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Roach's Introductory Clinical Pharmacology

Roach's Introductory Clinical Pharmacology
Roach’s Introductory Clinical Pharmacology, Edition 10
Roach’s Introductory
Clinical Pharmacology
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Roach’s Introductory
Clinical Pharmacology
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Roach's Introductory Clinical Pharmacology, Edition 10
Preface
Why This Book?

Roach's Introductory Clinical Pharmacology is one in a series of textbooks designed for the Licensed Practical/Vocational Nurse (LPN/LVN). As a front-line provider you are often times the first person to interact with a patient in the health care system. This textbook is designed to provide learners with a clear, concise introduction to pharmacology. The ease in reading lets you gain practical information on how to approach the patient about the drugs being prescribed. The basic explanations presented in this text are not intended to suggest that pharmacology is an easy subject. As we know it, drug therapy is one of the most important and complicated treatment modalities in modern health care.

As a novice provider, this book gives you the introduction you need to begin gaining knowledge about drugs and medication management. The learner may find that certain drugs or drug dosages available when this textbook went to publication may no longer be available. Likewise, there may be new drugs on the market that were not approved by the U.S. Food and Drug Administration (FDA) at the time of publication. With the availability of computers, smart phones, and Internet resources, current information is always there for verification of any drug question and should be checked when you do have a question before administering a drug. Don't forget that your colleagues, clinical pharmacists, and primary health care providers are also resources for information concerning a specific drug, including dosage, adverse reactions, contraindications, precautions, interactions, or administration.

What's New in This Edition?

The tenth edition of Roach's Introductory Clinical Pharmacology reflects the ever-changing science of pharmacology and the nurse's responsibilities in administering pharmacologic agents. Content is arranged to help the learner connect concepts and information. Key terms and drug class lists are now easily accessible at the beginning of every chapter. A new chapter (47) adds to your understanding about the drugs used to deal with the changes of aging on the urinary and reproductive systems. Every chapter begins with a case study to help you connect people to the drugs they take.

Key Themes in the New Edition

Mathematics and Prevention of Medication Errors

Chapter improvements are designed to support your learning of pharmacologic concepts. Chapter 3 provides you with ways to look at medication calculation using principles of safe practical information rather than mathematical formulas used in traditional math classes. You are guided through the chapter on the basics such as name, dose, and drug strength, then shown how to apply these elements in calculating medication doses from pill to liquid form. Learning focuses on reducing medication errors that result from mathematical mistakes rather than on the traditional arithmetic exercises. Up to seven dosage calculations for each chapter are provided when the textbook is used with the accompanying Study Guide. Should you wish to review math and less frequently used calculations, they are provided in Appendix F.

Communication Among Patients, Family, and Health Care Providers

Health literacy and communication are key components in Chapter 5. The patient—provider relationship has changed; patients are assuming a greater role and responsibility in their health care. Providers need to know the importance of good communication, health literacy, and cultural competence to practice patient-centered care. Your ability to use outcome strategies and communicate what you do to support patient and family confidence in learning self-management skills of medication administration is highlighted in patient teaching information.

Simple, Logical Drug Classification

Pharmacologic concepts are made easy and practical in the drug chapters, too. In Unit II, learning the different types of antibacterial drugs can be challenging. In this edition we have simplified the task by grouping the drugs according to what they do to a bacterial cell. This presentation helps in understanding how the different classes are similar and what to look for in terms of similar actions or adverse reactions. Unit III has a greater emphasis on teaching you pain assessment strategies as well as the drugs for pain relief. One of the main categories of drugs to treat Alzheimer's disease, the cholinesterase inhibitors, was moved to Unit IV and is now grouped with other drugs that affect the central nervous system. Lastly, diuretics

work in the urinary system primarily to treat diseases like hypertension, so the chapter on diuretics with cardiovascular system drugs now appears in Unit VIII.

What Makes This Book Unique?

The unique feature of this book is drug therapy from a nursing perspective. Publishers give you many choices of textbooks offering information on drug action and activity. This text is written by nurses for nurses in easy-to-read language and is designed to teach you not only about the drugs but also how to relay this information to patients. The more you understand the drugs and their effects on the human body, the better you can help your patients understand and deal with the drugs they are taking. The nursing process uses a step-by-step method to show how medications are used in the care of patients. Elements of the nursing process—assessment, analysis, planning, intervention, and evaluation—show you basic and practical nursing skills to help people understand the treatment, to meet their health care needs, and to improve adherence to treatment, all designed for better patient outcomes.

This textbook is written by authors bringing well over 30 years of nursing experience each from working in mental health settings, acute care hospitals, operating rooms, ambulatory clinics, home health, and hospice settings, as well as holding nursing certification in areas such as oncology, holistic nursing, and medical surgical clinical nurse specialist. As certified nurse educators (CNEs) and from experiences of teaching at vocational, associate degree, and baccalaureate nursing programs, the authors understand how to design and communicate learning in a way that will maximize your knowledge of pharmacology.

Roach’s Introductory Clinical Pharmacology, Edition 10

User’s Guide

Unit Structure and Organization

Learners are more successful when they know how to use the textbook as well as what is in the textbook. Here are some quick tips on how to use your textbook more effectively. Thirteen units offer 54 chapters providing information in learnable segments that are not overwhelming to the learner. Organization of the text in this manner allows you to move about the book easily when these areas are covered in your program curriculum.

The book starts with the basic fundamentals of drug therapy. Then units about infection and pain, followed by units about drugs related to different body systems. These units are written in a head-to-toe sequence, making the specific drugs easier to find.

Learning about drug therapy is easier when you can connect the information with life-like clinical experiences. In Chapter 5 you will be introduced to a group of clients in the clinic setting. Their stories establish for you a context in which to begin learning about the selected drugs and their real-world application.

Beginning of the Chapter

The chapter opening page is designed to guide you, the learner, in organizing your study routine as you learn the essential elements of drug therapy in each chapter.

Learning Objectives

These define what you will learn in a specific chapter. Review the objectives first to help you understand what you need to learn after reading the chapter.

Key Terms

With accompanying definitions, the Key Terms help you build your vocabulary. Look for bold type in the text at first mention of the word in the chapter to remind you of the definition.

Drug Classes

This gives you a sense of how drugs are grouped according to like properties. Learning these groupings helps you identify potential errors and safety concerns.

Pharmacology in Practice

Each chapter features a case study about an individual dealing with an issue related to drugs featured in the chapter. Scenarios focus on assessment, administration, or teaching issues that have an impact on real-life patients. Their stories help you to focus your attention on the concepts important to patient care.

Drug Information

Consistent Framework

Each chapter presents the drugs in such a way that you learn to recognize and respond to patient questions quickly and accurately. Illustrated concepts guide you as each chapter features information about the drug class in a logical and sequential order as Action, Uses, and Adverse Reactions— the concepts you, the nurse, deal with on a consistent basis. This is followed by Contraindications, Precautions, and Interactions—all items typically reviewed earlier and considered by other health providers, yet at the same time important for you to know to provide safe drug administration to your patients.

Nursing Alerts

Quickly identify urgent nursing actions in the management of the patient receiving a specific drug or drug category.

Lifespan Considerations

Draw your attention to specific populations at risk or needing specific administration considerations (e.g., gerontology and pediatric).

Drug Interaction Tables

A quick visual scan of these tables can tell you if a patient is likely to have a problem when multiple drugs are given.

Herbal Considerations

Provide information on herbs and complementary and alternative remedies used by patients under your care. Additional information is provided in Appendix D where examples of a number of natural products are provided.

Special Features

Special features are sprinkled throughout the text to direct you to priority information about the drugs or individuals who will receive the drugs.

Nursing Process and Drug Therapy

Uniquely presented, nursing actions regarding drug information are provided in the context of a nurse's clinical practice. The nursing process is featured as a practical guide to connect patients and drug therapy.

End of the Chapter

Here is where you determine what you have learned from reading each chapter. Information is summarized in an easy-to-read format, giving you the opportunity to demonstrate what you learned by applying information in the chapter case study. Once you review the chapter, use the review questions to demonstrate your skill as you would when you take the NCLEX-PN examination.

Pharmacology in Practice: Think Critically

Each chapter ends with a return to the case study patient. Realistic patient care situations help learners apply the material contained in the chapter by exploring options and making clinical judgments related to the administration of drugs. The case histories of seven patients are used, and different aspects of care are presented in different chapters like puzzle pieces, making connections for learners to appreciate the complex issues in providing care to both individuals and families.

Key Points

Key points are summarized and the important concepts of the chapter are listed to help you determine if you have mastered the learning objectives.

Summary Drug Tables

Conveniently placed, these tables provide a list of drugs from the classes discussed in each chapter. Names, uses, frequent adverse reactions, and general dosing information are given in an accessible format.

Chapter Review

Know Your Drugs

Use the matching exercise to identify drug names and connect generic with brand names to help you recognize the potential for and prevention against using the wrong drug.

Calculate Medication Dosages

Practice the math skills to learn accurate drug dosing and recognize the potential for error, thus ensuring that you give the correct dose.

Prepare for the NCLEX

Here questions allow you to test your knowledge of the material.

Build Your Knowledge – information and fact-based questions are presented to get you 'warmed up' to apply what you've learned.

Apply Your Knowledge – keyed to the actual 2011 NCLEX-PN test plan (see examples in Appendix H), these application and analysis questions about concepts in the chapter help you apply what you've learned as well as prepare for the NCLEX-PN examination.

Alternate-Format Questions – provide you experience in applying what you've learned in a different manner.

Special Features

Questions are structured like the NCLEX examination. The design helps you become familiar with the language and format of NCLEX testing.

Patient or Client

In this section of each chapter, you see wording change from "patient" to "client." This is specifically designed because often you are taught using the terms patient, resident, consumer, or client. The ability to recognize the interchange of words helps you to adapt to testing format.

Numbered (1, 2, 3, 4) Distractors

The NCLEX provides a single question on a computer screen. The options you are given are listed as numbers. Distracter options in these questions are labeled 1, 2, 3, 4 instead of A, B, C, D—again, to simulate the NCLEX-PN examination.

Roach's Introductory Clinical Pharmacology, Edition 10

Teaching/Learning Package

Resources for the Learner

Online Student Resources

Learning goes where you go! Free access to all your LWW resources at the Point, at http://thepoint.lww.com/Ford10e Student resources on the Point include eBook, NCLEX alternative-format tutorial, more than 1,000 NCLEX-style questions in an easy and accessible form, watch & learn videos, concepts in action animation 3-D depictions of pharmacology concepts, a Spanish-English audio glossary, and monographs of the 100 most commonly prescribed drugs.

Study Guide to Accompany Roach's Introductory Clinical Pharmacology, 10th Edition

Completely revised — offering exercises, puzzles, and the same seven patients as the textbook in real-life case studies connected to situations in the textbook.

PrepU

Practice makes perfect. And this is the perfect practice.

PrepU is an adaptive learning system designed to improve students' competency mastery and provide instructors with real-time analysis of their students' knowledge at both a class and individual student level.

PrepU demonstrates formative assessment—it determines what students know as they are learning and focuses them on what they are struggling with so they don't spend time on what they already know. Feedback is immediate and remediates students back to this specific text so they know where to go back to the text, read, and help understand a concept.

Adaptive and Personalized

No student has the same experience—PrepU recognizes when a student has reached 'mastery' of a concept before moving the student on to higher levels of learning. This will be a different experience for each student based on the number of questions he or she answers and whether he or she answers them correctly. Each question is also 'normed' by all students in PrepU around the country—how every student answers a specific question generates the difficulty level of each question in the system. This adaptive experience allows students to practice at their own pace and study much more effectively.

Personalized Reports

Students get individual feedback about their performance, and instructors can track class statistics to gauge the level of understanding. Both get a window into performance to help identify areas for remediation. Instructors can access the average mastery level of the class, students' strengths and weaknesses, and how often students use PrepU. Students can see their own progress charges and strengths and weaknesses—so they can continue quizzing in areas where they are weaker.

Mobile Optimized

Students can study anytime, anywhere with PrepU, as it is mobile optimized. More convenience equals more quizzing and more practice for students!

There is a PrepU resource available with this book! For more information, visit http://thepoint.lww.com/PrepU

Resources for the Instructor

Classroom resources: PowerPoint presentations; Guided Lecture Notes; Discussion Topics; Assignments; Image Bank.

Even more NCLEX-style questions: this time presented within a test generator that allows you to create and edit your own exams.

Roach’s Introductory Clinical Pharmacology, Edition 10

Acknowledgments

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To Sally S. Roach for trusting and believing in my efforts to continue the legacy of her book.

Dedication

To two very special women in my life, Sylvia Jones and Viola Oberholtzer. Sylvia is the first nurse I ever met, because she is my mother—and encouraged me to become a nurse, too. Aunt Vi (Viola O.), the person who told me to look at alternative routes to the Registered Nurse pathway, encouraging me to start at the community college and advance from there. Without the support of these two women in my life, I would not be authoring this book now.

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To my extended family, friends, colleagues and students-turned-fellow nurses—thanks for being there with ideas and stories to share.

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Roach’s Introductory Clinical Pharmacology, Edition 10

Contents

Unit I provides a foundation for understanding pharmacology in the context of nursing clinical practice. Three of the five chapters specifically discuss concepts focal to nursing: drug administration, nursing process, and patient teaching. The general principles of pharmacology and the mathematics involved in dosage calculation are concepts used by all providers involved with patients and medications and are included in their own chapters. This first unit of study is the foundation to build understanding of drug therapy in the subsequent units. Provided is a brief summary of the content in each chapter.

Basic principles are covered in Chapter 1, beginning with how drugs are derived from natural sources, such as plants, or made synthetically. Other concepts include how drug categories are based on the body system they influence or the way they are made chemically. Some drugs require a prescription (those given under the supervision of a licensed health care provider) or may be purchased as nonprescription (those obtained over the counter and designated as safe when taken as directed). When taken by a patient, drugs undergo a series of steps to be processed, utilized, and eliminated by the body—this is the basis for the study of pharmacology for health care providers.

Administration of a drug is primarily the responsibility of the nurse and is discussed in Chapter 2. Nurses have the duty to safely provide patient care by correctly administering the medication prescribed by the primary health care provider. This is achieved by learning and following the principles of drug administration, proper technique, and using medication systems correctly.

Your ability to correctly calculate mathematical problems is one of the most important steps in providing safe care to patients. Multiple steps in drug administration and delivery help to ensure accuracy in those math calculations. Chapter 3 provides both the opportunity to practice calculations and an overview of the tasks that you will undertake to be sure doses of

drugs are correct before administration.

Most patients experience problems of anxiety or deficient knowledge regarding new medication routines. The nursing process is used to help members of the health care team provide effective patient care. This process is used to develop an individualized care and teaching plan for the patient. These concepts are covered in Chapter 4.

It is crucial that the patient understand the important information about the medication prescribed, including the dosage, how to take the medication, the expected effect, and adverse reactions. In Chapter 5, components needed for successful patient teaching are described. Additionally, a group of individuals receiving nursing care in an ambulatory setting are introduced. Their stories are designed to help nurses understand how all this information is used in the nursing care of patients receiving drug therapy. You will learn how concepts are put into practice using case studies throughout the textbook.

By understanding the basic principles of pharmacology, you can build a sound knowledge base of the drugs used to help patients maintain their highest levels of wellness.

Roach’s Introductory Clinical Pharmacology, Edition 10

1

General Principles of Pharmacology

LEARNING OBJECTIVES

On completion of this chapter, the student will:

1. Define the term pharmacology.
2. Identify the different names assigned to drugs.
3. Distinguish between prescription drugs, nonprescription drugs, and controlled substances.
4. Discuss drug development in the United States.
5. Discuss the various types of drug activity and reactions produced in the body.
6. Identify factors that influence drug action.
7. Define drug tolerance, cumulative drug effect, and drug idiosyncrasy.
8. Discuss the types of drug interactions that may be seen with drug administration.
9. Discuss the nursing implications associated with drug actions, interactions, and effects.
10. Discuss the use of herbal medicines.

KEY TERMS

absorption • a drug is moved from site of administration to body fluids; first process during pharmacokinetics

adverse reaction • undesirable drug effect

allergic reaction • immediate hypersensitive reaction by the immune system; it presents as itching, hives, swelling, and difficulty breathing

anaphylactic shock • sudden, severe hypersensitivity reaction with symptoms that progress rapidly and may result in death if not treated; also called anaphylactic reaction or anaphylactoid reaction

angioedema • localized wheals or swellings in subcutaneous tissues or mucous membranes, which may be due to an allergic response; also called angioneurotic edema

controlled substances • drugs that have the potential for abuse and dependency, both physical and psychological

cumulative drug effect • when the body is unable to metabolize and excrete one dose of a drug before the next is given

distribution • drug moves from circulation to body tissue or a target site

drug idiosyncrasy • any unusual or abnormal response that differs from the response normally expected to a specific drug and dosage

drug tolerance • decreased response to a drug, requiring an increase in dosage to achieve the desired effect

excretion • elimination of a drug from the body

first-pass effect • action by which an oral drug is absorbed and carried directly to the liver, where it is inactivated by enzymes before it enters the general bloodstream

half-life • time required for the body to eliminate 50% of a drug

herbal medicine • type of complementary/alternative therapy that uses plants or herbs to treat various disorders; also called herbalism

hypersensitivity • undesirable reaction produced by a normal immune system

metabolism • drug is changed to a form that can be excreted

metabolite • inactive form of the original drug

nonprescription drugs • drugs that are designated by the U.S. Food and Drug Administration (FDA) to be safe (if taken as directed) and obtainable without a prescription; also called over-the-counter (OTC) drugs

pharmaceutic • pertaining to the phase during which a drug dissolves in the body

pharmacodynamics • study of the drug mechanisms that produce biochemical or physiologic changes in the body

pharmacokinetics • study of drug transit (or activity) after administration

physical dependency • habitual use of a drug, where negative physical withdrawal symptoms result from abrupt discontinuation

prescription drugs • drugs the federal government has designated as potentially harmful unless their use is supervised by a licensed health care provider, such as a nurse practitioner, physician, or dentist

psychological dependency • compulsion or craving to use a substance to obtain a pleasurable experience

receptor • in pharmacology, a reactive site on the surface of a cell; when a drug binds to and interacts with the receptor, a pharmacologic response occurs

teratogen • drug or substance that causes abnormal development of the fetus, leading to deformities

toxic • poisonous or harmful

Pharmacology is the study of drugs and their action on living organisms. A sound knowledge of basic pharmacologic principles is essential for nurses to administer medications safely and monitor patients who receive these medications. This chapter gives a basic overview of pharmacologic principles that you will need to understand when administering medications. The chapter also discusses drug development, federal legislation affecting the dispensing and use of drugs, and the use of herbal medicines as they relate to pharmacology.

Drugs have changed the way in which health care providers treat patients over the last century. In the early 1900s, individuals died of infections, from medical and surgical causes,

due in part to lack of sanitary conditions and the fact that medicines to combat infection did not exist. The discovery of drug substances has changed an infection from being a death sentence into a deviation in health status. Additionally, patients lacking certain substances in their bodies, such as insulin, or diagnosed with cancerous tumors can now live long and productive lives due to drug therapy.

Medications are derived from natural sources, such as plants and minerals, or synthetically produced in a laboratory. Examples of natural sources include digitalis, which is an extract from the foxglove plant that acts as a potent heart medication. On the other hand, mipomersen is a chemically engineered drug being studied to target specific cell components in people with high cholesterol.

Drug Names

The first task in learning about drug therapy is to understand how drugs are named. Throughout the process of development, drugs may have several names assigned to them: a chemical name, a generic (nonproprietary, official) name, and a trade (or brand) name. These different names can be confusing. When you have a clear understanding of the different names used, you promote patient safety by reducing errors.

The chemical name is the scientific term that describes the molecular structure of a drug; it typically is the chemical components of the drug. The generic name is considered the official name of a drug and is the name given to a drug that can be made or marketed by any company; it is nonproprietary (meaning it is not owned by any specific agency). This name is typically written in smaller letters on a container. The generic name is the official name that is given a drug by the U.S. Food and Drug Administration (FDA). It also is the name found in the National Formulary or the U.S. Pharmacopeia for an approved drug.

When a drug name is followed by a trademark symbol ™ or a registered trademark symbol ®, this signifies that it is the trade or brand name. The trade name is selected by a specific company for marketing purposes. To avoid confusion, it is best to use the generic name. Table 1.1 identifies the various names and provides an explanation of each.

Drug Classes and Categories

A drug may be classified by the chemical type of the active ingredient or by the way it is used to treat a particular condition. Each drug can be classified into one or more drug classes. To help learn these classes a list will be included on each chapter’s title page. For instance, in Unit II, drugs that retard or destroy pathogens are classified as anti-infectives. In each chapter, these drugs are further categorized by the way they work (such as antivirals) or their chemical structure (e.g., penicillins). Additionally, once a drug is approved for use, the FDA assigns it to one of the following categories: prescription, nonprescription, or controlled substance.

NURSING ALERT

Study the patterns used in the naming of drugs. This may help you to identify names and prevent medication errors. Certain portions of the drug name may be similar in specific drug classes or categories. For example, beta ()-adrenergic blocking drug names end with “lol.” Atenolol, metoprolol, and propranolol are all antihypertensive drugs from the same category.

Table 1.1 Drug Names

Figure 1.1 Example of a prescription form.

Prescription Drugs

Prescription drugs, also called legend drugs, are the largest category of drugs. Prescription drugs are prescribed by a licensed health care provider. The prescription (Fig. 1.1) contains the name of the drug, the dosage, the method and times of administration, and the signature of the licensed health care provider prescribing the drug.

Prescription drugs are designated by the federal government as potentially harmful unless their use is supervised by a licensed health care provider, such as a nurse practitioner, physician, or dentist. Supervision is important because, although these drugs have been tested for safety and therapeutic effect, prescription drugs may cause different reactions in some individuals.

In institutional settings, the nurse administers the drug and monitors the patient for therapeutic effect and adverse reactions. Some drugs have the potential to be toxic (harmful). You will play a critical role in evaluating the patient for toxic effects. When these drugs are prescribed to be taken at home, you will provide patient and family education about the drug.

Nonprescription Drugs

Nonprescription drugs are designated by the FDA as safe (when taken as directed) and can be obtained without a prescription. These drugs are also referred to as over-the-counter (OTC) drugs and may be purchased in a variety of settings, such as a pharmacy, drugstore, or the local supermarket. Over-the-counter drugs include those given for symptoms of the common cold, minor aches and pains, constipation, diarrhea, and heartburn.

These drugs are not without risk and may produce adverse reactions. For example, acetylsalicylic acid, commonly known as aspirin, is potentially harmful and can cause gastrointestinal (GI) bleeding and salicylism (see Chapter 13). Labeling requirements give the consumer important information regarding the drug, dosage, contraindications, precautions, and adverse reactions. Consumers are urged to read the directions carefully before taking OTC drugs.

Controlled Substances

Controlled substances are the most carefully monitored of all drugs. These drugs have a high potential for abuse and may cause physical or psychological dependency. Physical dependency is the habitual use of a drug, in which negative physical withdrawal symptoms res-

ult from abrupt discontinuation; it is the body's dependence on repeated administration of a drug. Psychological dependency is a compulsion or craving to use a substance to obtain a pleasurable experience; it is the mind's desire for the repeated administration of a drug. One type of dependency may lead to the other.

The Controlled Substances Act of 1970 established a schedule, or classification system, for drugs with abuse potential. The act regulates the manufacture, distribution, and dispensing of these drugs. The Controlled Substances Act divides drugs into five schedules, based on their potential for abuse and physical and psychological dependence. Appendix A describes the five schedules.

Prescription practices of the primary health care provider for controlled substances are monitored by the Drug Enforcement Agency (DEA). Under federal law, limited quantities of certain schedule V drugs may be purchased without a prescription, with the purchase recorded by the dispensing pharmacist. In some cases, state laws are more restrictive than federal laws and impose additional requirements for the sale and distribution of controlled substances. In hospitals or other agencies that dispense controlled substances, the scheduled drugs are counted every 8 to 12 hours to account for each injectable, tablet, or other form of the drug. Any discrepancy in the number of drugs must be investigated and explained immediately.

Drug Development

Drug development is a long and arduous process that can take from 7 to 12 years, and sometimes longer. The FDA has the responsibility for approving new drugs and monitoring drugs currently in use for adverse or toxic reactions. The development of a new drug is divided into the pre-FDA phase and the FDA phase. During the pre-FDA phase, a manufacturer conducts in vitro testing (testing in an artificial environment, such as a test tube) using animal and human cells to discover new drugs. This testing is followed by studies in live animals. The manufacturer then makes application to the FDA for Investigational New Drug (IND) status.

Figure 1.2 Phases of drug development.

Next, clinical (i.e., human) testing of the new drug begins. Clinical testing involves three phases, with each phase involving a larger number of people (Fig. 1.2). All effects, both pharmacologic and biologic, are noted. Phase 1 involves 20 to 100 individuals who are healthy volunteers. If Phase 1 studies are successful, the testing moves to Phase 2, in which tests are performed on people who have the disease or condition for which the drug is thought to be effective. If those results are positive, the testing progresses to Phase 3, in which the drug is given to large numbers of patients in medical research centers to provide information about adverse reactions. Phase 3 studies offer additional information on dosing and safety. Clinical trial studies can extend for many years.

A New Drug Application (NDA) is submitted after the investigation of the drug in Phases 1, 2, and 3 is complete and the drug is found to be safe and effective. With the NDA, the manufacturer submits all data collected concerning the drug during the clinical trials. A panel of experts, including pharmacologists, chemists, physicians, and other professionals, reviews the application and makes a recommendation to the FDA. The FDA then either approves or disapproves the drug for use.

After FDA approval, continued surveillance is done to ensure safety. Postmarketing surveillance (Phase 4) occurs after the manufacturer places the drug on the market. During this surveillance, an ongoing review of the drug occurs with particular attention given to adverse reactions. Health care providers are encouraged to help with this surveillance by reporting adverse effects of drugs to the FDA by using MedWatch (Display 1.1) or the Institute for Safe Medication Practices (ISMP) Medication Errors Reporting Program (MERP).

Display 1.1 MedWatch and Reporting Adverse Events

• The U.S. Food and Drug Administration (FDA) established a safety information and adverse event reporting program called MedWatch, by which nurses or other health care providers can learn about or report observations of serious adverse drug effects. Anyone can access the website (http://www.fda.gov/medwatch/index.html) to obtain safety alerts on drugs, devices, or dietary supplements.

• A drug must be used and studied for many years before all of the adverse reactions are identified. Nurses play an important role in monitoring for adverse reactions. The website provides a standardized form for reporting, which can be submitted electronically or downloaded, filled out, and mailed/faxed in to the program. It is important to submit reports, even if there is uncertainty about the cause–effect relationship. The FDA protects the identity of those who voluntarily report adverse reactions.

• The FDA considers serious adverse reactions those that may result in death, life-threatening illness, hospitalization, or disability or those that may require medical or surgical intervention. This form also is used to report an undesirable experience associated with the use of medical products (e.g., latex gloves, pacemakers, infusion pumps, anaphylaxis, blood, blood components).

Special Food and Drug Administration Programs

Although it takes considerable time for most drugs to get FDA approval, the FDA has special programs to meet different needs. Examples of these special programs include the orphan drug program and accelerated programs for urgent needs.

Orphan Drug Program

The Orphan Drug Act of 1983 was passed to encourage the development and marketing of products used to treat rare diseases. The act defines a rare disease as a condition affect-

ing fewer than 200,000 individuals in the United States or a condition affecting more than 200,000 persons in the United States but for which the cost of producing and marketing a drug to treat the condition would not be recovered by sales of the drug. The National Organization of Rare Disorders reports that there are more than 6800 rare disorders that affect approximately 30 million individuals. Examples of rare disorders include multiple myeloma, cystic fibrosis, and phenylketonuria.

The act provides for incentives such as research grants, protocol assistance by the FDA, and special tax credits to encourage manufacturers to develop orphan drugs. If the drug is approved, the manufacturer has 7 years of exclusive marketing rights. More than 360 new drugs have received FDA approval since the law was passed. Examples of orphan drugs include Valortim for anthrax infection, TOL-101 for acute organ transplant rejection, and atiprimod for the treatment of multiple myeloma.

Accelerated Programs

Accelerated approval of drugs is offered by the FDA as a means to make promising products for life-threatening diseases available on the market, based on preliminary evidence and before formal demonstration of patient benefit. The approval that is granted is considered a “provisional approval,” with a written commitment from the pharmaceutical company to complete clinical studies that formally demonstrate patient benefit. This program seeks to make life-saving investigational drugs available before granting final approval to treat diseases that pose a significant health threat to the public. If the drug continues to prove beneficial, the process of approval is accelerated.

One example of a disease that qualified as posing a significant health threat is acquired immunodeficiency syndrome (AIDS). When first diagnosed, because AIDS was so devastating to the individuals affected and because of the danger the disease posed to public health, the FDA and pharmaceutical companies worked together to shorten the IND approval process for some drugs that show promise in treating AIDS. This accelerated process allowed primary health care providers to administer medications that indicated positive results in early Phase 1 and 2 clinical trials, rather than wait until final approval was granted.

Drug Activity within the Body

Once in the body, drugs act in certain ways or phases. Oral drugs go through three phases: the pharmaceutic phase, pharmacokinetic phase, and pharmacodynamic phase (Fig. 1.3). Liquid and parenteral drugs (drugs given by injection) go through the latter two phases only.

Figure 1.3 Drug activity within the body: pharmaceutic, pharmacokinetic, and pharmacodynamic phases.

Pharmaceutic Phase

In the pharmaceutic phase, the drug dissolves. Drugs must be a soluble liquid to be absorbed. Drugs that are liquid or drugs given by injection (parenteral drugs) are already dissolved and are absorbed quickly. A tablet or capsule (solid forms of a drug) goes through this phase as it disintegrates into small particles and dissolves into the body fluids in the GI tract. Tablets that have an enteric coating or time-release capsules do not disintegrate until they reach the alkaline environment of the small intestine.

Pharmacokinetic Phase

Pharmacokinetics refers to the transportation activity of drugs in the body after administration. These activities include absorption, distribution, metabolism, and excretion. Subcomponents of these pharmacokinetic activities include transport, first-pass effect during absorption, and half-life during excretion of the drug.

Absorption

Absorption involves moving the drug from the site of administration into the body fluids and is the process by which a drug is made available for use in the body. It occurs after dissolution of a solid form of the drug or after the administration of a liquid or parenteral drug. In this process, the drug particles in the GI tract are moved into the body fluids. This movement can be accomplished in several ways:

Active transport—cellular energy is used to move the drug from an area of low concentration to one of high concentration.Passive transport—no cellular energy is used as the drug moves from an area of high concentration to an area of low concentration (small molecules diffuse across the cell membrane).Pinocytosis—cells engulf the drug particle (the cell forms a vesicle to transport the drug into the inner cell).

Several factors influence the rate of absorption, including the route of administration, the solubility of the drug, and specific conditions of the body’s tissues. The most rapid route of drug absorption occurs when the drug is given by the intravenous route. Absorption occurs more slowly when the drug is administered orally, intramuscularly, or subcutaneously. This is because the complex membranes of the GI mucosal layers, muscle, and skin delay drug passage. Bodily conditions such as lipodystrophy (the atrophy of subcutaneous tissue from repeated subcutaneous injections) inhibits absorption of a drug given in the affected site.

The first-pass effect may also affect absorption. When a drug is absorbed by the small intestine, it travels to the liver before being released to circulate within the rest of the body. The liver may metabolize a significant amount of the drug before releasing it into the body. When the drug is released into the circulation from the liver, the remaining amount of active drug may not be enough to produce a therapeutic effect, and the patient will need a higher dosage.

Distribution

The systemic circulation transports and distributes drugs to various body tissues or target sites. Distribution of an absorbed drug in the body depends on protein binding, blood flow, and solubility.

When a drug travels through the blood, it comes into contact with proteins such as the plasma protein albumin. The drug can remain free in the circulation or bind to the protein. Only free drugs can produce a therapeutic effect. Drugs bound to protein are pharmacologically inactive. Only when the protein molecules release the drug can the drug diffuse into the tissues, interact with receptors, and produce a therapeutic effect. A drug is said to be highly protein bound when more than 80% of the circulating drug is bound to protein.

A drug is distributed quickly to areas with a large blood supply, such as the heart, liver, and kidneys. In other areas, such as the internal organs, skin, and muscle, distribution of the drug occurs more slowly.

Solubility, or the drug's ability to cross the cell membrane, affects its distribution. Lipid-soluble drugs easily cross the cell membrane, whereas water-soluble drugs do not.

Metabolism

Metabolism, also called biotransformation, is the process by which the body changes a drug to a more or less active form that can be excreted. Usually the resulting form is a metabolite (an inactive form of the original drug). In some drugs, one or more of the metabolites may have some drug activity. Metabolites may undergo further metabolism or may be excreted from the body unchanged. Most drugs are metabolized by the liver, although the kidneys, lungs, plasma, and intestinal mucosa also aid in the metabolism of drugs.

Excretion

The elimination of drugs from the body is called excretion. After the liver renders drugs inactive, the kidney excretes the inactive compounds from the body. Also, some drugs are excreted unchanged by the kidney without liver involvement. Patients with kidney disease may require a dosage reduction and careful monitoring of kidney function. Children have immature kidney function and may require dosage reduction and kidney function tests. Similarly, older adults have diminished kidney function and require careful monitoring and lower dosages. Other drugs are eliminated in sweat, breast milk, or breath, or by the GI tract through the feces.

Half-life refers to the time required for the body to eliminate 50% of the drug. Knowledge of the half-life of a drug is important in planning the frequency of dosing. Drugs with a short half-life (2 to 4 hours) need to be administered frequently, whereas drugs with a long half-life (21 to 24 hours) require less frequent administration. For example, digoxin (Lanoxin) has a long half-life (36 hours) and requires once-daily dosing. However, aspirin has a short half-life

and requires frequent dosing. It takes five to six half-lives to eliminate approximately 98% of a drug from the body. Although half-life is fairly stable, patients with liver or kidney disease may have problems excreting a drug. Difficulty in excreting a drug increases the half-life and increases the risk of toxicity, because these organs do not remove the substances and the drug remains in the body longer. Older patients or patients with impaired kidney or liver function require frequent diagnostic tests measuring renal or hepatic function.

Onset, Peak, and Duration

The therapeutic effect of a drug determines the timing of drug administration. Three pharmacokinetic factors are important when considering how a drug acts in the body:

Onset of action—time between administration of the drug and onset of its therapeutic effect-Peak concentration—when absorption rate equals the elimination rate (not always the time of peak response)Duration of action—length of time the drug produces a therapeutic effect

These factors are taken into consideration when determining the dose schedule of a specific drug. This ensures that proper blood levels are maintained in the body for the drug to work properly.

Pharmacodynamic Phase

Pharmacodynamics is the study of the drug mechanisms that produce biochemical or physiologic changes in the body. Pharmacodynamics deals with the drug's action and effect in the body. After administration, most drugs enter the systemic circulation and expose almost all body tissues to possible effects of the drug. This exposure in all tissue causes the drug to produce more than one effect in the body. The primary effect of a drug is the desired or therapeutic effect. Secondary effects are all other effects, desirable or undesirable, produced by the drug.

Most drugs have an affinity for certain organs or tissues and exert their greatest action at the cellular level on those specific areas, which are called target sites. A drug exerts its action by one of two main mechanisms:

1. Alteration in cellular function
2. Alteration in cellular environment

Alteration in Cellular Function

Most drugs act on the body by altering cellular function. A drug cannot completely change the function of a cell, but it can alter its function. A drug that alters cellular function can increase or decrease certain physiologic functions, such as increasing heart rate, decreasing blood pressure, or increasing urine output.

Receptor-Mediated Drug Action

Many drugs act through drug–receptor interaction. The function of a cell is altered when a drug interacts with a receptor. This occurs when a drug molecule selectively joins with a reactive site—the receptor—on the surface of a cell. When a drug binds to and interacts with the receptor, a pharmacologic response occurs.

An agonist is a drug that binds with a receptor and stimulates the receptor to produce a therapeutic response. An antagonist is a drug that joins with receptors but does not stimulate the receptors. The therapeutic action in this case consists of blocking the receptor's function.

Receptor-Mediated Drug Effects

The number of available receptor sites influences the effects of a drug. When only a few receptor sites are occupied, although many sites are available, the response will be small. When the drug dose is increased, more receptor sites are used, and the response increases. When only a few receptor sites are available, the response does not increase when more of the drug is administered. However, not all receptors on a cell need to be occupied for a drug to be effective. Some extremely potent drugs are effective even when the drug occupies few receptor sites.

Alteration in Cellular Environment

Some drugs act on the body by changing the cellular environment, either physically or chemically. Physical changes in the cellular environment include changes in osmotic pressure, lubrication, absorption, or the conditions on the surface of the cell membrane.

An example of a drug that changes osmotic pressure is mannitol, which produces a change in the osmotic pressure in brain cells, causing a reduction in cerebral edema. A drug that acts by altering the cellular environment by lubrication is sunscreen. An example of a drug that acts by altering absorption is activated charcoal, which is administered orally to absorb a toxic chemical ingested into the GI tract. The stool softener docusate is an example of a drug that acts by altering the surface of the cellular membrane. Docusate has emulsifying and lubricating activity that lowers the surface tension in the cells of the bowel, permitting water and fats to enter the stool. This softens the fecal mass, allowing easier passage of the stool.

Chemical changes in the cellular environment include inactivation of cellular functions or alteration of the chemical components of body fluid, such as a change in the pH. For example, antacids neutralize gastric acidity in patients with peptic ulcers.

Other drugs, such as some anticancer drugs and some antibiotics, have as their main site of action the cell membrane and various cellular processes. They incorporate themselves into the normal metabolic processes of the cell and cause the formation of a defective final product, such as a weakened cell wall, which results in cell death, or reduce a needed energy substrate that leads to cell starvation and death.

Pharmacogenomics

Most pharmacodynamic mechanisms deal with principles that affect each cell in the same way, whereas pharmacogenomics is the study of how people's responses to medications are variable due to individual genetic variation. In other words, the genetic makeup of a person can affect the pharmacodynamics of a drug. This discovery was made during the Human Genome Project when many scientists were able to determine the different components of the human genetic code. Pharmacogenetics is the creation of individualized drug therapy that allows for the best choice and dose of drugs.

Drug Use, Pregnancy, and Lactation

The use of any medication (prescription or nonprescription) carries a risk of causing birth defects in the developing fetus. Drugs administered to pregnant women, particularly during the first trimester (3 months), may have teratogenic effects. A teratogen is any substance that causes abnormal development of the fetus, often leading to severe deformation. Some drugs are classified as teratogens.

To prevent teratogenic effects, the FDA has established five categories suggesting the potential of a drug for causing birth defects (Appendix A). Information regarding the pregnancy category of a specific drug is found in reliable drug literature, such as the inserts accompanying drugs and approved drug references. In general, most drugs are contraindicated during pregnancy and lactation unless the potential benefits of taking the drug outweigh the risks to the fetus or the infant.

During pregnancy, no woman should consider taking any drug, legal or illegal, prescription or nonprescription, unless the drug is prescribed or recommended by the primary health care provider. Smoking or drinking any type of alcoholic beverage also carries risks, such as low birth weight, premature birth, and fetal alcohol syndrome. Children born of mothers using addictive drugs, such as cocaine or heroin, often are born with an addiction to the drug abused by the mother. Women who are pregnant should also be very careful about the use of herbal supplements because these products can act like drugs. Women should not take an herbal supplement without discussing it first with her primary health care provider.

When a mother breastfeeds, her child has a risk of exposure to harmful medications. A number of drugs can be excreted in breast milk. Therefore, if a mother is lactating (breastfeeding), some of the drug she is taking may be ingested and absorbed by the infant or breastfeeding child. It is important for both mothers and nurses to know the potential of exposure to a breastfeeding child when the mother is taking a drug.

The National Library of Medicine provides a free online database with information on drugs and lactation called LactMed (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT). This website is geared to the health care practitioner and nursing mother and contains over 450

drug records. It includes information such as maternal levels in breast milk, infant levels in blood, and potential effects in breastfeeding infants. A pharmacist, Dr. Thomas Hale, from Texas Tech University has developed a system of lactation risk categories similar to that of the FDA pregnancy risk categories for drugs. Drugs are assigned an L1 to L5 risk according to the drug's transmission in breast milk and the effect it may have on the child. Hale's listing of certain drugs may differ from those published by organizations such as the American Academy of Pediatrics, yet it is a good starting point for discussion with mothers who are breastfeeding.

Drug Reactions

Drugs produce many reactions in the body. The following sections discuss adverse drug reactions, allergic drug reactions, drug idiosyncrasy, drug tolerance, cumulative drug effect, and toxic reactions.

Adverse Drug Reactions

Patients may experience one or more adverse reactions or side effects when they are given a drug. Adverse reactions are undesirable drug effects. Adverse reactions may be common or may occur infrequently. They may be mild, severe, or life-threatening. They may occur after the first dose, after a few doses, or after many doses. Often, an adverse reaction is unpredictable, although some drugs are known to cause certain adverse reactions in many patients. For example, drugs used in treating cancer are very toxic and are known to produce adverse reactions in many patients receiving them. Other drugs produce adverse reactions in fewer patients. Some adverse reactions are predictable, but many adverse drug reactions occur without warning.

Some texts use both the terms side effects and adverse reactions, using side effects to explain mild, common, and nontoxic reactions and adverse reactions to describe more severe and life-threatening reactions. For the purposes of this text, only the term adverse reaction is used, with the understanding that these reactions may be mild, severe, or life-threatening.

Allergic Drug Reactions

An allergic reaction is an immediate hypersensitivity reaction. Allergy to a drug usually begins to occur after more than one dose of the drug is given. On occasion, the nurse may observe an allergic reaction the first time a drug is given, because the patient has received or taken the drug in the past.

A drug allergy occurs because the individual's immune system responds to the drug as a foreign substance called an antigen. When the body responds to the drug as an antigen, a series of events occurs in an attempt to render the invader harmless. Lymphocytes respond by forming antibodies (protein substances that protect against antigens). Common allergic reactions occur when the individual's immune system responds aggressively to the antigen.

Chemical mediators released during the allergic reaction produce symptoms ranging from mild to life-threatening.

Even a mild allergic reaction produces serious effects if it goes unnoticed and the drug is given again. Any indication of an allergic reaction is reported to the primary health care provider before the next dose of the drug is given. Serious allergic reactions require contacting the primary health care provider immediately, because emergency treatment may be necessary.

Some allergic reactions occur within minutes (even seconds) after the drug is given; others may be delayed for hours or days. Allergic reactions that occur immediately often are the most serious.

Allergic reactions are manifested by a variety of signs and symptoms observed by the nurse or reported by the patient. Examples of some allergic symptoms include itching, various types of skin rashes, and hives (urticaria). Other symptoms include difficulty breathing, wheezing, cyanosis, a sudden loss of consciousness, and swelling of the eyes, lips, or tongue.

Anaphylactic shock is an extremely serious allergic drug reaction that usually occurs shortly after the administration of a drug to which the individual is sensitive. This type of allergic reaction requires immediate medical attention. Symptoms of anaphylactic shock are listed in Table 1.2.

All or only some of these symptoms may be present. Anaphylactic shock can be fatal if the symptoms are not identified and treated immediately. Treatment is to raise the blood pressure, improve breathing, restore cardiac function, and treat other symptoms as they occur. Epinephrine (adrenalin) may be given by subcutaneous injection in the upper extremity or thigh and may be followed by a continuous intravenous infusion. Hypotension and shock may be treated with fluids and vasopressors. Bronchodilators are given to relax the smooth muscles of the bronchial tubes. Antihistamines and corticosteroids may also be given to treat urticaria and angioedema (swelling).

Table 1.2 Symptoms of Anaphylactic Shock

Angioedema (angioneurotic edema) is another type of allergic drug reaction. It is manifested by the collection of fluid in subcutaneous tissues. Areas that are most commonly affected are the eyelids, lips, mouth, and throat, although other areas also may be affected. Angioedema can be dangerous when the mouth is affected, because the swelling may block the airway and asphyxia may occur. Difficulty in breathing and swelling in any area of the body are reported immediately to the primary health care provider.

Drug Idiosyncrasy

Drug idiosyncrasy is a term used to describe any unusual or abnormal reaction to a drug. It is any reaction that is different from the one normally expected from a specific drug and dose. For example, a patient may be given a drug to help him or her sleep (e.g., a hypnotic). Instead of falling asleep, the patient remains wide awake and shows signs of nervousness or excitement. This response is idiosyncratic because it is different from what one expects from this type of drug. Another patient may receive the same drug and dose, fall asleep, and after 8 hours be difficult to awaken. This, too, is abnormal and describes an overresponse to the drug.

The cause of drug idiosyncrasy is not clear. Study in the science of genetics can give us insight into possible explanations. The inability to tolerate certain chemicals and drugs is believed to be due to a genetic deficiency. Pharmacogenetics, the study of ways that specific genes can enhance sensitivity or resistance to certain drugs, helps to explain some drug idiosyncrasies. A pharmacogenetic disorder is a genetically determined abnormal response to normal doses of a drug. This abnormal response occurs because of inherited traits that cause abnormal metabolism of drugs. For example, individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency have abnormal reactions to a number of drugs. These patients exhibit varying degrees of hemolysis (destruction of red blood cells) when these drugs are administered. More than 100 million people are affected by this disorder. Examples of drugs that cause hemolysis in patients with a G6PD deficiency include aspirin, chloramphenicol, and the sulfonamides.

Drug Tolerance

Drug tolerance is a term used to describe a decreased response to a drug, requiring an increase in dosage to achieve the desired effect. Drug tolerance may develop when a patient takes certain drugs, such as opioids and tranquilizers, for a long time. The individual who takes these drugs at home increases the dose when the expected drug effect does not occur. The development of drug tolerance is a sign of physical drug dependence. Drug tolerance may also occur in the hospitalized patient. When the patient begins to ask for the drug at more frequent intervals, the nurse needs to assess whether the dose is not adequate based on the disease process or whether the patient is building a tolerance to the drug's effects.

Cumulative Drug Effect

A cumulative drug effect may be seen in those people with liver or kidney disease because these organs are the major sites for the breakdown and excretion of most drugs. This drug effect occurs when the body is unable to metabolize and excrete one (normal) dose of a drug before the next dose is given. Thus, if a second dose of the drug is given, some drug from the first dose remains in the body. A cumulative drug effect can be serious because too much of the drug can accumulate in the body and lead to toxicity.

Patients with liver or kidney disease are usually given drugs with caution because a cumulative effect may occur. When the patient is unable to excrete the drug at a normal rate, the drug accumulates in the body, causing a toxic reaction. Sometimes, the primary health care provider lowers the dose of the drug to prevent a toxic drug reaction.

Toxic Reactions

Most drugs can produce toxic or harmful reactions if administered in large dosages or when blood concentration levels exceed the therapeutic level. Toxic levels build up when a drug is administered in dosages that exceed the normal level or if the patient's kidneys are not functioning properly and cannot excrete the drug. Some toxic effects are immediately visible; others may not be seen for weeks or months. Some drugs, such as lithium or digoxin, have a narrow margin of safety, even when given in recommended dosages. It is important to monitor these drugs closely to detect and avoid toxicity.

Drug toxicity can be reversible or irreversible, depending on the organs involved. Damage to the liver may be reversible, because liver cells can regenerate. However, hearing loss from damage to the eighth cranial nerve caused by toxic reaction to the anti-infective drug streptomycin may be permanent. Sometimes drug toxicity can be reversed by administering another drug that acts as an antidote. For example, in serious instances of digitalis toxicity, the drug Digibind may be given to counteract the effect.

Carefully monitor the patient's blood level of drug to ensure that the level remains within the therapeutic range. Any deviation should be reported to the primary health care provider. Because some drugs can cause toxic reactions even in recommended doses, you should be aware of the signs and symptoms of toxicity of commonly prescribed drugs.

Minimizing Drug Reactions Through Pharmacogenomics

Drug developers are also researching ways to target cell structures and selected cells to minimize reactions in other body tissues, thereby reducing or eliminating adverse reactions. Genetic specialists search for genetic variations associated with drug efficiency. The goal of pharmacogenomics is the creation of drugs that can be tailor-made for individuals, target specific cells in the body, and adapt to each person's own individual genetic makeup.

Drug Interactions

It is important when administering medications to be aware of the various drug interactions that can occur, especially drug–drug interactions and drug–food interactions. This section gives a brief overview of drug interactions. Specific drug–drug and drug–food interactions are discussed in subsequent chapters.

Drug–Drug Interactions

A drug–drug interaction occurs when one drug interacts with or interferes with the action of another drug. For example, taking an antacid with oral tetracycline causes a decrease in

the effectiveness of the tetracycline. The antacid chemically interacts with the tetracycline and impairs its absorption into the bloodstream, thus reducing the effectiveness of the tetracycline. Drug categories known to cause interactions with other drugs include oral anticoagulants, oral hypoglycemics, anti-infectives, antiarrhythmics, cardiac glycosides, and alcohol. Drug–drug interactions can produce effects that are additive, synergistic, or antagonistic.

Additive Drug Reaction

An additive drug reaction occurs when the combined effect of two drugs is equal to the sum of each drug given alone. The equation 1 + 1 = 2 is sometimes used to illustrate the additive effect of drugs. For example, taking the drug heparin with alcohol will increase bleeding.

Synergistic Drug Reaction

Drug synergism occurs when drugs interact with each other and produce an effect that is greater than the sum of their separate actions. The equation 1 + 1 = 3 may be used to illustrate synergism. Drug synergism is exemplified when a person takes both a hypnotic and alcohol. When alcohol is taken shortly before or after the hypnotic drug, the action of the hypnotic increases considerably. The individual experiences a drug effect that is greater than each drug taken alone. On occasion, the occurrence of a synergistic drug effect is serious and even fatal.

Antagonistic Drug Reaction

An antagonistic drug reaction occurs when one drug interferes with the action of another, causing neutralization or a decrease in the effect of one of the drugs. For example, protamine is a heparin antagonist. This means that the administration of protamine completely neutralizes the effects of heparin in the body and blood clotting will happen in the body.

Drug–Food Interactions

When a drug is given orally, food may impair or enhance its absorption. A drug taken on an empty stomach is absorbed into the bloodstream more quickly than when the drug is taken with food in the stomach. Some drugs (e.g., captopril) must be taken on an empty stomach to achieve an optimal effect. Drugs that should be taken on an empty stomach are administered 1 hour before or 2 hours after meals. Other drugs—especially drugs that irritate the stomach, result in nausea or vomiting, or cause epigastric distress—are best given with food or meals. This minimizes gastric irritation. The nonsteroidal anti-inflammatory drugs (NSAIDs) and salicylates are examples of drugs that are given with food to decrease epigastric distress. Still other drugs combine with a food, forming an insoluble food–drug mixture. For example, when tetracycline is administered with dairy products, a drug–food mixture is formed that is not absorbable by the body. When a drug cannot be absorbed by the body, no pharmacologic effect occurs.

Factors Influencing Drug Response

Certain factors may influence drug response and are considered when the primary health care provider prescribes and the nurse administers a drug. These factors include age, weight, sex, disease, and route of administration.

Age

The age of the patient may influence the effects of a drug. Infants and children usually require smaller doses of a drug than adults. Immature organ function, particularly of the liver and kidneys, can affect the ability of infants and young children to metabolize drugs. An infant's immature kidneys impair the elimination of drugs in the urine. Liver function is poorly developed in infants and young children. Drugs metabolized by the liver may produce more intense effects for longer periods. Parents must be taught the potential problems associated with administering drugs to their children. For example, a safe dose of a nonprescription drug for a 4-year-old child may be dangerous for a 6-month-old infant.

Elderly patients may also require smaller doses, although this may depend on the type of drug administered. For example, the elderly patient may be given the same dose of an antibiotic as a younger adult. However, the same older adult may require a smaller dose of a drug that depresses the central nervous system, such as an opioid. Changes that occur with aging affect the pharmacokinetics (absorption, distribution, metabolism, and excretion) of a drug. Any of these processes may be altered because of the physiologic changes that occur with aging. Table 1.3 summarizes the changes that occur with aging and their possible pharmacokinetic effects.

Table 1.3 Factors Altering Drug Response in Children and Older Adults

Polypharmacy is the taking of numerous drugs that can potentially react with one another. This is seen particularly in elderly patients who may have multiple chronic diseases; polypharmacy leads to an increase in the number of potential adverse reactions. Although multiple drug therapy is necessary to treat certain disease states, it always increases the possibility of adverse reactions. You need good assessment skills to detect any problems when monitoring the geriatric patient's response to drug therapy.

Weight

In general, dosages are based on a weight of approximately 170 lb, which is calculated to be the average weight of men and women. A drug dose may sometimes be increased or decreased because the patient's weight is significantly higher or lower than this average. With opioids, for example, higher- or lower-than-average dosages may be necessary, depending on the patient's weight, to produce relief of pain.

Sex

The sex of an individual may influence the action of some drugs. Women may require a smaller dose of some drugs than men. This is because many women are smaller and have a different body fat–to-water ratio than men.

Disease

The presence of disease may influence the action of some drugs. Sometimes disease is an indication for not prescribing a drug or for reducing the dose of a certain drug. Both hepatic (liver) and renal (kidney) disease can greatly affect drug response.

In liver disease, for example, the ability to metabolize or detoxify a specific type of drug may be impaired. If the average or normal dose of the drug is given, the liver may be unable to metabolize the drug at a normal rate. Consequently, the drug may be excreted from the body at a much slower rate than normal. The primary health care provider may then decide to prescribe a lower dose and lengthen the time between doses because liver function is abnormal.

Patients with kidney disease may exhibit drug toxicity and a longer duration of drug action. The dosage of drugs may be reduced to prevent the accumulation of toxic levels in the blood or further injury to the kidney.

Route of Administration

Intravenous administration of a drug produces the most rapid drug action. Next in order of time of action is the intramuscular route, followed by the subcutaneous route. Giving a drug orally usually produces the slowest drug action.

Some drugs can be given only by one route; for example, antacids are given only orally. Other drugs are available in oral and parenteral forms. The primary health care provider selects the route of administration based on many factors, including the desired rate of action. For example, the patient with a severe cardiac problem may require intravenous administration of a drug that affects the heart. Another patient with a mild cardiac problem may experience a good response to oral administration of the same drug.

Nursing Implications with Drug Actions

Many factors can influence drug action. Consult appropriate references or the clinical pharmacist if there is any question about the dosage of a drug, whether other drugs the patient is receiving will interfere with the drug being given, or whether the oral drug should or should not be given with food.

Drug reactions are potentially serious. Observe all patients for adverse drug reactions, drug idiosyncrasy, and evidence of drug tolerance (when applicable). It is important to report all drug reactions or any unusual drug effect to the primary health care provider.

Use good judgment when reporting adverse drug reactions to the primary health care provider. Accurate observation and evaluation of the circumstances are essential; record all ob-

servations in the patient's record. If there is any question regarding the events that are occurring, withhold the drug and immediately contact the primary health care provider.

Herbal Medicine and Health Care

Herbal medicine, herbalism, and herbal therapy are all names used for complementary/alternative therapy that uses plants or herbs to treat various disorders. Individuals worldwide use herbal therapy and dietary supplements extensively. According to the World Health Organization (WHO), 80% of the world's population relies on herbs for a substantial part of their health care. Herbs have been used by virtually every culture in the world throughout history. For example, Hippocrates prescribed St. John's wort, currently a popular herbal remedy for depression. Native Americans use plants such as coneflower, ginseng, and ginger for therapeutic purposes. Herbal therapy is part of the group of nontraditional therapies commonly known as complementary and alternative medicine (CAM).

Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) is one of the 27 institutes and centers that make up the National Institutes of Health (NIH). The NCCAM explores complementary and alternative healing practices through scientific research. It also trains CAM scientists and disseminates the information gleaned from the research it conducts. Among the various purposes of the NCCAM is to evaluate the safety and efficacy of widely used natural products, such as herbal remedies and dietary and food supplements. The NCCAM is dedicated to developing programs and encouraging scientists to investigate CAM treatments that show promise. The NCCAM budget has steadily grown, reflecting the public's interest and need for CAM information that is based on rigorous scientific research.

The NCCAM defines CAM as a "group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine." Examples of complementary therapies are relaxation techniques, massage, aromatherapy, and healing touch. Complementary therapies are often used with traditional health care to "complement" conventional medicine. Alternative therapies, on the other hand, are therapies used in place of or instead of conventional or Western medicine. The term complementary/alternative therapy often is used as an umbrella term for many therapies from all over the world.

Dietary Supplement Health and Education Act

Herbs are not sold and promoted in the United States as drugs. In addition to vitamins and minerals, herbs are classified as dietary or nutritional supplements. Nutritional or dietary substances are terms used by the federal government to identify substances that are not regulated by the FDA but purported to be effective for use to promote health. This means that they do not have to meet the same standards as drug and OTC medications for proof of safety and

effectiveness and what the FDA calls “good manufacturing practices.”

Because natural products cannot be patented in the United States, it is not profitable for drug manufacturers to spend the millions of dollars and the 7 to 12 years needed to study and develop these products as drugs. In 1994, the U.S. government passed the Dietary Supplement Health and Education Act (DSHEA). This act defines substances such as herbs, vitamins, minerals, amino acids, and other natural substances as “dietary supplements.” The act permits general health claims such as “improves memory” or “promotes regularity” as long as the label also has a disclaimer stating that the supplements are not approved by the FDA and are not intended to diagnose, treat, cure, or prevent any disease. The claims must be truthful and not misleading and supported by scientific evidence. Some manufacturers have abused the law by making exaggerated claims, but the FDA has the power to enforce the law, which it has done, and these claims have decreased.

Educating Patients About Herbs and Dietary Supplements

The use of herbs and dietary supplements to treat various disorders is common. Herbs are used for various effects, such as boosting the immune system, treating depression, and promoting relaxation. Individuals are becoming more aware of the benefits of herbal therapies and dietary supplements. Advertisements, books, magazines, and Internet sites concerning these topics are prolific. People eager to cure or control various disorders take herbs, teas, megadoses of vitamins, and various other natural products. Although much information is available on dietary supplements and herbal therapy, obtaining the correct information can be difficult at times. Medicinal herbs and dietary substances are available at supermarkets, pharmacies, health food stores, and specialty herb stores and through the Internet. The potential for misinformation abounds. Because these substances are “natural products,” many individuals incorrectly assume that they are without adverse effects. When any herbal remedy or dietary supplement is used, it should be reported to the nurse and the primary health care provider. Many of these natural substances have strong pharmacologic activity, and some may interact with prescription drugs or be toxic in the body. For example, comfrey, an herb that was once widely used to promote digestion, can cause liver damage. Although it may still be available in some areas, it is a dangerous herb and is not recommended for use as a supplement.

When obtaining the drug history, always question the patient about the use of herbs, teas, vitamins, or other dietary supplements. Many patients consider herbs as natural and therefore safe. Some also neglect to report the use of an herbal tea as part of the health care regimen because they do not think of it as such. Explain to the patient that just because an herbal supplement is labeled “natural,” it does not mean the supplement is safe or without harmful effects. Herbal supplements can act the same way as drugs and can cause medical problems if

not used correctly or if taken in large amounts. Display 1.2 identifies teaching points to consider when discussing the use of herbs and dietary supplements with patients.

Because herbal supplements are not regulated by the FDA, products lack standardization with regard to purity and potency. In addition, multiple ingredients in products and batch-to-batch variation make it difficult to determine if reactions occur as a result of the herb itself. To assist with the identification of herb–drug interactions, report any potential interactions to the FDA through its MedWatch program (see Display 1.1). It is especially important to take special care when patients are taking any drugs with a narrow therapeutic index (the difference between the minimum therapeutic and minimum toxic drug concentrations is small—such as warfarin, a blood thinner) and herbal supplements. Because the absorption, metabolism, distribution, and elimination characteristics of most herbal products are poorly understood, much of the information on herb–drug interactions is speculative. Herb–drug interactions are sporadically reported and difficult to determine.

Display 1.2 Teaching Points When Discussing Herbal Therapy

- Herbal preparations are not necessarily safe because they are natural. Unlike prescription and over-the-counter (OTC) medicines, herbal products and supplements do not have to be tested to prove they work well and are safe before they're sold. Also, they may not be pure. They might contain other ingredients, such as plant pollen, that could make you sick. Sometimes they contain drugs that are not listed on the label, such as steroids or estrogens.
- If you have health problems, there may be an increased danger in taking herbal preparations. These conditions include blood-clotting problems, cancer, diabetes, an enlarged prostate gland, epilepsy, glaucoma, heart disease, high blood pressure, immune system problems, psychiatric problems, Parkinson's disease, liver problems, stroke, and thyroid problems.
- If you are going to have surgery, be sure to tell your doctor if you use herbal products. Herbal products can cause problems with surgery, including bleeding and problems with anesthesia. Stop using herbal products at least 2 weeks before surgery, or sooner if your doctor recommends it.
- Herbal products can change the way prescription and OTC drugs work. Herbal health products or supplements can affect the way the body processes drugs. When this happens, your medicine may not work the way it should. This may mean the drugs aren't absorbed at high enough levels to help the conditions for which they are prescribed. This can cause serious problems. You should be especially cautious about using herbal health products or supplements if you take a drug in one of the following categories:
  - Drugs to treat depression, anxiety, or other psychiatric problems
  - Antiseizure drugs