Pharmacology, the science with which this book is concerned, includes a fascinating range of topics. It is the study of drugs—their sources, chemical and physical properties, physiologic actions, absorption, distribution, metabolism, excretion and therapeutic uses. Because an overall view of drug therapy as one of the components of total patient care is essential to the nurse, each of the various disciplines involved in

pharmacology will be developed in this text to the extent that it contributes to this purpose.

The term *pharmacology* stems from the Greek words *pharmakon,* meaning "drug," and *logos,* meaning "a rational discussion." Pharmacology in practice, however, is as old as man. The first primitive man who observed that a leaf he chewed caused diarrhea or somnolence was already concerned with the science of drug therapy. In this simple way, countless drugs have been discovered, only to be forgotten and rediscovered many times. Such agents as opium, belladonna, rauwolfia, quinine, digitalis and curare were components of ancient remedies long before even the foundations of our modern civilization were laid.

Early Egyptian papyri contained prescriptions including materials still in use today, such as magnesia, lime, soda, iron salts and sulfur. Simple compounds of arsenic and poisons found in plants—for example, hemlock and strychnine—were used by the ancient Greeks and Romans. Quinine, an antimalarial drug, was discovered when Peruvian cinchona bark was used to treat the fever and chills of a Spanish officer. The symptoms quickly subsided upon its use, it is said, whereupon it was brought to Europe and used as a drug for fevers of various causes.

Until recent times most of our medicinal agents were portions of plants (roots, bark, leaves and sap), but with the advances in pharmaceutical chemistry, many of the active principles have been isolated and made available in pure form. Furthermore, hundreds of additional drugs are prepared synthetically. The expansion of our knowledge and the increasing complexity of our society have made possible the phenomenal growth of the drug industry. Billions of dollars are spent annually in pharmacologic research.

Modern Attitudes Toward Use of Drugs

The attitudes toward drug use and the demands on medical personnel are quite different today from those of a few generations past. The average consumer today has read rather extensively of new drugs and scientific advancements in magazines and newspapers and has heard and seen still more advertisements on the radio and television. As a result consumers feel qualified to prescribe drugs for themselves and to urge physicians to prescribe antibiotics, tranquilizers and other new drugs of which they have read even before these compounds are released by the drug companies for general use.

Many qualified persons have become alarmed at this situation and have pointed out the dangers of using drugs promiscuously. Numerous monographs have been written also about the iatrogenic (physician-produced) diseases. Side effects of drugs used to treat illnesses can at times be much more serious than the original conditions. The increased usage of multiple drugs has led to increased awareness and concern about dangerous interactions of drugs with other drugs and also with certain foods. There is no doubt that drug-induced diseases represent one of the most important problems facing medicine today.

A nurse's attitude toward the use of drugs is important; the formation of a correct attitude should be one of the primary aims of any course in pharmacology. *Common sense* is the key phrase in this connection. The nurse and all others who are concerned with prescribing, administering or dispensing medications must recognize first and foremost that the normal body functions optimally when it is supplied with a balanced diet and an adequate amount of rest and recreation. Under circumstances of abnormal emotional stress or physical or functional abnormalities, however, supportive therapy must be given temporarily to restore, at least in part, normal body processes. The "miracle drugs," although often lifesaving, may well be a two-edged sword, because they can produce serious and even permanent damage if used unwisely.

Even in his or her personal life the nurse must be convinced of the extreme importance of taking drugs only when absolutely necessary. Since the nurse has constant access to potent, habit-forming and dangerous drugs, the temptation may well arise to use them indiscriminately. Dexamyl Spansules are *not* necessary every time one wants to lose five pounds; Darvon capsules are *not* necessary for a simple headache; sleeping capsules are *not* necessary for daytime sleeping after a night shift. The fact that nurses rank high among drug addicts in the medical field is unfortunate, for in most instances the serious consequences could easily have been avoided by the maintenance of a proper respect for drugs. An intelligent appreciation of the lifesaving properties of drugs is necessary; so also is a healthy awareness of the serious side effects that may be produced when drugs are misused.

Terms Used In Pharmacology

Drug. The term *drug* has been defined by the Federal Food, Drug and Cosmetic Act as applying to (1) articles recognized in the official pharmaceutical standards such as *The United States Pharmacopeia/National Formulary,* the *British Pharmacopoeia,* the *Pharmacopoeia Internationalis* or other such official volumes; (2) articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or animals; (3) articles other than food that are intended to affect the structure or any function of the body of humans or animals; and (4) articles intended for use as a component of any article specified in clauses (1), (2) or (3).

Pharmacodynamic Agent. A drug classified as a pharmacodynamic agent can stimulate or depress either biochemical or physiologic functions and thus either relieve the symptoms or alter the course of the disease.

Chemotherapeutic Agent. Chemotherapeutic agents are intended primarily to inhibit or destroy aberrant cells, such as cancer cells, or microbial parasites that cause disease, while at the same time having minimal effect on healthy living tissue.

Pharmacology. Pharmacology is the study of the responses of living organisms to chemical stimuli. This is a broad definition and includes virtually all the biologic disciplines. Pharmacology comprises chiefly the sciences of pharmacodynamics, pharmacotherapeutics, pharmacognosy, pharmacy and toxicology. The science of pharmacology involves specific knowledge of the sources of drugs, their physical and chemical properties, their physiologic actions in the body and their metabolic fate and therapeutic uses.

Pharmacodynamics. The study of the biochemical and physiologic effects of drugs and their mechanisms of action is given the name *pharmacodynamics.* Much of the subject matter of this science involves biochemistry, microbiology, physiology and pathology. The study is unique in that its focal point is the action of drugs—their absorption, distribution, biotransformation and excretion. Structure-activity relationships, or the prediction of drug action on the basis of chemical structure, have recently become an important facet of pharmacodynamics. The synthesis of many new drugs has resulted from research performed in this area.

Pharmacotherapeutics. Pharmacotherapeutics is the branch of pharmacology concerned only with the use of drugs in the treatment of disease. In this study the therapeutic effects of one agent are compared with those of another on the basis of ability to halt a disease or disease process.

Pharmacognosy. *Pharmacognosy*, a term derived from the Greek words *pharmakon,* meaning "drug," and *gnosis,* meaning "knowledge," is concerned with the history, production, commerce, selection, identification, preservation and use of drugs of plant and animal origin.

Pharmacogenetics. Pharmacogenetics is a relatively new field that involves the study of genetically determined variations in drug response.

Pharmacy. Pharmacy involves knowledge of the physical and chemical properties of drugs and available dosage forms. The pharmacist is concerned primarily with preparing, compounding and dispensing medicines upon the written order of a licensed practitioner.

Toxicology. The science of toxicology deals with the noxious effects of drugs. This study involves not only the natural and synthetic compounds used in therapy but also the numerous other substances that may be responsible for toxic reactions.

Drug Names

Chemical Name. The chemical name describes the drug's structural formula.

Official Name. *The United States Pharmacopeia/National Formulary* designates an official name for the drug. The official name is often identical with the generic name.

Generic Name. The laboratory or company that first develops the drug usually assigns a generic name, which is often an abbreviation of the chemical name.

Trade Name. Each manufacturer may assign a trade or brand name to the drug.

Sources of Drugs

Drugs may be obtained from animal, vegetable and mineral sources. They may be used in the crude or raw form, or as dried or fresh organs or organisms and their natural exudations; or the active ingredients, such as the various alkaloids, glycosides, alcohols, esters or aldehydes, may be isolated from these crude substances and employed for various therapeutic purposes.

Many drugs that were formerly obtained only from natural sources are now prepared synthetically; this method is generally more satisfactory when it can be used. Synthetic procedures have contributed greatly to the advancement of pharmacology and are responsible for the great majority of the new "miracle drugs" in present use. Very often only a slight alteration in chemical structure can greatly change the action of a drug in the body. Drugs can be given a more selective action, and the number of undesirable side effects can be greatly reduced by such slight changes.

Following are a few examples of drugs obtained from the various sources:

Animal Sources. Drugs obtained from the animal kingdom vary greatly in their pharmaceutical applications. Many drugs are prepared from the glands of animals (e.g., thyroid hormone, insulin, and sex hormones); other drugs may be prepared from shells and exoskeletons (e.g., prepared chalk) or from substances, such as beeswax and cobra venom, that are secreted by animals.

Vegetable Sources. In the past, most of the substances used as drugs were of vegetable origin (Fig. 1–1). Almost every part of the plant has been used for pharmaceutic or healing purposes: roots (digitalis, glycyrrhiza or licorice, sarsaparilla); rhizomes (aspidium, iris); barks (cinchona, sassafras, wild cherry); leaves (hyoscyamus, belladonna, digitalis, peppermint, senna); fruits (*Rhamnus cathartica,* colocynth, caraway, juniper berries); flowers (clove, corn silk); and seeds (flaxseed, black mustard, castor oil).

Mineral Sources. Only a few minerals in their pure forms are used in current therapy. These include copper sulfate, magnesium sulfate and aluminum.

Figure 1–1. *Atropa belladonna* showing the alternate, petiolate, ovate, entire leaves, in the axils of which are the solitary fruits or flowers with large, leafy bracts.

Synthetic Drugs. In addition to active ingredients of plant and animal drugs that are now prepared synthetically, hundreds of drugs that are classified as corticosteroids, antianxiety agents, antidepressants, chemotherapeutic agents and germicides are prepared by synthetic chemical procedures.

Development and Evaluation of New Drugs

Procedure

In the United States the development and use of new drugs for interstate commerce is controlled by regulations of the Food and Drug Administration (F.D.A.). Clinical data that have been developed during the investigation of the drug must be submitted.

The investigational phase is controlled by F.D.A. regulations and involves the thorough investigation and study of the pharmacologic effects of the drug in animals in order to find evidence that the drug has some effectiveness and is sufficiently safe to warrant further testing in studies on humans. Early studies are done on all actions and effects of the drug, dosage, chemical properties, metabolism, side effects and acute and chronic toxicity. From these data, the drug's safety margin is estimated, i.e., the ratio between the dose causing the desirable effect and the dose causing toxic effects. The drug's therapeutic index—its safety relative to that of standard drugs—is also determined and is considered in the decision to conduct further studies. Further studies are conducted on animals in order to determine chronic toxic effects on organs and tissues, especially the kidney, liver, bone marrow and blood, and on the fetuses of pregnant female animals.

Initially in human studies, the new drug is administered carefully to normal, healthy volunteers and to patients. Ethical and moral aspects of such human investigations have been specified by F.D.A. guidelines. If the experiments with patients give indications that the drug may have some effectiveness, further pharmacologic studies and controlled clinical studies are done to determine the drug's efficacy and safety.

In clinical studies it may be necessary for the nature of the medication to be concealed from the patient (single-blind experiment) or from both the patient and all persons involved in the conduct and administration of the study (double-blind experiment). The "blind" experiments are necessary particularly when the subjective aspects of the drug's effect, such as relief from pain or anxiety, are being evaluated. These studies attempt to reduce the possibility that the patient's response may be from conscious or unconscious