Pharmacologic Basis of Nursing Practice

FOURTH EDITION

CLARK • QUEENER • KARB

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FOURTH EDITION

with 89 illustrations

Mosby

St. Louis Baltimore Boston Chicago London Philadelphia Sydney Toronto

Mosby
Dedicated to Publishing Excellence

Editor: Robin Carter
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Designer: Gail Morey Hudson
Illustrator: Mark Swindle

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A NOTE TO THE READER
The authors and publisher have made every attempt to check dosages and nursing content for accuracy. Because the science of pharmacology is continually advancing, our knowledge base continues to expand. Therefore, we recommend that the reader always check product information for changes in dosage or administration before administering any medication. This is particularly important with new or rarely used drugs. The National Institutes of Health do not necessarily endorse the views expressed in this book.

Printed in the United States of America

Mosby–Year Book, Inc.
11830 Westline Industrial Drive, St. Louis, Missouri 63146

Library of Congress Cataloging in Publication Data

Freeman, Julia B.
Pharmacologic basis of nursing practice / Julia B. Freeman Clark, Sherry F. Queener, Virginia Burke Karb.—4th ed.
p. cm.
Rev. ed. of: Pharmacological basis of nursing practice. 3rd ed. 1990.
Includes bibliographical references and index.
ISBN 0-8016-6673-2 : $45.95
1. Pharmacology. 2. Nursing. I. Freeman, Julia B. Pharmacological basis of nursing practice. II. Queener, Sherry F. III. Karb, Virginia Burke. IV. Title.
[DNLM: 1. Drug Therapy—nurses' instruction. 2. Pharmacology—nurses' instruction. QV 4 F855p]
RM300.F72 1992
615'.1'024613—dc20
DNLC/DLC
for Library of Congress 92-49911
CIP

94 95 96 97 GW/VH 9 8 7 6 5 4 3 2

Preface

Pharmacology is a rapidly changing field. Newly acquired knowledge about the molecular basis of medicine has expanded the therapeutic strategies available. The role of the nurse is increasingly sophisticated as new drugs and new strategies are applied to patient care.

CONTENT AND FEATURES

This fourth edition of *Pharmacologic Basis of Nursing Practice* contains information on **over 70 new drugs** that have appeared in the 3 years since the last edition. We have thoroughly revised the appropriate portions of the book, including the addition of new drugs in tables and integration of these agents into the text. The entire text has been reviewed, revised, and, in many cases, entirely reformatted to keep up with current knowledge on drug mechanisms and therapeutic uses of agents. The rapidly developing area of immunopharmacology, first added in the third edition, has been updated extensively, as have antihypertensive agents, antianginal agents, antibiotics, and others.

The fourth edition also contains the following new features to facilitate use of the book and to integrate more fully the nursing-related aspects of pharmacology into the text:

- **Learning Objectives** now appear at the beginning of each chapter to guide students in their study. These objectives specifically highlight the nursing relevance of the drugs presented within each chapter.
- **Chapter Overviews** describe the range of material to provide a focus and to allow the student to place individual drug and drug-group content into a nursing practice context. These brief overviews follow the learning objectives. Together, the learning objectives and chapter overviews provide a solid nursing-oriented approach to content in each chapter.
- **Nursing Process Overviews** introduce each therapeutic segment or drug-group discussion. This content is subdivided into a nursing process framework: Assessment, Nursing Diagnoses, Management, and Evaluation. Included under the management heading are the planning and implementation steps of the nursing process. This approach is a highly practical one in that it eliminates unnecessary repetition of content that applies to both the planning and evaluation steps of the nursing process and thus enables us to keep the book to a more manageable length.
- **Nursing Implications Summaries,** which were formerly called *Patient Care Implications,* have been moved to the end of each chapter and highlighted with color to draw attention to them. These summaries serve two functions. First, they present general guidelines on the nursing implications for drug groups or specific therapies covered in each chapter. Second, they provide detailed, specific nursing implications for each therapeutic agent. This is the focal content for nursing students; it builds on the foundational content that is presented within each chapter. These extensive summaries can also be used by the student as a quick yet thorough review before each assignment in the clinical setting.
- **Chapter Review** sections have been added to the end of each chapter to facilitate review of key content and encourage comprehension. These reviews include **key terms,** which are bold-faced in the text where introduced, and **review questions,** which have been thoroughly revised to reflect a stronger nursing focus. Summaries that formerly appeared at the end of each chapter have been moved to the *Instructor's Resource Manual* to aid in preparing lecture content.
- To facilitate use of the book in programs where pharmacology is integrated into the curriculum and not offered as a separate course, we have included a separate **Disorder Index** at the beginning

of the comprehensive index. The disorder index presents all disorders discussed in the book to permit students to locate and read all disorder-specific content more readily. The comprehensive index also includes this information should the student desire to locate material in traditional index form.

Several content features have been retained from the previous edition and, in some cases, retitled to clarify their content.

- **Geriatric Considerations** are boxed for emphasis and included wherever there are significant implications of specific agents among elderly patients. These boxes are cross-referenced if pertinent to other chapters and, as are the features noted below, listed on the endpapers with page-number references to facilitate retrieval.
- **Pediatric Considerations** are also boxed and included where important. These life-span boxes are set off to allow the student to identify them readily and to locate age-related content.
- **Drug Abuse Alerts** are boxed to bring attention to this increasingly timely topic and to make the nursing student more aware of the nurse's responsibility in this area.
- **Dietary Considerations** feature information on drug-food interactions or health maintenance and promotion.
- **Patient Problem** boxes highlight patient problems that occur as side effects of drug therapy or otherwise present nursing challenges. These problems are emphasized because they are relatively common yet highly treatable, and, therefore, the nurse will encounter them frequently in practice.
- **Over 50 two-color illustrations** have been redrawn for better presentation and several new ones have been added. Illustrations have been enlarged, wherever possible, for clarity and visual appeal.

GOALS

Our goal remains to provide an up-to-date, scientifically based pharmacology book that assists nursing students studying drugs. Specifically, we seek to present clearly the concepts of pharmacology that guide all drug use; to discuss the major drug classes with an emphasis on mechanisms of action; and to detail the nursing implications for drug administration throughout the nursing process.

Our approach is to emphasize the rationale for drug therapy by relating the physiologic factors of disease processes to drug mechanisms. Although more thorough in describing the scientific basis of drug action than most textbooks for nursing students, this book carefully reviews pertinent physiologic facts so students can readily see how drugs modify physiologic processes and apply this to nursing practice.

Students of nursing look forward to pharmacology as one of the important background courses for their professional education, but they often express frustration about trying to remember the large number of drugs they must learn. We seek to minimize that difficulty by dealing with drug classes first and then by emphasizing the similarities among drugs of a single drug class. Chapters are focused on the grouping of drugs according to their mechanism of action.

For the instructor, our goal is to provide a book that can be adapted to varied curricula. The book is divided into twelve sections. Each section contains three or more chapters, and a chapter has distinct segments for different therapeutic situations. For example, antianginal drugs are covered in a section of the chapter on drugs to improve circulation; the chapter is one of nine chapters in the section on drugs affecting the cardiovascular and renal systems. This organization allows the instructor to rearrange the order in which material is presented and also gives students succinct sections to master.

ORGANIZATION

Sections I through III contain introductory material on the general principles of pharmacology, patient care, and neuropharmacology. These areas are the cornerstones of pharmacology. The goal of these chapters is to provide the background information for discussing drug actions and use. These concepts provide a guide for study of the drug classes presented later in the text. It has been our experience as teachers that basic concepts need to be reinforced throughout the study of pharmacology. We refer students to these early chapters at logical points throughout the text to assist the student in recalling basic concepts.

Sections IV through XII present drug classes by broad categories grouped on body systems or processes. Each section consists of three or more chapters with each chapter targeted to a general therapeutic goal. A chapter may contain several therapeutic segments, and a segment covers one or more drug classes.

Each chapter follows a consistent and logical format. The student is first presented the Learning Objectives for the chapter. The Chapter Overview describes the range of material covered in the chapter and is followed by the Nursing Process Overview, a section on the application of nursing process to content in that chapter or section. A therapeutic goal is then introduced, and the student is presented with the physiology and cell biology required as background. Disease processes are discussed briefly to explain the aberrant physiologic processes involved. Il-

lustrations are used to clarify the biologic processes reviewed. Specific drug classes are presented, with the mechanisms of action of the particular class discussed first, followed by pharmacokinetics, side effects, toxicity, drug interactions, and special comments on clinical use of the drugs. Each drug group is also listed in a table that gives both the generic and trade names, information on administration, and comments about the drug. Each chapter closes with an extensive Nursing Implications Summary, Key Terms, Review Questions, and Selected Readings, a list of suggested readings primarily from the nursing literature.

NURSING CONTENT

Much attention is given to emphasizing the relevant nursing information for the drugs discussed.

The Nursing Process Overview guides the nursing student in relating knowledge of medications to the overall plan of care for the patient. It is not meant to supplant the use of additional textbooks of nursing or current literature. Focus is on the pharmacologic factors rather than on the disease process itself. As mentioned previously, each Nursing Process Overview is divided into four parts. The first, Assessment, briefly summarizes key aspects of the assessment database. The second part, Nursing Diagnoses, gives examples of appropriate nursing diagnoses. The third part, Management, encompasses the planning and implementation phase of the nursing process. It identifies the type of data that should be monitored throughout therapy and some of the nursing activities needed to promote the drug activity or to foster patient well-being. The fourth part, Evaluation, describes the desired outcome of drug therapy.

The Nursing Implications Summary section supplements the Nursing Process Overview in assisting new practitioners and nursing students in translating knowledge of a drug action into appropriate nursing interventions. The specific clinical details of drug administration and of patient and family education are purposely separated from the body of the text and detailed in the Nursing Implications Summary section. The Nursing Implications Summary section does presuppose familiarity with the drug being discussed. A person using this section for reference on a completely unfamiliar drug would be well advised to first read the appropriate material on the drug in the body of the text.

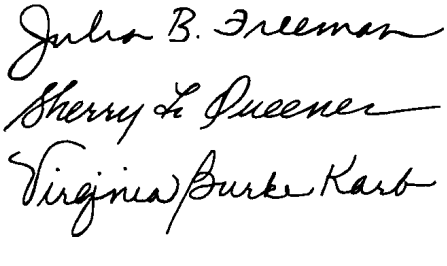
We believe the presentation we have used to integrate basic pharmacology with nursing practice enables students to use the book effectively. Students can first master the scientific basis of the action of a particular drug. General comments on nursing assessment and management of patients are made in the text and are summarized and brought into focus in the Nursing Process Overview and in Alert boxes. However, when students enter the clinical setting, they require much more specific information than can be effectively included in the body of the text. By gathering this information in the Nursing Implications Summary and in the drug tables, we provide students concrete material for clinical use.

ACKNOWLEDGMENTS

The production of this textbook has involved several able and experienced members of the editorial staff at Mosby–Year Book. We wish to thank Robin Carter and Don Ladig for their special editorial contributions. We also thank Linda Wendling for the Instructor's Resource Manual; Shannon Canty and Carol Sullivan Wiseman for production; and Gail Morey Hudson for design.

Henry R. Besch, Jr., Ph.D., Chairman of the Department of Pharmacology and Toxicology at Indiana University School of Medicine, deserves special mention for the support and help he has given us during the continued development of all editions of this book. Mrs. Janie Siccardi, Administration Assistant in the Department of Pharmacology and Toxicology, has greatly aided us in this effort. Thanks also for the support of Lynne Goodykoontz, Ph.D., R.N., Dean of the School of Nursing, University of North Carolina at Greensboro. The continued contributions of Dr. Lynn R. Willis, Professor of Pharmacology, Indiana University School of Medicine, and Dr. Stephen Hatfield, Research Scientist, Eli Lilly and Company, are much appreciated. Illustrations in several chapters were rendered by Mark Swindle, Phil Wilson Artcraft, and Sylvia Eidam.

We would also like to thank two special colleagues who have lived with the book as long as we have. They are Dr. Stephen W. Queener, Research Scientist, Department of Antibiotic Culture Development, Eli Lilly and Company; and Dr. Kenneth S. Karb, Medical Oncologist, Greensboro, North Carolina.



Contents

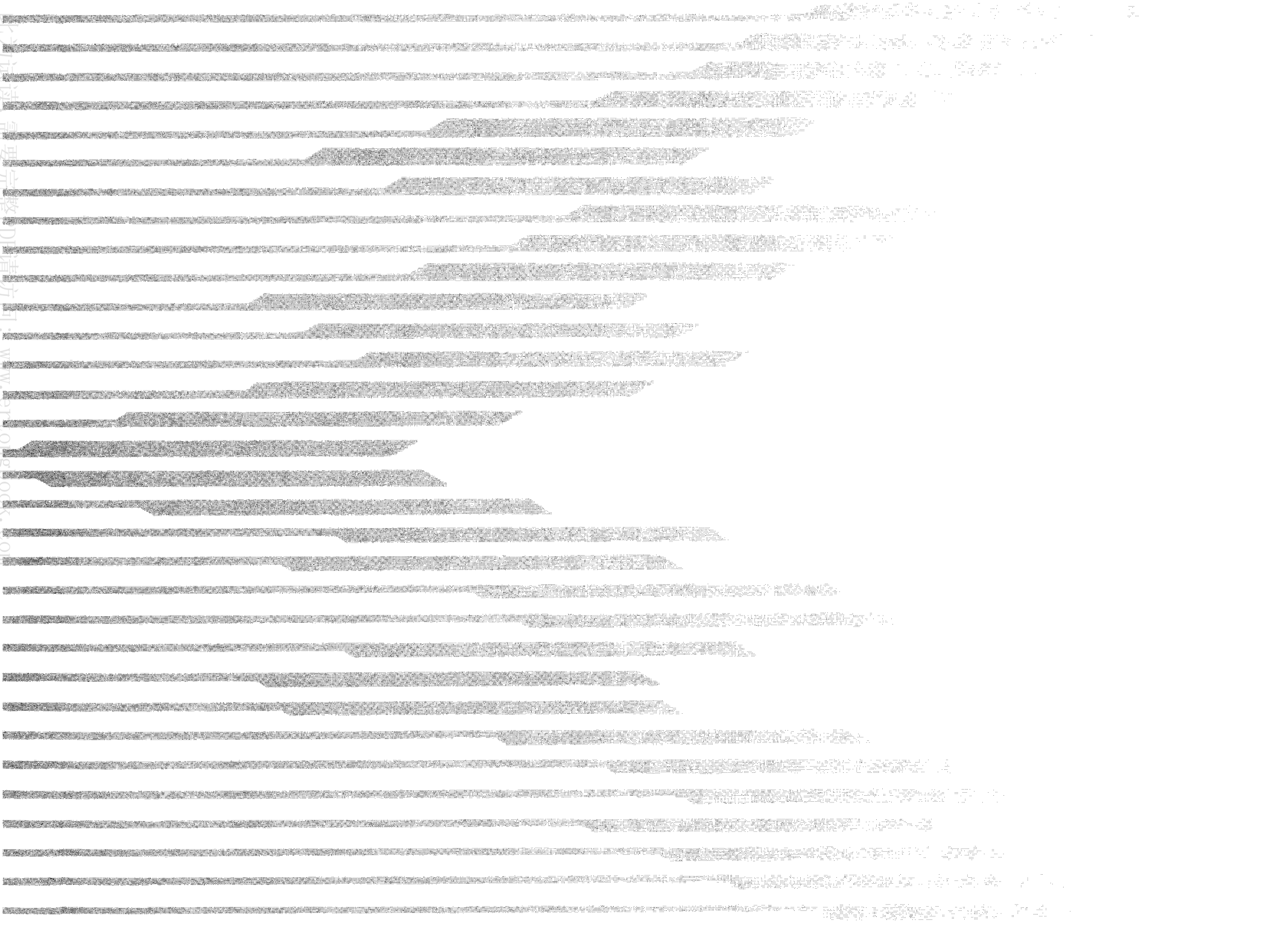
SECTION I

PRINCIPLES OF PHARMACOLOGY

Chapter 1, General Principles of Drug Action, covers the principles that govern the action of all drugs in the body. These basic concepts and terms recur repeatedly throughout the study of pharmacology. Initial study of these concepts will help the student approach the study of individual drugs and rationalize the manner in which they are used clinically.

Chapter 2, Legal Implications of Drug Therapy, places the legal status of modern drugs in perspective. This chapter also introduces the Schedule of Controlled Substances and the Drug Efficacy Study Implementation (DESI) rating—topics that recur at appropriate places throughout the text. Canadian drug classifications are covered in this chapter and referred to elsewhere in the text.

Chapter 3, Application of the Nursing Process to Drug Therapy, discusses the use of the nursing process with patients receiving drug therapy. The chapter also discusses patient education; medication errors; the roles of the nurse, physician, and pharmacist; and patient compliance.



CHAPTER 1

General Principles of Drug Action

LEARNING OBJECTIVES

After studying this chapter, you should be able to:

- Describe the three principles of drug action.
- Describe three ways in which drugs interact with the body.
- Discuss the mechanisms producing unwanted drug reactions.
- Describe four types of allergic responses.
- Explain how drug dissolution, the lipid solubility of the drug, and the presence of gastric contents can influence absorption of drugs by enteral routes.
- Discuss factors influencing persistence, distribution, metabolism, and excretion of drugs from the body.
- Discuss advantages and disadvantages to common routes of administration.
- Explain how the elimination half-life of a drug influences the time required to attain a steady-state concentration of drug given at fixed intervals.
- Give examples of kinds of drug interactions.
- Suggest three possible explanations for biologic variation in patients' responses to drugs.

CHAPTER OVERVIEW

◆ Pharmacology is the study of the interaction of chemicals with living organisms to produce biologic effects. This book presents those chemicals that produce therapeutically useful effects, chemicals referred to as *drugs*. This chapter reviews the general principles of drug action that form the basis for understanding the actions of specific drugs.

◆ Most drugs produce biologic effects by interacting with specific receptors at the drug's site of action. The magnitude of the biologic effect produced by a drug is related to the concentration of the drug present at the site of action. Drugs differ not only in their intrinsic ability to produce an effect, but also in their ability to penetrate to the site of action and in their rates of removal from that site. **Pharmacokinetics** is the study of how drugs enter the body, reach their site of action, and are removed from the body. **Pharmacodynamics** is the study of drug action at the biochemical and physiologic level. Both the pharmacokinetics and the pharmacodynamics of a drug determine how a drug is administered, how often it is given, and what the dose is.

Nursing Process Overview

GENERAL PRINCIPLES OF PHARMACOLOGY

Assessment

The material presented in this chapter forms the framework on which subsequent specific information about drugs may be placed.

Study the mechanism of action of each drug class presented. Does this drug operate through specific receptors? Does it alter a body fluid or cell membranes? What are the anticipated effects? How does the typical patient manifest these effects? How does the patient's age influence drug administration?

Management

Consider the possible side effects of the action of the drug in tissues. For example, does the drug affect receptors in more than one organ or tissue? Note whether experience has indicated that allergies or idiosyncratic reactions are common with the drug. How might the drug's half-life influence the patient's response? What is the drug's dosing schedule?

Evaluation

Consider the balance between the positive effects of the drug and the negative reactions to understand what place a drug has in clinical practice. For example, some very effective drugs have limited clinical use because the side effects that they produce are unacceptable for most patients. Understanding the pharmacology of individual drugs thus becomes a more rational process and is much more easily accomplished. Chapter 3 deals with the application of the nursing process to drug therapy.

MECHANISMS OF DRUG ACTIONS

Drug Action is Determined by How a Drug Interacts with the Body

Drugs may chemically alter body fluids

Drugs that chemically alter body fluids directly enter a body fluid or compartment. An example is an antacid, which enters the stomach and neutralizes excess stomach acid. Alteration of the pH of stomach fluid is the only intended action of these drugs. Other examples are drugs that accumulate in the urine and alter the pH of that fluid. By acidifying the urine with ammonium chloride or alkalinizing the urine with sodium bicarbonate, the ion flow in the kidney is altered, and drug excretion patterns are changed.

Drugs may chemically alter cell membranes

Drugs that chemically alter cell membranes interact nonspecifically. The interaction involves a chemical attraction and is usually based on the lipid nature of the cell membrane and the lipid attraction of the drugs. General anesthetic gases act in this way. These agents dissolve in lipid-containing membranes and thereby alter the properties of the cells involved.

Drugs may act through specific receptors

The biologic activity of most drugs is determined by the ability of the drug to bind to a specific receptor; this is in turn determined by the chemical structure of the drug. The interaction of a drug with a specific receptor is similar to a lock-and-key fit (Figure 1-1). Only a certain critical portion of the drug is usually involved in binding, not the entire molecule. Drugs that have similar critical regions but differ in other parts of the molecule might also be expected to have similar biologic activity (*drugs D, E,* and *F* in Figure 1-1).

The ability to bind to the receptor and the capability of stimulating an action by the receptor are two different aspects of drug action. The ability to bind to the receptor is known as **affinity.** Drugs with high affinities have a high attraction to the receptor. The capability of stimulating the receptor to some action is called **efficacy.**

When receptors are highly specific and have high affinities for the compounds that bind to them, very low concentrations of these compounds may show biologic activity. For example, hormones naturally found in the body act through specific receptors. Some of these hormones are found in the bloodstream at concentrations of less than 1 picomole, or less than one part per trillion. Nevertheless, these tiny amounts are biologically effective because the hormone is detected and bound by the specific receptor.

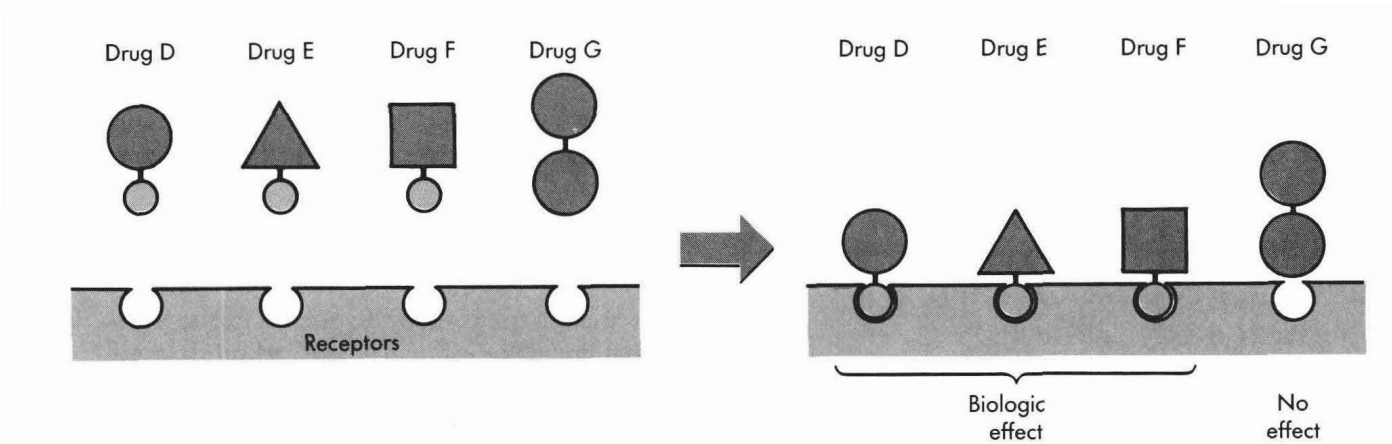


FIGURE 1-1

Lock-and-key fit between drugs and receptors through which they act. Site on receptor that interacts with drug has definite shape. Those drugs conforming to that shape can bind and produce biologic response. In example, only shape along lower surface of drug molecule is important in determining whether drug will bind to receptor.

Receptors also allow localization of drug effects to certain tissues. Each tissue or cell type possesses a unique array of specific receptors. For example, certain cells in the kidney possess specific receptors for antidiuretic hormone (see Chapter 50). These cells therefore have the capacity to respond to this hormone. Cells in other tissues that lack these receptors cannot respond to antidiuretic hormone.

The concept of drug receptors is one of the major concepts in pharmacology. The specific receptors called *drug receptors* are actually natural components of the body intended to respond to some chemical normally present in blood or tissues. For example, specific receptors within the brain respond to morphine and related compounds from the opium poppy, but the natural function of these receptors was not known until 1975 when endogenous morphine-like substances were discovered. It is now known that the brain and other tissues contain compounds called *enkephalins* and *endorphins*. These natural compounds bind to the so-called morphine receptor and are more potent than morphine in producing analgesia (see Chapter 44).

Any compound, either natural or synthetic, that binds to a specific receptor and produces a biologic effect by stimulating that receptor is called an **agonist.** For example, the hormone norepinephrine binds to specific sites in the heart called *beta-1 adrenergic receptors*. Stimulation of these receptors causes the heart to beat faster. The synthetic drug isoproterenol acts on the same receptors in the heart and produces the same effects. Both norepinephrine and isoproterenol are therefore called *agonists* for the beta-1 adrenergic receptor (see Chapter 10). Agonists have both affinity for receptors and efficacy because they cause some action by the receptor.

Some drugs produce their action not by stimulating receptors but by preventing natural substances from stimulating receptors. These drugs are called **antagonists.** For example, the drug propranolol blocks beta-1 adrenergic receptors and prevents agonists such as norepinephrine from stimulating the receptor normally. Propranolol therefore is classed as an antagonist of the action of norepinephrine. Antagonists have affinity for receptors but lack efficacy. When the receptor is occupied by an antagonist, the receptor cannot carry out its normal function.

Drugs do not Create Functions but Modify Existing Functions Within the Body

This principle explains the necessity for understanding the physiology of healthy humans and the changes caused by disease as a background for pharmacology. Drugs must always be considered in terms of the physiologic functions they alter in the body. In no case do drugs *create* a function in a tissue or organ. For example, digitalis is a drug used to strengthen the action of the heart. Digitalis produces this effect by altering the existing pattern of ion flow into and out of heart cells; it does not create a new way for the heart to contract. Digitalis simply alters the natural process.

To emphasize this principle, subsequent chapters on drug families start with a brief description of the normal physiology influenced by that group of drugs.

No Drug Has a Single Action

The **desired action** of a drug is an expected, predictable response. Ideally, each drug would have the desired effect on one physiologic process and produce no other effect. However, all drugs have the potential for altering more than one function in the body. These unwanted actions are known as **side effects** or drug reactions. For example, digitalis strengthens the failing heart; this is the desired clinical effect of the drug. At the same time, however, it may cause erratic heartbeats. This action is an undesirable side effect.

Predictable reactions arising from the known pharmacologic action of a drug account for between 70% and 80% of all drug reactions. For example, barbiturates put a patient to sleep because they depress the central nervous system. However, excessive depression of the central nervous system is lethal because the brain centers that control breathing will be depressed. Respiratory depression would therefore be an expected toxic reaction when barbiturates are used at doses that allow the drug to accumulate in the body. This type of toxic reaction to excessive amounts of the drug may be distinguished from predictable side effects seen at normal doses of the drug. These predictable side effects are related to the secondary actions of the drug. For example, at normal therapeutic doses, barbiturates increase the drug-metabolizing activity of the liver. This ability is unrelated to the therapeutically desired activity of these drugs and, in fact, is the mechanism by which barbiturates cause a number of reactions with other drugs.

Unpredictable reactions to drugs account for between 20% and 30% of all drug reactions. Although experience shows that a certain percentage of the population may be expected to react to a drug in an unusual manner, it is often not possible to predict which individual will show the reaction. The unpredictable drug reactions are of two types: idiosyncratic and allergic.

Idiosyncratic reactions are unusual, unexpected reactions to a drug that are most often explained by a genetic difference between the patient and the normal population. For example, a small percentage of the population lacks the enzyme pseudocholinesterase,

which is usually found in the bloodstream. Persons lacking this enzyme show no signs of this abnormality until they are exposed to drugs such as succinylcholine. Succinylcholine is a paralyzing agent used before surgery to relax the muscles and allow easy tracheal intubation. In most persons the drug is very short acting because it is destroyed by pseudocholinesterase. In persons lacking this enzyme, succinylcholine stays in the bloodstream, and the drug is very long acting. These patients require artificial ventilation until the paralyzing effects of succinylcholine wear off, whereas normally, people recover within a minute or so and require no assistance. This prolonged reaction to succinylcholine is one example of an idiosyncratic reaction.

Allergic reactions to drugs account for between 6% and 10% of all drug reactions. The allergic reaction may be triggered by the drug in its original form or by a metabolite of the drug formed in the body. Most drugs are not very allergenic, but others are very efficient at stimulating reactions from the immune system.

Drug allergies can be divided into four types, based on the mechanism of the immune reaction. Type I reactions occur soon after exposure and commonly produce **urticaria,** also called *hives*. These raised, irregularly shaped patches on the skin are frequently accompanied by severe itching. Although allergic reactions involving the skin are annoying, they are not usually serious; they can, however, progress to a severe acute allergic reaction that involves the cardiovascular and respiratory systems. This dangerous reaction is called **anaphylaxis** or anaphylactic shock. Anaphylaxis is marked by sudden contraction of the bronchiolar muscles and frequently by edema of the mouth and throat. These reactions may completely cut off air flow to the lungs. In addition, blood pressure falls, and the patient may go into shock. These violent reactions may occur within a very short time, and aggressive therapy is required to save the patient's life. Few people react to drugs in this way. All symptoms of type I reactions are caused by immunoglobulin E (IgE) antibodies, which are released in response to the drug and prompt target cells to discharge immune modulators such as histamine (see Chapter 24). Drugs associated with type I reactions include penicillins, cephalosporins, and iodides.

Type II reactions to drugs involve immunoglobulin M (IgM) or immunoglobulin G (IgG) antibodies, which can trigger lysis of specific blood cells under the appropriate conditions. These delayed reactions are sometimes called *autoimmune responses*. Examples include hemolytic anemia induced by methyldopa and thrombocytopenic purpura induced by quinidine. Procainamide and hydralazine can induce a condition resembling systemic lupus erythematosus.

Type III reactions are frequently described as serum sickness, but symptoms include urticaria, pain in the joints, swollen lymph nodes, and fever. Penicillins, iodides, sulfonamides, and phenytoin can cause this type of delayed reaction, which may involve IgE, IgM, or IgG antibodies.

The type IV reaction is contact dermatitis, caused by topical application of drugs.

Any patient can suffer an allergic reaction in response to any drug, but certain drugs are more prone to cause reactions. Patients receiving these agents should be closely monitored to detect early signs of allergic responses and thereby protected from injury.

Allergic reactions do not occur during the first exposure to a drug because time is required for the immune system to develop the antibodies that cause these reactions. In theory, this should help predict which patients are at risk of allergic reactions; however, documenting prior exposure to a drug is not always easy. Patients do not always know the names of drugs they have received and are not always reliable sources of information on prior reactions to drugs. Moreover, persons may be unknowingly exposed to antibiotics or other drugs through food or milk, if the drugs are improperly used in animal medicine.

PRINCIPLES RELATING DRUG DOSE TO DRUG ACTION

Pharmacokinetics

Factors controlling drug absorption by enteral routes

To be effective systemically, a drug must be present in the blood in a free or available form. For most medications, less than the total amount of administered drug is ultimately available to produce effects on target tissues. The term **bioavailability** describes what proportion of the administered drug is available to produce systemic effects. With a drug having low bioavailability, most of the administered dose of the drug is lost or destroyed, never reaching the blood in a form that can be effective. Drugs that are freely and rapidly absorbed have a high bioavailability. The many factors that can influence bioavailability are discussed in the following sections.

Drug dissolution. About 80% of drugs used in clinical practice are administered orally, primarily because of the ease and convenience of administration by this route. The drug may be given in liquid form, but most often it is given in a solid form such as a pill, tablet, or capsule (Table 1-1). To achieve this solid form, the drug is usually mixed with other compounds that serve various functions. Starches and other compounds may be added as inert fillers, especially when the actual amount of drug required per

Table 1-1 Forms of Medications

Form	Description
Capsules	Solid dosage forms for oral use in which medication is enclosed in gelatin shell that dissolves in stomach or intestine. Gelatin of capsules is colored to aid in product identification. Manufacturers use distinctive shapes for identifying their capsules.
Douche	Aqueous solution used as cleansing or antiseptic agent for part of body or body cavity. Douches are usually sold as powder or liquid concentrate to be dissolved or diluted before use.
Elixirs	Clear fluids for oral use that contain primarily water and alcohol with glycerin and sorbitol or another sweetener sometimes added. Alcohol content of these preparations varies.
Glycerites	Solutions of drugs in glycerin for external use. Solution must be at least 50% glycerin.
Patches	Inner surface of the patch contacts skin and allows transdermal absorption of lipid-soluble drugs. The total amount of drug on the patch is very large, but typically only a small fraction is absorbed.
Pills	Solid dosage forms for oral use in which drug and various vehicles are formed into small globules or ovoids. True pills are rare; most have been replaced by compressed tablets.
Solution	Liquid preparations, usually in water, containing one or more dissolved compounds. Solutions for oral use may contain flavoring and coloring agents. Solutions for intravenous injection must be sterile and particle free. Other injectable solutions must be sterile. Solutions of certain drugs may also be used externally.
Suppositories	Solid dosage forms to be inserted into body cavity where medication is released as solid melts or dissolves. Suppositories frequently contain cocoa butter (cacao butter or theobroma oil), which is solid at room temperature but liquid at body temperature, or glycerin, polyethylene glycol, or gelatin, which dissolves in secretions from mucous membranes.
Suspension	Finely divided drug particles that are suspended in suitable liquid medium before being injected or taken orally. Suspensions must not be injected intravenously.
Sustained action drug	Form of medication that is altered so that dissolution is slow and continuous for extended period. Total dosage in sustained action medication is greater than for regular formulations because drug is not all released at once.
Syrups	Medication dissolved in concentrated solution of sugar such as sucrose. Flavors may be added to mask unpleasant taste of certain medications.
Tablets	Solid dosage forms, frequently shaped like disks or cylinders, that contain, in addition to drug, one or more of following ingredients: binder (adhesive substance that allows tablet to stick together), disintegrators (substances promoting tablet dissolution in body fluids), lubricants (required for efficient manufacturing), and fillers (inert ingredients to make tablet size convenient).
Enteric-coated drugs	Solid dosage forms for oral use. Medication in tablet form is coated with materials designed not to dissolve in stomach. Coatings dissolve in intestine, where medication may be absorbed.
Press-coated or layered drugs	Preformed tablet that has another layer of material pressed on or around it. This practice allows incompatible ingredients to be separated and causes them to be dissolved at slightly different rates.
Tincture	Alcoholic or water-alcohol solutions of drugs.
Transdermal creams	Relatively lipid-soluble drugs that may be absorbed transdermally. Dosage is usually measured in inches of cream extruded from tube.
Troches (also called *lozenges* or *pastilles*)	Solid dosage forms, frequently shaped like disks or cylinders, that contain drug, flavor, sugar, and mucilage. Troches dissolve or disintegrate in mouth, releasing medication such as antiseptic or anesthetic for action in mouth or throat. Troches dissolve more slowly than tablets.

dose is too small to be conveniently handled. Adhesive substances called *binders* may also be added to allow the tablet to hold together after it is compressed in manufacture. Other compounds called *disintegrators* may be required to allow the tablet to absorb water and to break apart. Lubricants are frequently added to prevent the tablet from sticking to machinery during manufacture. These other additions to the dosage form may make up the bulk of the tablet. For example, in tablets containing 100,000 units of penicillin the active ingredient, potassium penicillin, makes up only 11% of the tablet mass.

To be effective, the solid dose of a drug must break apart in the gastrointestinal tract and allow the drug to go into solution. Only the dissolved drug is absorbed from the gastrointestinal tract into the blood. Breakdown of the solid dosage form is the required first step in absorption of the drug; therefore any

variability in this process can affect how rapidly and completely the drug is absorbed. The formulation of a tablet or capsule obviously affects dissolution rates. Tablets from different manufacturers that contain the same amount of active ingredient but different types and amounts of inert ingredients may not be identical in clinical action because each formulation may have different dissolution properties. Tablets may also change with age and conditions of storage. Older tablets tend to dry out and become more difficult to disintegrate, leading to reduced bioavailability of the drug.

The gastrointestinal tract. Food may interefere with dissolution and absorption of certain drugs. However, some drugs are so irritating to the stomach that food may be useful to dilute high local concentrations of the drug. There is considerable variation from person to person in gastric emptying times and, therefore, in the length of time the drug spends in the acid environment of the stomach. In addition, the amount of acid in the stomach varies with the individual and the time of day. The very young and the elderly have less stomach acid than middle-aged persons. Lower acidity may mean less drug is degraded and more is available for absorption.

Chemical properties of the drug. In addition to the physical state of the drug, its chemical nature determines how satisfactory oral administration will be. First, to pass through the membrane lining the gastrointestinal tract, a drug must be relatively **lipid soluble** because the membranes themselves contain a high concentration of lipid. Ionic (charged) forms of drugs do not easily pass through these membranes. Many drugs can exist in an ionic state or in an uncharged lipid-soluble state, depending on the chemical environment (pH) in which the drug is found. This environment changes along the gastrointestinal tract (Figure 1-2). The stomach fluid is highly acidic. A drug such as aspirin, which is a weak acid, is converted from a charged to an uncharged form by the strong acid in the stomach. Because the uncharged form of the drug can readily diffuse through the lipid membranes of the stomach cells, the drug is rapidly absorbed. In contrast, drugs such as penicillins are not stable in the acid of the stomach, and part of the dose is destroyed rather than absorbed.

Enteric coatings on tablets or capsules protect some drugs that are sensitive to the acid in the stomach (see Table 1-1). These coatings are inert at low (acidic) pH but soluble at higher (alkaline) pH. Therefore the drug passes through the stomach and is released in the intestine. Enteric coatings are also used for drugs that are highly irritating to the gastric mucosa.

The fluids in the small intestine are slightly alkaline.

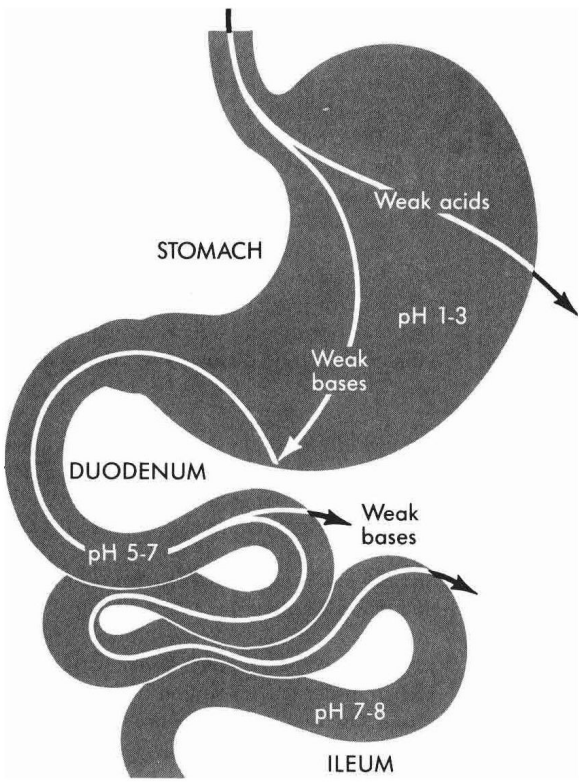


FIGURE 1-2

Effect of pH on ability of drugs to cross gastrointestinal membranes. Strongly acidic environment of stomach (pH 1 to 3) maintains weak acids in uncharged form, which is more easily absorbed. Weak bases remain charged in stomach but are converted to uncharged forms as pH approaches neutrality (pH 7) or becomes slightly alkaline (pH 7 to 8).

This higher pH favors the absorption of weakly basic drugs because at this pH range weak bases are uncharged (Figure 1-2). The small intestine also has an enormous surface area for drug absorption, which makes it a major site of absorption. However, some drugs, particularly proteins such as insulin or growth hormone, are destroyed in the small intestine by the action of digestive enzymes from the pancreas.

Drugs that are absorbed from the small intestine are transported by the portal circulation directly to the liver before entering the circulation to the rest of the body (Figure 1-3). The liver metabolizes a significant proportion of certain drugs before they can enter the general circulation. The term **first-pass phenomenon** refers to the process of absorption of a drug into the portal circulation, with metabolism of the drug in the liver before it reaches systemic circulation. Liver metabolism often inactivates drugs