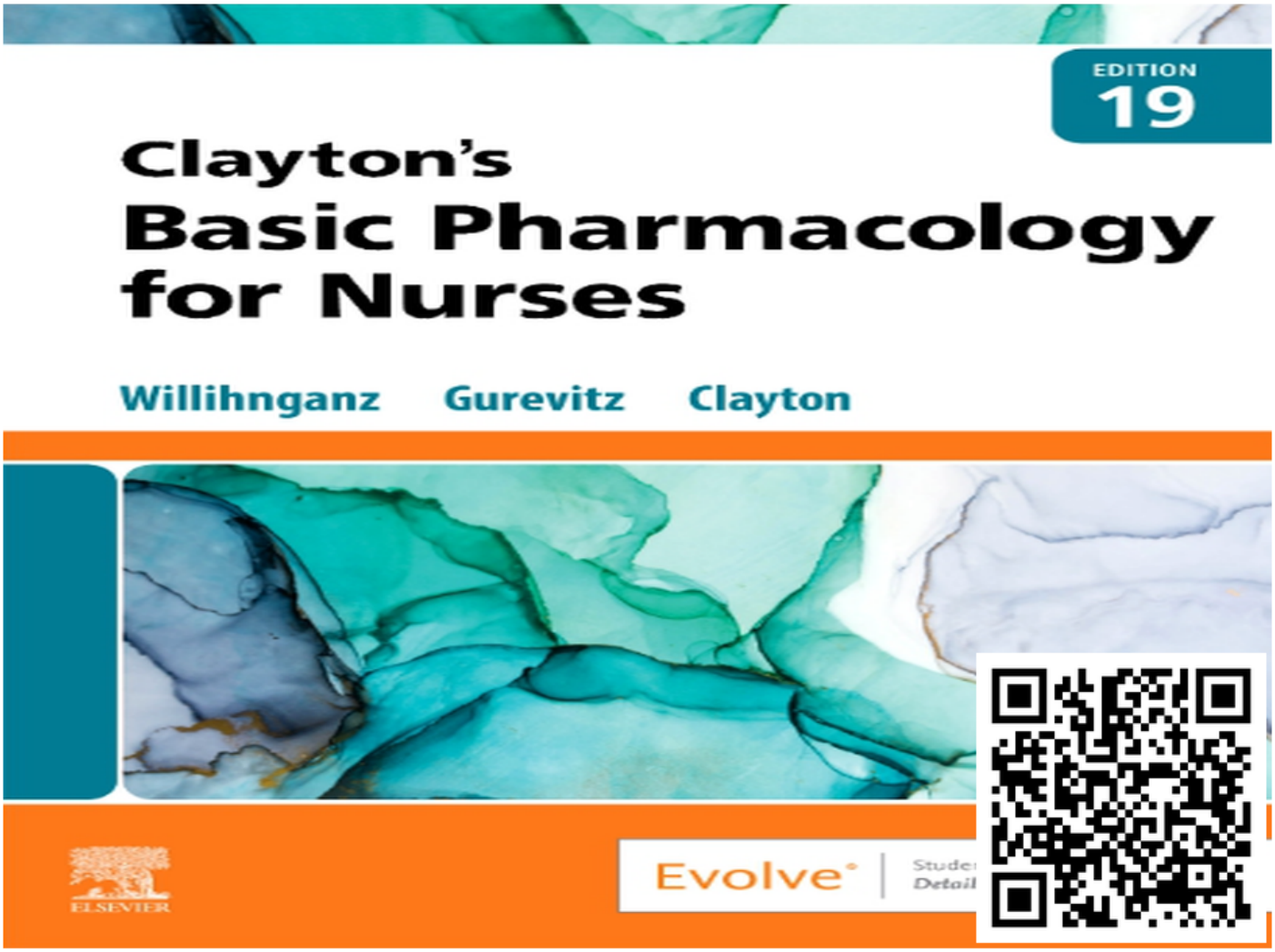

EDITION
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Basic Pharmacology for Nurses

Willihnganz Gurevitz Clayton

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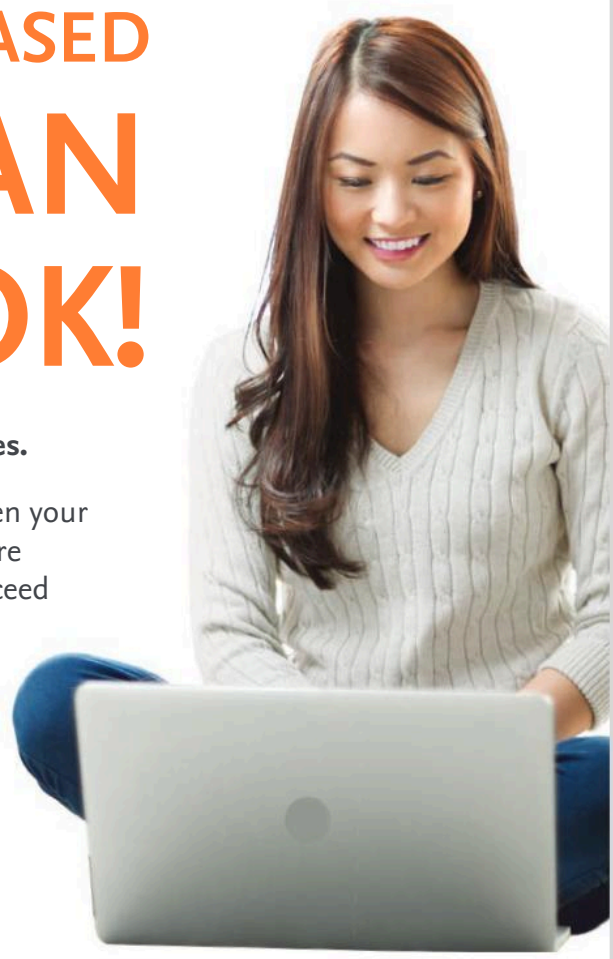

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Basic Pharmacology for Nurses

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EDITION
19

Basic Pharmacology for Nurses

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Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.
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To Kevin, the love of my life,
and to my wonderful daughters Katie and Jennifer,
who always stand beside me.

—MJW

To my wonderful wife Eileen
and to our daughter Maire.

—SLG

To Francine,
for her unfailing support and encouragement,
and to
Sarah, Nathaniel, Evelyn, and Grace
and
Beth, Clayton, and Arden,
the lights of our lives!

—BDC

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Preface

The 19th edition of *Basic Pharmacology for Nurses*, in the tradition of the book's standards first established in 1957, advocates the administration of medication with safety and precision while focusing on medication safety through medication monitoring and patient education. In the practice setting, the nurse not only must demonstrate knowledge of the underlying disease process but also must be able to perform an accurate assessment. The nurse must also plan and implement care in a manner that involves the patient as an active participant in decisions affecting care. Therefore a primary concern throughout this book is the integration of patient teaching about drug therapy to enable the patient to reach therapeutic goals and attain an optimum level of health. The nurse must also validate patient understanding to ensure that the individual has the ability to provide safe self-care and monitoring of the prescribed treatment plan. User friendly in content, structure, and layout, the text is concise and easy to read. With its emphasis on the seven Rights of Drug Administration (right drug, right time, right indication, right dosage, right patient, right route, and right documentation), *Basic Pharmacology for Nurses* provides students with the information needed to provide safe, effective nursing care for patients receiving drug therapy.

ORGANIZATION AND SPECIAL FEATURES

CONTENT THREADS

Basic Pharmacology for Nurses, 19th edition, shares some features and design elements with other Elsevier books that you may be using. The purpose of these Content Threads is to make it easier for students and instructors to use the variety of books required by a fast-paced and demanding curriculum.

The shared features in *Basic Pharmacology for Nurses*, 19th edition, include the following:

- Cover and internal design similarities; the colorful, student-friendly design encourages reading and learning of this core content
- Numbered lists of Objectives that begin each chapter
- Key Terms with pronunciations at the beginning of each chapter; the Key Terms are in color when they are defined in the chapter
- Bulleted lists of Key Points at the end of each chapter

Next Generation (NG) NCLEX style questions are at the end of each chapter. These questions use single-episode and unfolding cases. They include the six NCSBN Clinical Judgment Measurement Model cognitive processes and skills; answers are provided on the Evolve student website.

In addition to content and design threads, these textbooks benefit from the advice and input of the Elsevier Advisory Board.

CONTENTS

Unit I explores pharmacology foundations, principles, life span considerations, the nursing process with pharmacology, and patient education. Unit II contains the unique Illustrated Atlas of Medication Administration that provides extensive step-by-step instructions and illustrations that show primary routes of administration and proper administration techniques for all forms of medications.

Units III through X provide an overview of each drug class, followed by narrative discussions of the most common individual drugs. The units and chapters are organized by body system.

CHAPTER ORGANIZATION

- Each drug chapter in Units III through X begins with an overview of a clinical problem and its management.
- The general nursing implications section includes clearly identified headings for Assessment, Implementation, and Patient Education. The Patient Education section helps the nurse incorporate patient education designed to promote health into the overall treatment plan.
- Drug monographs are provided for each major drug class. These monographs describe Actions, Uses, and Therapeutic Outcomes for each class.
- A drug class–specific nursing implications section for each drug monograph highlights Premedication Assessment, Product Availability, Dosing Instructions, Common Adverse Effects, Serious Adverse Effects, and Drug Interactions.

SPECIAL FEATURES

Basic Pharmacology for Nurses includes special features designed to foster effective learning and comprehension.

- Chapter-opening features include lists of Objectives and Key Terms with pronunciations.

- Clinical Pitfall and Medication Safety Alert boxes highlight critically important clinical considerations to help students practice safety and reduce medication errors.
- Clinical Goldmine boxes put a spotlight on tips and best practices for clinical procedures.
- Life Span Considerations boxes focus on the implications of drug therapy for children, pregnant and breastfeeding women, and older adults.
- Herbal Interactions boxes discuss well-documented interactions among drugs, herbal therapies, and dietary supplements.
- A handy bulleted list of Key Points at the end of most chapters facilitates review of essential chapter content.

NEW TO THIS EDITION

- This edition includes the latest US Food and Drug Administration (FDA) approvals, including up-to-date clinical drug indications, guidelines for use, and recently released new drugs.
- Increased emphasis on medication safety that stresses imperative information for patient protection.
- Additional information on genetics, pharmacogenomics, and racial/gender factors in drug actions is included to highlight current research.
- New figures have been added to illustrate proper medication administration.
- End-of-chapter NCLEX-style questions that include NG types such as Cloze, Grid/Matrix, Drag and Drop, and Extended Multiple Response. These types cover the six cognitive skills: Recognize Cues, Analyze Cues, Prioritize Hypotheses, Generate Solutions, Take Action, and Evaluate Outcomes.

TEACHING AND LEARNING PACKAGE

FOR STUDENTS

- The Evolve Website provides free student resources, including answers and rationales for in-text Review Questions for the NCLEX® Examination, a math review, animations, video clips, a collection of Patient Teaching handouts, fully customizable Patient Self-Assessment Forms provided as "completable" PDF documents, and a collection of 500 NCLEX-style Review Questions.
- The revised Study Guide provides additional learning resources that complement those in the textbook. Questions for each chapter follow the objectives in the book for additional focus on these key concepts. Matching starts each chapter, and patient scenarios are included with the chapters that detail the medications. NG NCLEX-style questions are included, as are typical NCLEX questions. Each question includes the correct answer, rationale, NCLEX style used, and cognitive skill measured. Each question has a page number identified to help the student find the answer in the textbook. Answers to the Study Guide questions are available from instructors.

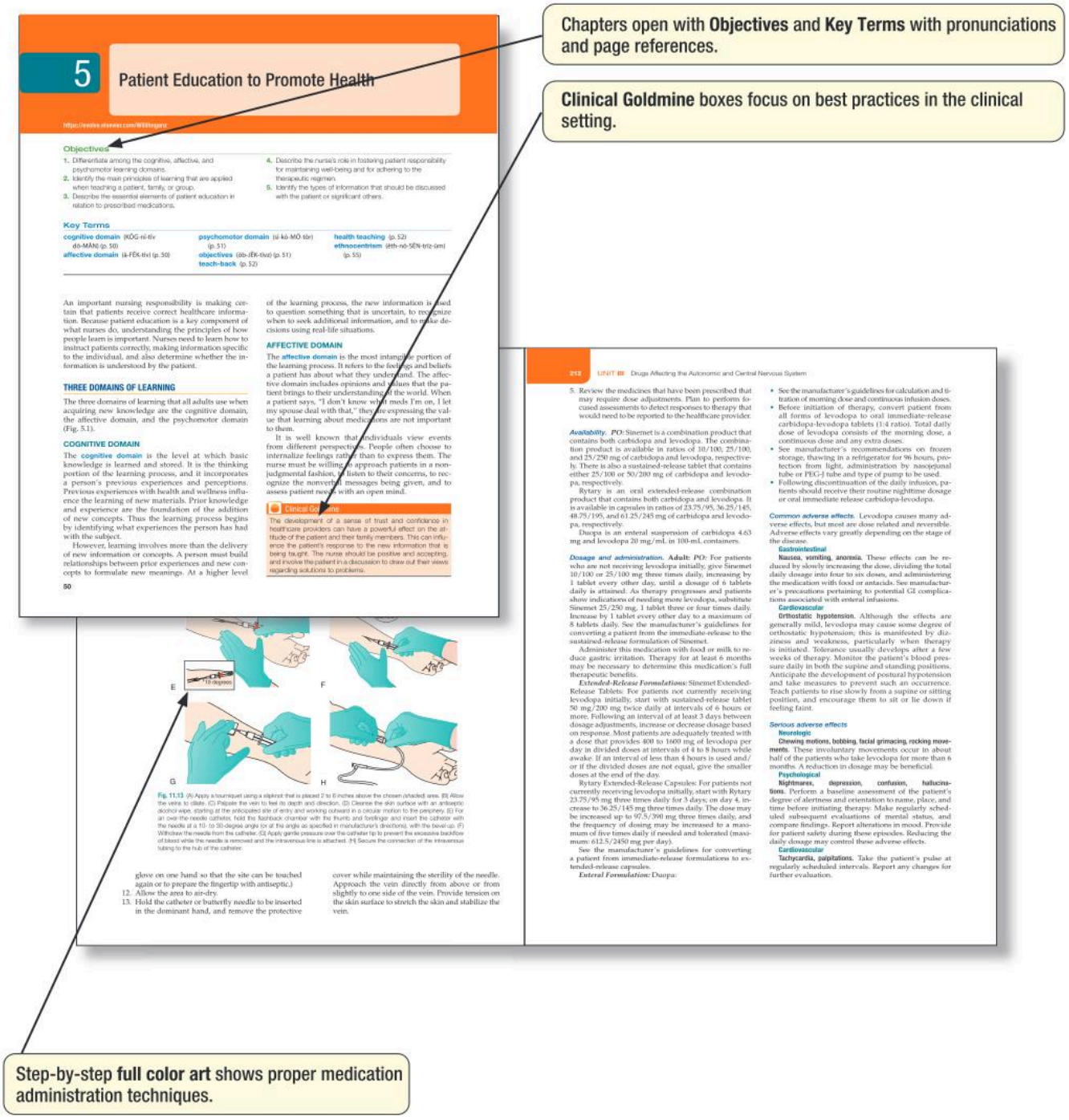
FOR INSTRUCTORS

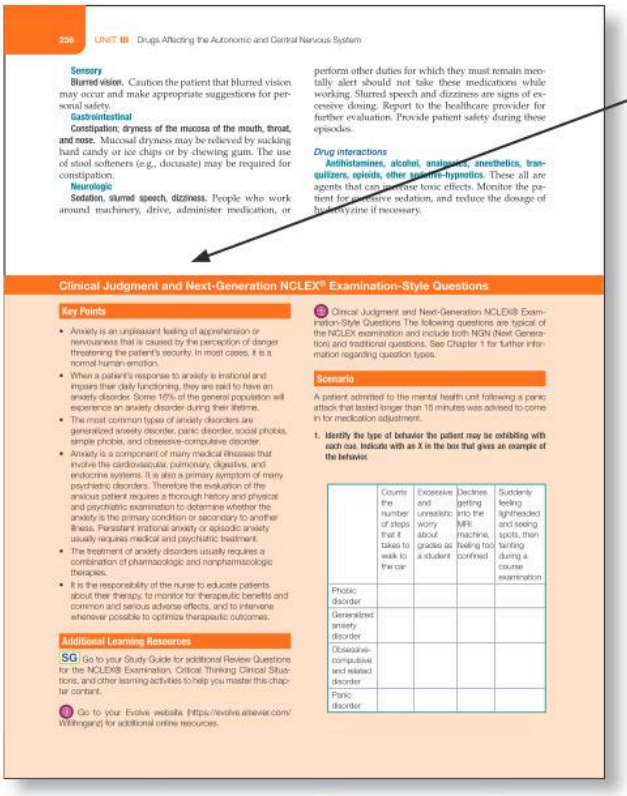
The comprehensive *Evolve Resources with TEACH Instructor Resource* provides a rich array of resources that include the following:

- Updated TEACH Lesson Plans, based on textbook learning objectives, provide ready-to-use lesson plans that tie together all of the text and ancillary components provided for *Basic Pharmacology for Nurses.*
- The collection of PowerPoint Lecture Slides is specific to the text.
- A Test Bank, delivered in ExamView, now provides an expanded collection of approximately 900 multiple-choice and alternate-format NCLEX-style questions. Each question includes the Correct Answer, Rationale, and corresponding text page numbers.
- The Image Collection contains every reproducible image from the text. Images are suitable for incorporation into classroom lectures, PowerPoint presentations, or distance-learning applications.
- Answer keys are provided for the Study Guide.

Special Features

Basic Pharmacology for Nurses focuses on medication safety through medication monitoring and patient education. Full-color art and design features accompany detailed, understandable discussions of drugs organized by body system.





236 UNIT III Drugs Affecting the Autonomic and Central Nervous System

Sensory

Blurred vision. Caution the patient that blurred vision may occur and make appropriate suggestions for personal safety.

Gastrointestinal

Constipation; dryness of the mucosa of the mouth, throat, and nose. Mucosal dryness may be relieved by sucking hard candy or ice chips or by chewing gum. The use of stool softeners (e.g., docusate) may be required for constipation.

Neurologic

Sedation, slurred speech, dizziness. People who work around machinery, drive, administer medication, or perform other duties for which they must remain mentally alert should not take these medications while working. Slurred speech and dizziness are signs of excessive dosing. Report to the healthcare provider for further evaluation. Provide patient safety during these episodes.

Drug interactions

Antihistamines, alcohol, analgesics, anesthetics, tranquilizers, opioids, other sedative-hypnotics. These all are agents that can increase toxic effects. Monitor the patient for excessive sedation, and reduce the dosage of hydroxyzine if necessary.

Clinical Judgment and Next-Generation NCLEX® Examination-Style Questions

Key Points

- Anxiety is an unpleasant feeling of apprehension or nervousness that is caused by the perception of danger threatening the patient's security. In most cases, it is a normal human emotion.
- When a patient's response to anxiety is irrational and impairs their daily functioning, they are said to have an anxiety disorder. Some 16% of the general population will experience an anxiety disorder during their lifetime.
- The most common types of anxiety disorders are generalized anxiety disorder, panic disorder, social phobia, simple phobia, and obsessive-compulsive disorder.
- Anxiety is a component of many medical illnesses that involve the cardiovascular, pulmonary, digestive, and endocrine systems. It is also a primary symptom of many psychiatric disorders. Therefore the evaluation of the anxious patient requires a thorough history and physical and psychiatric examination to determine whether the anxiety is the primary condition or secondary to another illness. Persistent irrational anxiety or episodic anxiety usually requires medical and psychiatric treatment.
- The treatment of anxiety disorders usually requires a combination of pharmacologic and nonpharmacologic therapies.
- It is the responsibility of the nurse to educate patients about their therapy, to monitor for therapeutic benefits and common and serious adverse effects, and to intervene whenever possible to optimize therapeutic outcomes.

Additional Learning Resources

SG Go to your Study Guide for additional Review Questions for the NCLEX® Examination, Critical Thinking Clinical Situations, and other learning activities to help you master this chapter content.

Go to your Evolve website (https://evolve.elsevier.com/Willihnganz) for additional online resources.

Clinical Judgment and Next-Generation NCLEX® Examination-Style Questions The following questions are typical of the NCLEX examination and include both NGN (Next Generation) and traditional questions. See Chapter 1 for further information regarding question types.

Scenario

A patient admitted to the mental health unit following a panic attack that lasted longer than 15 minutes was advised to come in for medication adjustment.

1. **Identify the type of behavior the patient may be exhibiting with each cue. Indicate with an X in the box that gives an example of the behavior.**

	Counts the number of steps that it takes to walk to the car	Excessive and unrealistic worry about grades as a student	Declines getting into the MRI machine, feeling too confined	Suddenly feeling lightheaded and seeing spots, then fainting during a course examination
Phobic disorder				
Generalized anxiety disorder				
Obsessive-compulsive and related disorder				
Panic disorder				

Get Ready for the NCLEX® Examination! sections include Key Points, Additional Learning Resources, and Review Questions for the NCLEX® Examination.

- **Patient Education and Health Promotion** is emphasized in the overall treatment plan.
- **Life Span Considerations** boxes focus on implications of drug therapy for children, pregnant and breastfeeding women, and older adults.
- **Clinical Pitfall and Medication Safety Alert** boxes highlight critically important clinical considerations.
- **Herbal Interactions** boxes describe possible adverse effects of alternative therapies.
- Chapters open with **Objectives** and **Key Terms** with pronunciations and page references.

STUDY GUIDE

Includes *Practice Questions for the NCLEX® Examination* for each textbook chapter. Answers to the revised study guide are available from your instructor.

Contents

Drug Definitions, Standards, and Information Sources

1

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Objectives

1. Differentiate between the chemical, generic, and brand names of drugs.
2. Identify the various methods used to classify drugs.
3. Identify sources of drug information available for healthcare providers.
4. Discuss the difference between prescription and nonprescription drugs.
5. Describe the process of developing and bringing new drugs to market.
6. Differentiate between the Canadian chemical names and the proper name of a drug.

Key Terms

pharmacology (făr-mă-KŎL-ŏ-jē) (p. 1)
therapeutic methods (thĕr-ă-PYŪ-tĭk MĔTH-ĕdz) (p. 1)
drugs (p. 1)
biologic therapies (p. 1)
chemical name (KĔM-ĭ-kŭl) (p. 2)
generic name (jĕ-NĂR-ĭk) (p. 2)
brand name (p. 2)
prescription drugs (p. 2)
nonprescription drugs (p. 2)
over-the-counter (OTC) drugs (p. 2)
illegal drugs (ĭl-LĒ-gŭl) (p. 2)
biosimilars (p. 2)
schedules (SKĔD-jūlz) (p. 5)
black box warnings (p. 8)
orphan drugs (ŌR-făn) (p. 8)
Food and Drugs Act and Regulations (p. 9)
Controlled Drugs and Substances Act (p. 10)

Pharmacology (from the Greek *pharmakon,* meaning "drugs," and *logos,* meaning "science") deals with the study of drugs and their actions on living organisms. Diseases that cause illness may be treated in several different ways, which are referred to as *therapies.* The various approaches to therapy are called **therapeutic methods**. Examples of therapeutic methods include the following:

- **Drug therapy:** Treatment with drugs
- **Diet therapy:** Treatment with diet (e.g., a low-salt diet for patients with cardiovascular disease)
- **Physiotherapy:** Treatment with natural physical forces (e.g., water, light, heat)
- **Psychological therapy:** The identification of stressors and methods that can be used to reduce or eliminate stress

Most illnesses caused by diseases require a combination of therapeutic methods for successful treatment.

Drugs (from the Dutch *droog,* meaning "dry") are chemical substances that have an effect on living organisms. Therapeutic drugs, which are often called *medicines,* are those drugs that are used for the prevention or treatment of diseases. Up until the early to mid-20th century, dried plants were the most abundant source of medicines, thus the word *drug* was applied to them.

Whereas most drugs are individual chemicals that cause a response in living tissues, a new class known as **biologic therapies** have been discovered that have transformed treatment of patients with disorders that attack the body's own organs, tissues, and cells (autoimmune disorders), blood (hematologic disorders), and cancers. Biologic agents are large, complex proteins manufactured in a living system such as a microorganism, or within plant or animal cells. Biologics have added major therapeutic choices for the treatment of many diseases for which no effective therapies were available or previously existing therapies were clearly inadequate.

DRUG NAMES, STANDARDS, LEGISLATION, AND DEVELOPMENT IN THE UNITED STATES

DRUG NAMES

All drugs have several names, which may cause confusion. When administering the prescribed drug, the spelling on the drug package must correspond exactly with the spelling of the drug ordered to ensure that the proper medicine is administered.

Each drug has three names: (1) a *chemical* name, (2) a *generic* name, and (3) a *brand* name. The **chemical name** is most meaningful to the chemist. By means of the chemical name, the chemist understands the exact chemical constitution of the drug and the exact placement of its atoms or molecular groupings.

Before a drug becomes official, it is given a **generic name** or common name. The generic name is simpler than the chemical name. It may be used in any country and by any manufacturer. The first letter of the generic name is not capitalized. Students are strongly encouraged to learn and refer to drugs by their generic names because formularies (i.e., lists of medicines available through a pharmacy) are maintained by generic names. When a therapeutically equivalent drug becomes available in generic form, the generic medicine is routinely substituted for the brand-name medicine.

Generic names are provided by the United States Adopted Names Council, which is an organization sponsored by the United States Pharmacopeial Convention, the American Medical Association, and the American Pharmacists Association. The official name, which is virtually always the generic name in the United States, is the name under which the drug is listed by the US Food and Drug Administration (FDA). The FDA is empowered by federal law to generically name the drugs for human use in the United States.

A trademark or **brand name** is followed by the symbol ®. This symbol indicates that the name is registered and that the use of the name is restricted to the owner of the drug, which is usually the manufacturer. Most drug companies place their products on the market under brand names rather than generic names. The brand names are deliberately made easier to pronounce, spell, and remember. The first letter of the brand name is capitalized.

Example of Chemical, Generic, and Brand Names for Drugs

Chemical name: [2-[4-[(4-Chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]acetic acid dihydrochloride (Fig. 1.1)
Generic name: cetirizine
Brand name: Zyrtec Allergy

DRUG CLASSIFICATIONS

Drugs may be classified by a variety of methods according to the *body system* that they affect (e.g., the central nervous system, the cardiovascular system, the gastrointestinal system); their *therapeutic use* or *clinical indications* (e.g., antacids, antibiotics, antihypertensives, diuretics, laxatives); and their *physiologic* or *chemical action* (e.g., anticholinergics, beta-adrenergic blockers, calcium channel blockers, cholinergics).

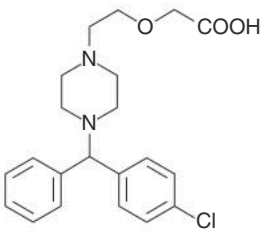

Fig. 1.1 Cetirizine, an antihistamine.

Drugs may be further classified as prescription or nonprescription. **Prescription drugs** require an order by a health professional who is licensed to prescribe drugs, such as a primary healthcare provider, a nurse practitioner, a physician assistant, a pharmacist, or a dentist. **Nonprescription drugs**, or **over-the-counter (OTC) drugs**, are sold without a prescription in a pharmacy or in the health section of department or grocery stores. **Illegal drugs**, sometimes referred to as *recreational drugs*, are drugs or chemical substances used for nontherapeutic purposes. These substances either are obtained illegally or have not received approval for use by the FDA. See Chapter 48 for further information about substance abuse.

A **biosimilar** is a biologic product that is close in structure and function to an existing approved biologic product, known as a *reference product*. For example, infliximab-dyyb (Inflectra) and infliximab-abda (Renflexis) are biosimilars for the reference product infliximab (Remicade) used to treat rheumatoid arthritis. With many patents for biologics expiring, biosimilar agents will become available. In 2010 legislation created an abbreviated licensure pathway for biologic products that are demonstrated to be biosimilar. Biosimilars offer an opportunity to increase access to biologics while lowering the cost of therapy. However, unlike generic medicines in which the active ingredients are identical to the reference small-molecule drugs, biosimilars will not be identical to the reference biologics. This is due to the inherent complexity of biologic proteins. Biosimilars made by different manufacturers will differ from the reference product and from each other, making each biosimilar a unique therapeutic option for patients (Table 1.1). Biosimilars are not generics and are not interchangeable. These agents cannot be substituted for the original reference molecule.

SOURCES OF DRUG STANDARDS AND DRUG INFORMATION

Drug products made by different manufacturers or in different batches by the same manufacturer must be uniformly pure and potent. The United States Pharmacopeial Convention is a nongovernment organization that promotes public health by establishing state-of-the-art standards to ensure the quality of medicines and other healthcare technologies. These standards are developed by a unique process of public involvement, and they are accepted worldwide. The Convention publishes a single-volume text, the *United States Pharmacopeia (USP)/National Formulary (NF)*, which is revised annually. The primary purpose of this volume is to provide standards for the identity, quality, strength, and purity of substances used in the practice of healthcare. The standards described in the *USP/NF* are enforced by the FDA as the

Table 1.1 Comparing and Contrasting Biosimilar and Generic Products

PROPERTIES	BIOSIMILAR DRUGS (BIOLOGICS)	GENERICS (SMALL-MOLECULE DRUGS)
Size	Large	Small
Structure	Complex with potential structural variations	Simple and well defined
Manufacturing	Unique bank of living cells Unlikely to achieve identical copy	Predictable chemical reaction Identical copy can be made
Complexity	Difficult to fully characterize	Easy to fully characterize
Stability	More sensitive to storage and handling conditions	Less sensitive to storage and handling conditions
Immunogenicity (promotes immune response; potential for allergy)	Higher potential	Lower potential
Approval requirements	Large clinical trials in patients	Small clinical trials for safety in healthy volunteers

official standards for the manufacture and quality control of medicines and nutritional supplements produced in the United States. The *USP/NF* is also recognized by the Canadian Food and Drugs Act as an authoritative source of drug standards in Canada.

Table 1.2 lists and describes the common sources of drug information available for the professional healthcare provider; additional resources are described in the following sections.

PACKAGE INSERTS

Manufacturers of drugs are required to develop a comprehensive but concise description of the drug, indications and precautions for clinical use, recommendations for dosage, known adverse reactions, contraindications, and other pharmacologic information relating to the drug. Federal law mandates that this material be approved by the FDA before the product is released for marketing and that it be presented on an insert that accompanies each package of the product.

The FDA adopted a format for package inserts to help reduce medication errors and to improve patient education. The labeling reduces practitioners' time looking for information, decreases the number of preventable medication errors, and improves treatment effectiveness and patient education. Because this labeling represents considerable effort and is most critical for newer and less familiar drugs, the formatting applies only to relatively new prescription drug products, developed since 2006.

Clinical Goldmine

DailyMed (see Online Resources), which is sponsored by the US National Library of Medicine, provides a database for new package inserts that is searchable by product name, indications, dosage and administration, warnings, description of drug product, active and inactive ingredients, and how the drug is supplied. See the section Electronic Databases.

NURSING JOURNALS

Many specialty journals have articles about drug therapy as it relates to a specific field of interest (e.g., *Geriatric Nursing*, *American Journal of Critical Care*). Nursing journals such as *RN* and *American Journal of Nursing* provide drug updates and articles that discuss nursing considerations related to drug therapy and drugs. Nurses must keep in mind that the purpose of using resources such as journals is to obtain professional knowledge of current evidence-based practice changes and they should not be used as a primary source for drug information. Nurses must be mindful of the accuracy of the information contained and should check the dates on articles to validate the currency of the information.

ELECTRONIC DATABASES

With the exponential growth of information about medicines and health, it is almost impossible to make the information available without the use of electronic databases. The National Library of Medicine (NLM) provides Medline and other searchable databases at no cost. Databases incorporated into the NLM include information on drugs and other chemicals that breastfeeding mothers may be exposed to and the levels in breast milk and infant blood with the possible adverse effects in the nursing infant. They also provide suggested therapeutic alternatives to the drugs. Information regarding the development and reproductive toxicology of drugs covering teratology is included. Most of the drug information sources listed in Table 1.2 are also available via electronic retrieval from libraries. Many college libraries subscribe to the Cumulative Index to Nursing and Allied Health Literature (CINAHL). These databases give nurses access to a wealth of information from sources published in the United States and other countries.

Databases for practitioners are also available by subscription. UpToDate, Lexicomp, and ePocrates are three vendors with several different packages of regularly updated information (see Online Resources). Lexicomp has a particularly strong database because the American Hospital Formulary Service is available through its portal.

Table 1.2 Sources of Drug Information for Healthcare Providers

SOURCES OF DRUG INFORMATION	DESCRIPTION
AHFS Drug Information	Contains monographs about virtually every single-entity drug available in the United States Describes therapeutic uses of drugs, including approved and unapproved uses Online version available
Drug Facts and Comparisons	Contains drug monographs that describe all drugs in a therapeutic class Monographs are formatted as tables to allow comparison of similar products, brand names, manufacturers, cost indices, and available dosage forms Online version available
ASHP's Handbook on Injectable Drugs	Collection of monographs about 360 injectable drugs with sections on available concentrations, compatibility with other drugs, dosage and rate of administration, stability, pH, and other useful information Interactive version available
Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care	Most comprehensive text available about over-the-counter medications that can be purchased in the United States Online version available
Martindale: The Complete Drug Reference	Considered one of the most comprehensive texts available for information about drugs in current use throughout the world Contains extensive referenced monographs about the international names, pharmacologic activity, and side effects of more than 6400 drugs Online subscription available
Natural Medicines Comprehensive Database	Scientific gold standard for evidence-based information about herbal medicines and combination products involving herbal medicines Only available in an online database by subscription or at libraries
CANADIAN DRUG STANDARDS	
European Pharmacopoeia *Pharmacopée Française* *The International Pharmacopoeia (Ph. Int.)* *British Pharmacopoeia* *Canadian Formulary* *The National Formulary* *Pharmaceutical Codex* *United States Pharmacopeia-National Formulary*	All recognized by the Canadian Food and Drugs Act as authoritative sources of drug standards
CANADIAN DRUG INFORMATION	
Compendium of Pharmaceuticals and Specialties (CPS)	Published annually by the Canadian Pharmacists Association Comprehensive list of the pharmaceutical products distributed in Canada, as well as other practical information e-CPS available
Patient Self-Care: Helping Patients Make Therapeutic Choices	Published by the Canadian Pharmacists Association Provides comprehensive information for health professionals and consumers about nonprescription drug products available in Canada e-Therapeutics available
Compendium of Self-Care Products (CSCP)	Nonprescription companion to *CPS* and *Patient Self-Care* Offers at-a-glance comparative tables for thousands of products and monographs about hundreds of commonly used nonprescription products

AHFS, American Hospital Formulary Service; *ASHP,* American Society of Health-System Pharmacists; *USP,* United States Pharmacopeia.

The DailyMed system (see Online Resources) was developed in collaboration with federal agencies—including the FDA, the NLM, the Agency for Healthcare Research and Quality, the National Cancer Institute in the US Department of Health and Human Services, and the US Department of Veterans Affairs—to provide high-quality information about marketed drugs. DailyMed makes available to healthcare providers and the public a standard, comprehensive, up-to-date resource about medicines.

UNITED STATES DRUG LEGISLATION

Drug legislation approved by Congress provides the legal basis (Table 1.3) for drug manufacturing and protects the consumer from false claims made by a drug

Table 1.3 Selected Major US Legislation Pertaining to Safety of Medicines

LEGISLATION (LAW)	PURPOSE AND EFFECT
Food, Drug, and Cosmetic Act of 1938	Requires that new drugs be safe, as well as pure (but did not require proof of efficacy). Enforcement by FDA.
Durham-Humphrey Amendment (1951) to the Food, Drug, and Cosmetic Act	Gives the FDA the power to determine which products may be sold with and without a prescription.
Kefauver-Harris Amendment (1962) to the Food, Drug, and Cosmetic Act	Requires proof of efficacy as well as safety for medicines released since 1938; establishes guidelines for reporting of information about adverse reactions, clinical testing, and advertising of new drugs.
Comprehensive Drug Abuse Prevention and Control Act (1970) (Controlled Substances Act, 1970)	Outlines strict controls in the manufacture, distribution, and prescribing of habit-forming drugs; establishes drug schedules and programs to prevent and treat drug addiction. Established the Drug Enforcement Administration (DEA).
Dietary Supplement Health and Education Act (1994) (DSHEA Act–1994)	Under this act, almost all herbal medicines, vitamins, minerals, amino acids, and chemicals used for health are reclassified as **dietary supplements**, a food category. The legislation allows the label to include information about how these products affect the human body. Labels must contain a statement that the product has not been evaluated by the FDA for treating, curing, or preventing any disease. The law does not prevent nonlicensed personnel from making founded or unfounded claims about the therapeutic effects of supplement ingredients. The result is that dietary supplements are not required to be safe and effective, and unfounded claims of therapeutic benefit abound. See Chapter 47.

manufacturer. The FDA is the administrative body that oversees the drug evaluation process in the United States and grants approval for or removal of drug products from the market.

CONTROLLED SUBSTANCES ACT

The Comprehensive Drug Abuse Prevention and Control Act, which is commonly referred to as the *Controlled Substances Act*, is designed to improve the administration and regulation of the manufacturing, distribution, and dispensing of drugs that require tighter control by the government because of their higher incidence of abuse and potential for addiction. The basic structure of the Controlled Substances Act consists of five classifications, or **schedules**, of controlled substances. The degree of control, the conditions of record keeping, the particular order forms required, and other regulations depend on which schedule the individual drug is assigned (Box 1.1).

Drugs that are listed as Schedule I are not available for other than highly controlled research purposes because of their very high potential for abuse and addiction. Drugs in Schedule II have a high potential for abuse and addiction, but are available by prescription only, in limited quantities, usually with no more than a 7- to 30-day supply. The prescription cannot be refilled; a new prescription must be issued for continued use. Drugs categorized as Schedule III, IV, or V have a lower potential for abuse and addiction and may be ordered by prescription with a maximum supply of 30 days of medicine. If so written by the prescriber, the prescription may be refilled up to five times but outdates at 6 months, at which time a new prescription is required if the medicine is to be continued. Prescription medicines that are not classified as controlled substances may be refilled for up to a period of time defined by individual state law, if

Box 1.1 Examples of Medicines in the Controlled Substances Drug Schedules

SCHEDULE I DRUGS
Examples: lysergic acid diethylamide (LSD), peyote, heroin, hashish

SCHEDULE II DRUGS
Examples: amphetamines, morphine, hydrocodone/acetaminophen (Vicodin), hydrocodone/acetaminophen (Lortab), hydrocodone/acetaminophen (Norco), methadone, oxycodone/aspirin (Percodan), methylphenidate (Ritalin), amphetamine/dextroamphetamine (Adderall)

SCHEDULE III DRUGS
Examples: aspirin/codeine (Empirin with codeine), aspirin/butalbital/caffeine (Fiorinal), acetaminophen/codeine (Tylenol with codeine)

SCHEDULE IV DRUGS
Examples: phenobarbital, chlordiazepoxide, diazepam, flurazepam, temazepam

SCHEDULE V DRUGS
Example: atropine/diphenoxylate (Lomotil, Virtussin AC)

approved by the prescriber. Most state laws mandate that a prescription outdates in 1 year and must be rewritten if therapy is to be continued.

Drug Enforcement Administration

The US Drug Enforcement Administration (DEA) was organized to enforce the Controlled Substances Act, to gather intelligence, to train its officers, and to conduct research in the area of dangerous drugs and drug abuse.

Every manufacturer, primary healthcare provider, nurse practitioner, physician assistant, dentist, pharmacy, and hospital that manufactures, prescribes, or dispenses any of the drugs listed in the five schedules must register biannually with the DEA. A healthcare provider's prescription for substances named in this law must contain the healthcare provider's name, address, DEA registration number, and signature; the patient's name and address; and the date of issue. The pharmacist cannot fill such a prescription for a controlled substance without this information on the prescription.

Possession of Controlled Substances by Individuals

Federal and state laws make the possession of controlled substances without a valid prescription a crime, except in specifically exempted cases. The law makes no distinction between professional and practical nurses with regard to the possession of controlled drugs. Nurses may give controlled substances only under the direction of a healthcare provider who has been licensed to prescribe or dispense these agents. Nurses may not have controlled substances in their possession unless the following conditions are met: (1) the nurse is giving them to a patient under an order from a healthcare provider, (2) the nurse is a patient for whom a healthcare provider has prescribed scheduled drugs, or (3) the nurse is the official custodian of a limited supply of controlled substances on a unit or for a department of the hospital. Controlled substances that are ordered for patients but not used must be returned to the source from which they were obtained (i.e., the primary healthcare provider or pharmacy). Violation of or failure to comply with the Controlled Substances Act is punishable by fine, imprisonment, or both and by the possible loss of professional licensing.

EFFECTIVENESS OF DRUG LEGISLATION

The effectiveness of drug legislation depends on the interest and determination used to enforce these laws, the appropriation by government of adequate funds for enforcement, and the vigor used by proper authorities in enforcement. The interest and cooperation of healthcare professionals and the public with regard to the benefits of appropriate drug use and the possible consequences of indiscriminate use of drugs can be very beneficial. Many individuals assist in this education through support of national and state professional organizations, consumer advocacy groups, and local, state, and county health departments.

NEW DRUG DEVELOPMENT

It currently takes an average of 8 to 15 years and more than $2 billion in research and development costs to bring a single new drug to market; healthcare professionals and consumers alike often have a lack of understanding about this process. The Pharmaceutical Research and Manufacturers of America estimates that only 1 of 10,000 chemicals investigated is actually found to be "safe and effective" and ultimately brought to the pharmacist's shelf.

The Food, Drug, and Cosmetic Act of 1938 charged the FDA with the responsibility of regulating new drugs. Rules and regulations evolved by the FDA divide new drug development into four stages: (1) preclinical research and development; (2) clinical research and development; (3) New Drug Application (NDA) review; and (4) postmarketing surveillance (Fig. 1.2).

PRECLINICAL RESEARCH AND DEVELOPMENT STAGE

The preclinical research phase of new drug development begins with the discovery, synthesis, and purification of the drug. The goal at this stage is to use laboratory studies to determine whether the experimental drug has therapeutic value and whether the drug appears to be safe in animals. Enough data must be gained to justify testing the experimental drug in humans.

The preclinical phase of data collection may require 1 to 3 years, although the average length of time is 18 months. Near the end of this phase, the investigator (often a pharmaceutical manufacturer) submits an Investigational New Drug (IND) application to the FDA; this application describes all of the studies completed to date, discusses the expected safety of the drug, and explains the testing that is planned for human subjects. Within 30 days, the FDA must make a decision on the basis of safety considerations about whether to allow the human study to proceed. Only about 20% of the chemicals tested in the preclinical phase advance to the clinical testing phase.

CLINICAL RESEARCH AND DEVELOPMENT STAGE

The stage in which humans are first tested (i.e., the clinical research or IND stage) is usually subdivided into three phases. Phase 1 studies determine an experimental drug's pharmacologic properties, such as its pharmacokinetics, metabolism, safe dosage range, potential for toxicity at a certain dosage, and safe routes of administration. The study population is composed of normal volunteers or the intended treatment population, such as those patients for whom the standard

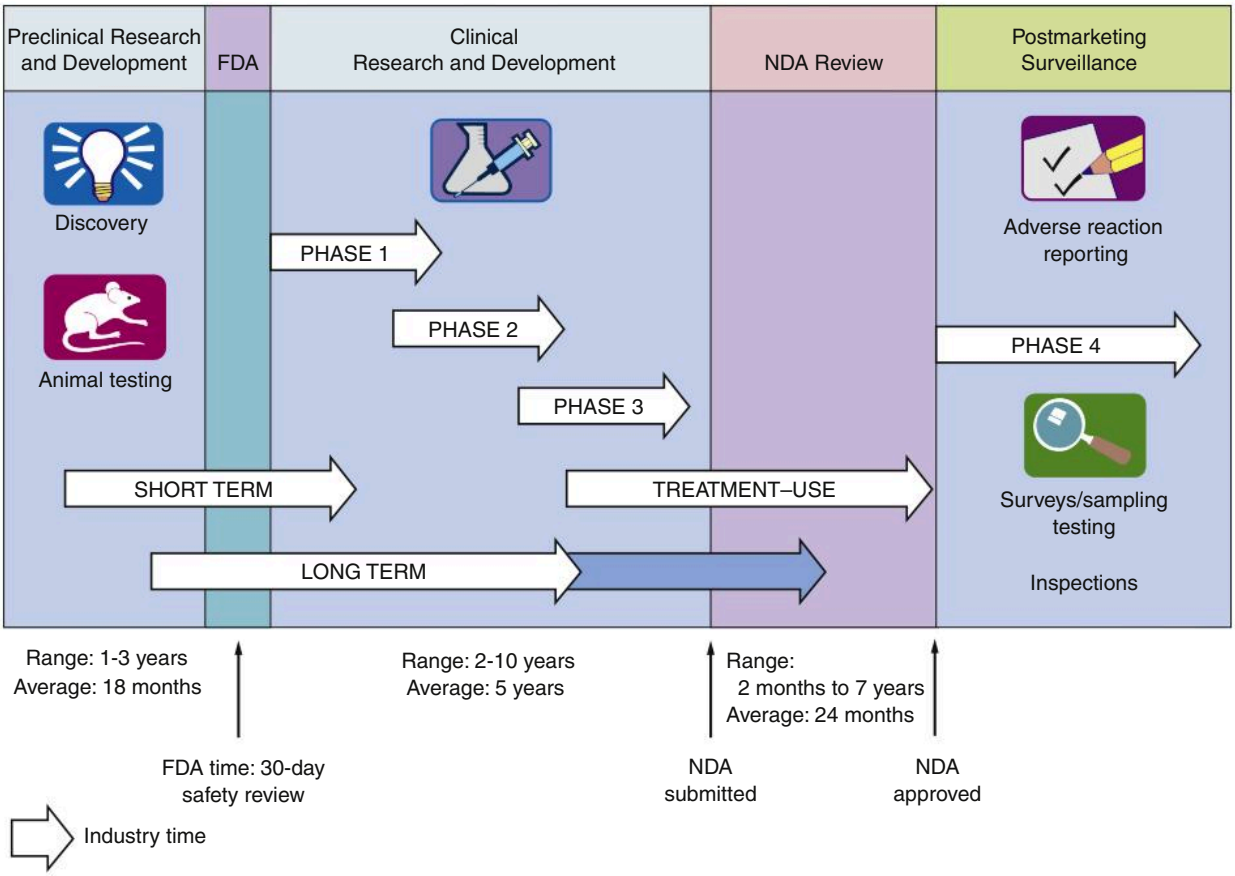

Fig. 1.2 The new drug review process. *FDA,* US Food and Drug Administration; *NDA,* New Drug Application.

treatments of certain cancers or dysrhythmias have been ineffective. Phase 1 studies usually require 20 to 100 subjects who are treated for 4 to 6 weeks.

If phase 1 trials are successful, the drug is moved to phase 2 trials, which involve a smaller population of patients who have the condition that the drug is designed to treat. Studies at various dosages are conducted to determine the success rate and safety of a drug for its intended use. If successful, the drug is advanced to phase 3 trials, in which larger patient populations are used to ensure the statistical significance of the results. Phase 3 studies also provide additional information about proper dosing and safety.

The entire clinical research phase may require 2 to 10 years, with the average experimental drug requiring 5 years. Each study completed is reviewed by the FDA to help ensure patient safety and efficacy. Only one of five drugs that enter clinical trials makes it to the marketplace. The others are eliminated because of efficacy or safety problems or a lack of commercial interest.

Fast Tracking

To expedite the development and approval of drugs for the treatment of life-threatening illnesses (e.g., acquired immunodeficiency syndrome), the FDA has drafted rules that allow certain INDs to receive the highest priority for review within the agency. This procedure is sometimes known as *fast tracking*. Additional rules allow INDs to be used for the treatment of a life-threatening disease in a particular patient—even if the patient does not fit the study protocol for the drug—when there is no alternative therapy. These cases are known as *treatment INDs*. A potentially lifesaving drug may be allowed for treatment IND status during late phase 2 studies, during phase 3 studies, or after all clinical studies have been completed but before marketing approval.

Parallel Tracking

Another mechanism to make INDs available to patients with life-threatening illnesses is known as *parallel tracking*. With this procedure, an IND may be used for patients who cannot participate in controlled clinical trials and when there is no satisfactory standard therapeutic alternative. Parallel track studies are conducted along with the principal controlled clinical trials; however, unlike a controlled study, the parallel track study does not involve a concurrent control group.

Investigators and patients must realize that there may be greater uncertainty regarding the risks and benefits of therapy with agents that are in relatively early stages of testing and development. Parallel tracking is similar to the treatment IND process but allows for access to investigational agents when there is less accumulated evidence of efficacy than required for a treatment

IND. A drug may be released through the parallel track mechanism when phase 2 trials have been given approval to proceed but have not necessarily been started.

NEW DRUG APPLICATION REVIEW

When sufficient data have been collected to demonstrate that the experimental drug is both safe and effective, the investigator submits an NDA to the FDA to formally request approval to market a new drug for human use. Thousands of pages of NDA data are reviewed by a team of pharmacologists, toxicologists, chemists, primary healthcare providers, and others (as appropriate), who then make a recommendation to the FDA about whether the drug should be approved for use. The average NDA review takes 24 months. After a drug is approved by the FDA, it is the manufacturer's decision as to when to bring a product to the marketplace.

POSTMARKETING SURVEILLANCE STAGE

If the manufacturer decides to market the medicine, the postmarketing surveillance stage begins; this is the fourth stage of drug product development. This process consists of an ongoing review of adverse effects of the new drug and periodic inspections of the manufacturing facilities and the resulting products. Other studies completed during the fourth stage include identifying other patient populations for whom the drug may be useful, refining dosing recommendations, and exploring potential drug interactions.

Clinical Goldmine

Healthcare providers make a significant contribution to the knowledge of drug safety by reporting adverse effects to the FDA using the MedWatch program for the voluntary reporting of adverse events and product problems (see Online Resources).

BLACK BOX WARNING

Although the FDA's drug approval process is one of the most stringent in the world, the value of ongoing safety review of medicines has been demonstrated through the use of the MedWatch program. If safety concerns are identified after a drug is approved for marketing, the FDA can issue **black box warnings** to the package insert of the product. When a medication's risks and known dangers outweigh its benefits, the FDA and/or the manufacturer may decide that the product should be withdrawn from the market.

The probability of a drug acquiring a new black box warning or being withdrawn from the market within 25 years of being released is estimated at 20%. Consequently, it is the responsibility of all healthcare professionals to constantly monitor their patients for adverse effects of drugs and to complete a MedWatch form when adverse effects are suspected. More than 200,000 MedWatch forms are filed with the FDA annually. Health Canada has a program for reporting adverse effects (Canada Vigilance Program: https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/canada-vigilance-program.html).

From a safety standpoint, prescribers and patients should be aware that recently marketed medicines carry a risk of causing unsuspected serious adverse effects. Even with the high probability that there will be no serious complications, the devastating—and sometimes fatal—consequences cannot be ignored. When choosing medicines for treatment, it becomes important to consider whether an equally effective alternative drug is already available. At a minimum, this reduces the risk of an undiscovered adverse drug reaction, and it is often less expensive. At a maximum, the patient, the family, and the prescriber are saved the anguish of an avoidable adverse drug reaction.

RARE DISEASES AND THE DEVELOPMENT OF ORPHAN DRUGS

The National Organization for Rare Disorders, which is a coalition of 140 rare-disease groups, estimates that more than 6000 rare health conditions exist in about 20 million Americans. Examples of these rare diseases are cystic fibrosis, Hansen disease (leprosy), sickle cell anemia, blepharospasm, infant botulism, and *Pneumocystis jiroveci* pneumonia (see Online Resources). Historically, pharmaceutical manufacturers have been reluctant to develop products that could be used to treat these illnesses. The medicines that are developed for these conditions are known as **orphan drugs** because the manufacturers have been unable to recover the costs of the research on account of the very limited use of the final product. Because no companies were willing to "adopt" the diseases to complete extensive research to develop products for treatment, the diseases became known as *health orphans.*

In 1983 Congress passed the Orphan Drug Act to stimulate the development and market availability of products that are used for the treatment of rare diseases. The act defines the term *rare disease* as a condition that affects fewer than 200,000 people in the United States. The FDA's Office of Orphan Products Development (OOPD) promotes the development of products that demonstrate promise for the diagnosis or treatment of rare diseases or conditions. The OOPD interacts with medical and research communities, professional organizations, academia, and the pharmaceutical industry, as well as with rare-disease groups. The OOPD administers the major provisions of the Orphan Drug Act, which provide incentives for sponsors to develop products for rare diseases.

The law provides research grants, protocol development assistance by the FDA, special tax credits for the cost of clinical trials, and 7 years of exclusive marketing rights after the product has been approved. On average, an orphan drug receives FDA approval 10 to 11 months sooner than a nonorphan drug. The act has been quite successful: more than 200 new drugs have been approved by the FDA for rare diseases, benefiting several million people. Examples include

pentamidine and atovaquone for *Pneumocystis jiroveci* pneumonia, thalidomide for Hansen disease, zidovudine for the human immunodeficiency virus, dornase alfa (Pulmozyme) for cystic fibrosis, and cladribine (Leustatin) for hairy cell leukemia.

DRUG NAMES, STANDARDS, AND LEGISLATION IN CANADA

CANADIAN DRUG NAMES

OFFICIAL DRUG

The term *official drug* pertains to any drug for which a standard is described specifically in the Food and Drug Regulations or in any publication named in the Food and Drugs Act as being satisfactory for officially meeting the standards for drugs in Canada.

CHEMICAL NAME

The *chemical name* is most meaningful to the chemist. By means of the chemical name the chemist understands the exact chemical constitution of the drug and exact placing of its atoms or molecular groupings. The chemical name is the same in both Canada and the United States.

PROPER NAME OR GENERIC NAME

The *proper name* is the nonproprietary (generic) name, which is used to identify an official drug in Canada. The *generic name* is the same in both Canada and the United States.

BRAND NAME

The *brand name* (or proprietary name) is the name assigned to the drug by its manufacturer to distinguish the drug for advertisement and sale. Brand names for the same generic drug product are frequently different between Canada and the United States. The following example and Fig. 1.3 depict the application of terminology to drug nomenclature.

Example of Canadian Drug Names

Chemical name: 4-dimethylamino-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11,dioxo-2-napthacene carboxamide (see Fig. 1.3)
Proper name: tetracycline
Official name: Tetracycline, USP
Brand names: Apo-Tetra; Nu-Tetra

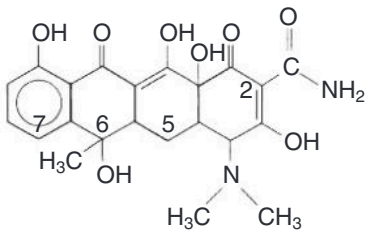

Fig. 1.3 Tetracycline, an antibiotic.

SOURCES OF CANADIAN DRUG STANDARDS

The Food and Drugs Act recognizes the standards described by international authoritative books as being acceptable for official drugs in Canada (see Table 1.2).

CANADIAN DRUG LEGISLATION

FOOD AND DRUGS ACT AND REGULATIONS

The **Food and Drugs Act** (1927) and **Regulations** (1953, 1954, 1979) empower Health Canada to protect the public from foreseeable risks related to the manufacture and sale of drugs, cosmetics, food, and therapeutic devices. The legislation provides for a review of the safety and efficacy of drugs before their clearance for marketing in Canada and determines whether the medicine is *prescription* or *nonprescription*. Also included in this legislation are requirements for good manufacturing practices, adequate labeling, and fair advertising.

In Canada (as in the United States), an effort has been made to align the provincial drug schedules so that the conditions for the sale of medicines are consistent across Canada. The National Association of Pharmacy Regulatory Authorities (NAPRA) governs national drug schedules but each province's regulatory body can regulate how a particular drug can be sold-sold/dispensed. The National Association of Pharmacy Regulatory Authorities (NAPRA) proposed a new national drug scheduling model. This model is in various stages of implementation across the provinces and territories of Canada. With the use of this model, all medicines in Canada are assigned to one of four categories:
Schedule I: All prescription drugs, including narcotics
Schedule II: Restricted-access nonprescription drugs
Schedule III: Pharmacy-only nonprescription drugs
Unscheduled: Drugs that are not assigned to the previous categories

Schedule II drugs are available for sale directly from the pharmacist and are kept "behind the counter." Examples include insulin, pseudoephedrine, glucagon, loperamide (for children younger than age 12 years), and nitroglycerin sublingual spray and tablets (other dosage forms are Schedule I). These medications are in two categories: (1) those that patients may require urgently and cannot delay taking until after an appointment with a prescriber (e.g., insulin, nitroglycerin, glucagon); and (2) those that require appropriate counseling to avoid improper use (e.g., loperamide, pseudoephedrine). Placement with a pharmacist does not allow for patient self-selection and allows for pharmacist intervention for these medications. This restriction is meant to ensure the following: (1) that patients are not self-diagnosing medically serious diseases (e.g., diabetes mellitus, angina); and (2) that patients are educated about the proper use of these drugs through appropriate counseling from the pharmacist.

Schedule III drugs are pharmacy-only nonprescription drugs. These medicines can be sold only

through pharmacies and include levonorgestrel emergency contraception, diphenhydramine, child preparations of antihistamines, and the low-dose histamine-2 antagonists. It is expected that if patients have questions, they could easily consult with a pharmacist.

Medicines that are not categorized in Schedule I, II, or III are considered to be "unscheduled" (e.g., nicotine gum and patches, acetylsalicylic acid, lower-dose ibuprofen, some lower-dosage "cough and cold" preparations) and can be sold at any retail outlet. Adequate information is available for the patient to make a safe and effective choice, and labeling is sufficient to ensure the appropriate use of the drug without professional supervision.

Drugs requiring a prescription—except for controlled drugs—are listed on Schedule F of the Food and Drug Regulations. Schedule F drugs may be prescribed only by qualified healthcare providers because they would normally be used most safely under supervision. Most antibiotics, antineoplastics, corticosteroids, cardiovascular drugs, and antipsychotics are Schedule F drugs.

CONTROLLED DRUGS AND SUBSTANCES ACT

The **Controlled Drugs and Substances Act** (1997) established the requirements for the import, production, export, distribution, and possession of substances classified as narcotics and substances of abuse in Canada. The Controlled Drugs and Substances Act describes eight schedules of controlled substances. Assignment to a schedule is based on the potential for abuse and the ease with which illicit substances can be manufactured in illegal laboratories. The degree of control; the conditions of record keeping; assignment of penalties for possession, trafficking, and manufacturing; and other regulations depend on these classifications. (Note that Schedules I, II, and III under the US Food and Drugs Act as described earlier are different from Schedules I through VIII of the Canadian Controlled Drugs and Substances Act). Examples of controlled substances schedule assignment are as follows:

Schedule I: Opium poppy and its derivatives (e.g., heroin, morphine); coca and its derivatives (e.g., cocaine), pethidine (meperidine), methadone, fentanyl

Schedule II: Cannabis

Schedule III: Amphetamines, methylphenidate, lysergic acid diethylamide (LSD), methaqualone, psilocybin, mescaline

Schedule IV: Sedative-hypnotic agents (e.g., barbiturates, benzodiazepines); butorphanol, anabolic steroids

Schedule V: Propylhexedrine, phenylpropanolamine, pyrovalerone

Schedule VI: Part I class A precursors (e.g., ephedrine, pseudoephedrine, norephedrine [phenylpropanolamine], ergotamine) and part II precursors (e.g., acetone, ethyl ether, hydrochloric acid, sulfuric acid, toluene)

Schedule VII: Cannabis resin (3 kg); cannabis (marijuana) (3 kg) (must be read in conjunction with Schedule II)

Schedule VIII: Cannabis resin (1 g); cannabis (marijuana) (30 g) (must be read in conjunction with Schedule II)

The Controlled Drugs and Substances Act and accompanying regulations provide for the nonprescription sale of certain codeine preparations (e.g., Tylenol No. 1 with codeine, Benylin with codeine). The content must not exceed the equivalent of 8 mg of codeine phosphate per solid dosage unit or 20 mg per 30 mL of a liquid preparation, and the preparation must also contain two additional nonnarcotic medicinal ingredients. These preparations may not be advertised or displayed, and they may be sold only by pharmacists (see previous discussion of Schedule II drugs). In hospitals, the pharmacy usually requires strict inventory control of these products and other narcotics.

Requirements for the legitimate administration of drugs to patients by nurses are generally similar in Canada and the United States. Individual hospital policy determines specific record-keeping requirements on the basis of federal and provincial laws. Violations of these laws will result in fines or imprisonment in addition to the loss of professional licensing.

NONPRESCRIPTION DRUGS

The NAPRA drug schedules list three categories of nonprescription drugs: Schedule II, Schedule III, and unscheduled drugs (see discussion under Food and Drugs Act and Regulations).

Clinical Judgment and Next-Generation NCLEX® Examination-Style Questions

Key Points

- In the classification system used in the United States, each drug has three names: a *chemical* name, a *generic* name, and a *brand* name. The chemical name is most meaningful to the chemist. The generic name is simpler than the chemical name. The first letter of the generic name is not capitalized. The brand names are selected by the manufacturer and deliberately made easier to pronounce, spell, and remember. A brand name is followed by the symbol ®. The first letter of the brand name is capitalized.
- Drugs may be classified by a variety of methods according to the *body system* that they affect (e.g., the central nervous system, the cardiovascular system, the gastrointestinal system); their *therapeutic use* or *clinical indications* (e.g., antacids, antibiotics, antihypertensives, diuretics, laxatives); and their *physiologic* or *chemical action* (e.g., anticholinergic agents, beta-adrenergic blockers, calcium channel blockers, cholinergic agents).
- Table 1.2 lists and describes the common sources of drug information available for the healthcare provider.
- Prescription drugs require an order by a healthcare provider who is licensed to prescribe drugs, such as a primary healthcare provider, a nurse practitioner, a physician assistant, a pharmacist, or a dentist. Nonprescription or over-the-counter (OTC) drugs are sold without a prescription in a pharmacy or in the health section of department or grocery stores.
- Rules and regulations evolved by the FDA divide new drug development into four stages: (1) preclinical research and development; (2) clinical research and development; (3) new drug application review; and (4) postmarketing surveillance (see Fig. 1.2).
- In Canada, the *proper name* is the nonproprietary (generic) name, which is used to identify an official drug. The *generic name* is the same in both Canada and the United States.

Additional Learning Resources

SG Go to your Study Guide for additional Review Questions for the NCLEX® Examination, Critical Thinking Clinical Situations, and other learning activities to help you master this chapter content.

Go to your Evolve website (https://evolve.elsevier.com/Clayton) for additional online resources.

Online Resources

- DailyMed: https://dailymed.nlm.nih.gov/dailymed/index.cfm
- ePocrates: http://www.epocrates.com/
- iPharmacy: https://itunes.apple.com/us/app/ipharmacy-drug-guide-pubmed-direct/id378721295
- Lexicomp: http://www.wolterskluwercdi.com/lexicomp-online/
- MedicinesComplete: https://about.medicinescomplete.com/#/
- MedWatch: https://www.fda.gov/Safety/MedWatch/default.htm
- National Organization for Rare Disorders (NORD): https://rarediseases.org/
- UpToDate: https://www.uptodate.com/home
- US National Library of Medicine: https://www.nlm.nih.gov/

Online Resources for Canadian Practitioners

- Controlled Substances and Drugs Act (Justice Laws Website): http://laws-lois.justice.gc.ca/eng/acts/c-38.8/
- Drug Product Database: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html
- National Association of Pharmacy Regulatory Authorities (NAPRA) proposal for drug schedule outlines: http://napra.ca/national-drug-schedules

Clinical Judgment and Next-Generation NCLEX® Examination-Style Questionsn

The National Council of State Boards of Nursing (NCSBN) is the body that develops and administers the NCLEX (National Council Licensure Exam). Recent studies indicate that graduates need to develop the skill of clinical decision making, so the NCLEX examination is changing with different types of questions that are designed to develop clinical judgment in patient situations. These type of questions are referred to as Next Generation NCLEX or NGN. The following questions are typical of the NCLEX examination and include both NGN (Next Generation) and traditional questions. Within each chapter the NCLEX section will identify the objective associated with it, the type of NCLEX question that will be used, and the cognitive skill associated with the item type. Six essential cognitive skills of clinical judgment are being tested: recognize cues; analyze cues; prioritize hypotheses; generate solutions; take action; and evaluate outcomes. These six clinical judgment skills build on and expand the nursing process (NCSBN, 2019).

TRADITIONAL NCLEX-TYPE QUESTIONS	NGN-TYPE QUESTIONS
Multiple Choice Test Item Multiple Response Test Item Ordering Test Item	• Enhanced Hot Spot Test Item • Cloze Test Item • Extended Multiple Response Test Item • Extended Drag and Drop Test Item • Matrix Text Item

1. **A patient has received a prescription from his primary care provider for the drug metoprolol (Lopressor). He asks the nurse why there are two names for the same drug. The nurse responds with which statements(s)?** *(Select all that apply.)*
   1. "One of the names is the brand name of the drug, and the other is the generic name."

2. "When drugs are discovered, all drugs are given a detailed chemical name and a simple generic name. If the company that discovered the drug brings it to the marketplace for sale, the manufacturer will give it a distinctive brand name."
3. "Lopressor is the generic name, and metoprolol is the brand name."
4. "The two names are used to determine whether the drug is a Schedule III or a Schedule IV drug."
5. "Generally, the generic product of the drug is less expensive than the brand name product."

Objective: Differentiate between the chemical, generic, and brand names of drugs.
NCLEX test item: Multiple response
Cognitive skill: Application

2. **Drugs can be classified using various methods; identify the different classification and examples as indicated.**

Choose the most likely option for the information missing from the statements below by selecting from the list of options provided.

Medications such as _____1_____ are classified by the _____2_____ method, whereas medications such as _____1_____ are classified by the _____2_____ method.

OPTIONS FOR 1	OPTIONS FOR 2
antacids antibiotics calcium channel blockers Diuretics Cholinergics	body systems chemical action clinical indication

Objective: Identify the various methods used to classify drugs.
NGN test item: Cloze
Cognitive skill: Analyze cues

3. **A young mother with a 2-month-old infant tells the nurse that she is concerned about the use of any medications because she is breastfeeding her baby. The nurse reviews the possible information sources to discuss with the mother.**

Indicate with an X in the "recommended by the nurse" column the source of drug information listed in the left column the nurse can recommend for the mother to use. Note that not all drug information sources will be used.

DRUG INFORMATION SOURCE	RECOMMENDED BY THE NURSE
Nursing journals Electronic databases Package inserts Natural medicines database	

Objective: Identify sources of drug information available for healthcare providers.
NGN test item: Extended drag and drop
Cognitive skill: Take action

4. **The nurse knows which of these factors are the differences between prescription and nonprescription drugs?** *(Select all that apply.)*

1. Nonprescription drugs are available over-the-counter.
2. Prescription drugs are those drugs that may be prescribed by dentists, pharmacists, nurse practitioners, and primary healthcare providers.
3. Recreational drugs are available by prescription only.
4. Over-the-counter drugs are available at a pharmacy or health section of grocery stores.
5. Prescription drugs have been approved for use by the FDA.

Objective: Discuss the difference between prescription and nonprescription drugs.
NCLEX test item: Multiple response
Cognitive skill: Application

5. **During which stage of the process of new drug development does testing on humans start?**

1. The preclinical research and development stage
2. The postmarketing surveillance stage
3. The postclinical research and development stage
4. The clinical research and development stage

Objective: Describe the process of developing and bringing new drugs to market.
NCLEX test item: Multiple choice
Cognitive skill: Knowledge

6. **A nurse is teaching a patient from Canada the names of her medications and reviews the differences between Canadian names. Which statement indicates that the patient understands the instructions?**

1. "The proper name of the medication is the same as the brand name in Canada."
2. "The proper name of the medication is the same as the generic name in Canada."
3. "The chemical name is the one used the most when buying medications in Canada."
4. "The chemical names and the brand names are the only names used in Canada."

Objective: Differentiate between the Canadian *chemical* name and the *proper* name of a drug.
NCLEX test item: Multiple choice
Cognitive skill: Evaluation

Basic Principles of Drug Action and Drug Interactions

2

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Objectives

1. Identify common drug administration routes.
2. Identify the meaning and significance of the term *half-life* when used in relation to drug therapy.
3. Describe the process of how a drug is metabolized in the body.
4. Compare and contrast the following terms that are used in relationship to medications: *desired action, common adverse effects, serious adverse effects, allergic reactions,* and *idiosyncratic reactions.*
5. Identify what is meant by a drug interaction.
6. Differentiate among the terms *additive effect, synergistic effect, antagonistic effect, displacement, interference,* and *incompatibility.*
7. Identify one way in which alternatives in metabolism create drug interactions.

Key Terms

receptors (rē-SĔP-tĕrz) (p. 13)
pharmacodynamics (făr-mă-kō-dī-NĂM-ĭks) (p. 13)
agonists (ĂG-ŏ-nĭsts) (p. 13)
antagonists (ăn-TĂG-ŏ-nĭsts) (p. 13)
partial agonists (PĂR-shŭl ĂG-ŏ-nĭsts) (p. 13)
enteral (ĔN-tĕr-ăl) (p. 14)
parenteral (pă-RĔN-tĕr-ăl) (p. 14)
percutaneous (pĕr-kū-TĀ-nē-ŭs) (p. 14)
pharmacokinetics (făr-mă-kō-kĭ-NĔT-ĭks) (p. 14)
absorption (ăb-SŎRP-shŭn) (p. 14)
distribution (dĭs-trĭ-BŪ-shŭn) (p. 15)
drug blood level (p. 15)
metabolism (mĕ-TĂB-ō-lĭz-ĕm) (p. 15)
excretion (ĕks-KRĒ-shŭn) (p. 15)
half-life (p. 16)
onset of action (p. 17)
peak action (p. 17)
duration of action (p. 17)
desired action (p. 17)
side effects (p. 17)
common adverse effects (ĂD-vŭrs ĕ-FĔKTS) (p. 17)
serious adverse effects (p. 17)
idiosyncratic reaction (ĭd-ē-ō-sĭn-KRĂT-ĭk rē-ĂK-shŭn) (p. 18)
allergic reactions (ă-LŬR-jĭk) (p. 18)
drug interaction (p. 18)
unbound drug (ŭn-BŎWND) (p. 18)
additive effect (ĂD-ĭ-tĭv) (p. 19)
synergistic effect (sĭn-ĕr-JĬS-tĭk) (p. 19)
antagonistic effect (ăn-tăg-ŏ-NĬST-ĭk) (p. 19)
displacement (dĭs-PLĀS-mĕnt) (p. 19)
interference (ĭn-tŭr-FĒR-ĕns) (p. 19)
incompatibility (ĭn-kŏm-păt-ĭ-BĬL-ĭ-tē) (p. 19)

BASIC PRINCIPLES RELATED TO DRUG THERAPY

DRUG RESPONSES IN THE BODY

When administered to the body, drugs do not create new responses but rather alter existing physiologic activity in several different ways. Usually the drug forms chemical bonds with specific sites, called **receptors**, within the body. This bond forms only if the drug and its receptor have similar shapes and if the drug has a chemical affinity for the receptor. The relationship between a drug and a receptor is similar to that seen between a key and lock (Fig. 2.1A). The study of the interactions between drugs and their receptors and the series of events that result in a pharmacologic response is called **pharmacodynamics**. Most drugs have several different atoms within each molecule that interlock into various locations on a receptor. The better the fit between the receptor and the drug molecule, the better the response from the drug. The intensity of a drug response is related to how well the drug molecule fits into the receptor and to the number of receptor sites that are occupied. Drugs that interact with a receptor to stimulate a response are known as **agonists** (Fig. 2.1B). Drugs that attach to a receptor but do not stimulate a response are called **antagonists** (Fig. 2.1C). Drugs that interact with a receptor to stimulate a response but inhibit other responses are called **partial agonists** (Fig. 2.1D).

Drug response must be stated in relation to the physiologic activity expected in response to the drug therapy (e.g., an antihypertensive agent is successful if the patient's blood pressure is lower after receiving the drug than it was before the drug was started). Therefore it is important to perform a thorough nursing assessment to identify the baseline data. After that is done, results from regular assessments can be compared

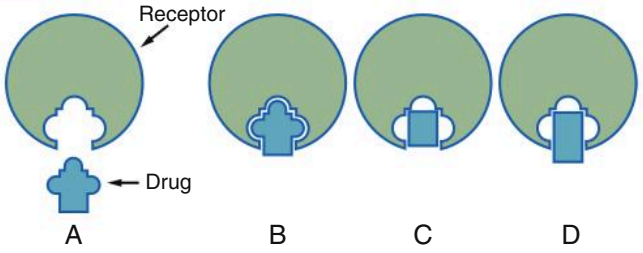

Fig. 2.1 (A) Drugs act by forming chemical bonds with specific receptor sites, similar to a key and lock. The better the fit, the better the response. (B) Drugs with complete attachment and response are called *agonists.* (C) Drugs that attach but do not elicit a response are called *antagonists.* (D) Drugs that attach and elicit a small response but also block other responses are called *partial agonists.*

Table 2.1 Drug Therapy Used in Disease Management[a]

DISEASES/ILLNESSES	CLASSIFICATION OF THE DRUGS USED
Cancer	Chemotherapy, immunotherapy
Mental illness	Antidepressants and antipsychotic agents
Hypertension	Antihypertensive agents
Diabetes	Antidiabetic agents
Infections	Antimicrobial agents
Inflammatory diseases	Antiinflammatory agents
Nausea and vomiting	Antiemetic agents
Constipation	Laxatives
Diarrhea	Antidiarrheal agents
GERD	Antacids

[a]List is not inclusive.
GERD, Gastroesophageal reflux disease.

with the baseline data by the primary healthcare provider, the nurse, and the pharmacist to evaluate the effectiveness of the drug therapy. Table 2.1 lists examples of drug therapies and their related diseases.

ROUTES OF DRUG ADMINISTRATION

The most common routes of drug administration are the enteral, parenteral, and percutaneous routes. When using the **enteral** route, the drug is administered directly into the gastrointestinal (GI) tract by the oral, rectal, or nasogastric route. The **parenteral** route bypasses the GI tract with the use of subcutaneous (subcut), intramuscular (IM), or intravenous (IV) injection. The **percutaneous** route involves drugs being absorbed through the skin and mucous membranes. Methods of the percutaneous route include inhalation, sublingual (under the tongue), and topical (on the skin) administration.

LIBERATION, ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

After they have been administered, all drugs go through five stages: ***l***iberation, ***a***bsorption, ***d***istribution, ***m***etabolism, and ***e***xcretion (LADME). After liberation from the dosage form, each drug has its own unique ADME characteristics. The study of the mathematical relationships among the ADME features of individual medicines over time is called **pharmacokinetics**.

Liberation

Regardless of the route of administration, a drug must be released from the dosage form (i.e., liberated) and dissolved in body fluids before it can be absorbed into body tissues. For example, before a solid drug that is taken orally can be absorbed into the bloodstream for transport to the site of action, the dosage form (usually a capsule or tablet) must disintegrate and the active drug must dissolve in the GI fluids so that it can be transported across the stomach or intestinal lining into the blood. The process of converting the drug into a form that will activate a response can be partially controlled by the pharmaceutical dosage form used (e.g., solution, suspension, capsule, tablet [with various coatings]). This conversion process can also be influenced by administering the drug with or without water or food in the patient's stomach.

Absorption

Absorption is the process whereby a drug is transferred from its site of entry into the body to the circulating fluids of the body (i.e., blood and lymph) for distribution around the body. The rate at which this occurs depends on the route of administration, the blood flow through the tissue where the drug is administered, and the solubility of the drug. It is therefore important to do the following: (1) administer oral drugs with an adequate amount of fluid (usually a large [8-ounce] glass of water); (2) give parenteral forms properly so that they are deposited in the correct tissue for enhanced absorption; and (3) reconstitute and dilute drugs only with the diluent recommended by the manufacturer in the package literature so that drug solubility is not impaired. Equally important are nursing assessments that reveal poor absorption (e.g., if insulin is administered subcutaneously and a lump remains at the site of injection 2 to 3 hours later, absorption from that site may be impaired).

The rate of absorption when a drug is administered by a parenteral route depends on the rate of blood flow through the tissues. Circulation or blood flow must be determined before the administration of drugs by the parenteral route to identify any circulatory insufficiency. If any such insufficiency is noted, injections will not be absorbed properly, and the drug will not be effective. Subcut injections have the slowest absorption rate, especially if peripheral circulation is impaired. IM injections are more rapidly absorbed because of greater blood flow per unit weight of muscle compared with subcut tissue. Cooling the area of injection slows the rate of absorption, whereas heat or massage hastens the rate of absorption. Drugs are dispersed throughout the body most rapidly when they are administered by IV injection. The nurse must be thoroughly educated

regarding the responsibilities and techniques associated with administering IV medications. It is important to remember that after a drug enters the patient's bloodstream, it cannot be retrieved.

The absorption of topical drugs that have been applied to the skin can be influenced by the drug concentration, the length of contact time, the size of the affected area, the thickness of the skin surface, the hydration of the tissue, and the degree of skin disruption. Percutaneous (i.e., across-the-skin) absorption is greatly increased in newborns and young infants, who have thin, well-hydrated skin. When drugs are inhaled, their absorption can be influenced by the depth of the patient's respirations, the fineness of the droplet particles, the available surface area of the patient's mucous membranes, the contact time, the hydration state, the blood supply to the area, and the concentration of the drug itself.

Distribution

The term **distribution** refers to the ways in which a drug is transported throughout the body by the circulating body fluids to the sites of action or to the receptors that the drug affects. *Drug distribution* refers to the transport of the drug throughout the entire body by the blood and lymphatic systems and the transport from the circulating fluids into and out of the fluids that bathe the receptor sites. Organs with the most extensive blood supplies (e.g., heart, liver, kidneys, brain) receive the distributed drug most rapidly. Areas with less extensive blood supplies (e.g., muscle, skin, fat) receive the drug more slowly.

After a drug has been dissolved and absorbed into the circulating blood, its distribution is determined by the chemical properties of the drug and how it is affected by the blood and tissues that it contacts. Two factors that influence drug distribution are protein binding and lipid (fat) solubility. Most drugs are transported in combination with plasma proteins (especially albumin), which act as carriers for relatively insoluble drugs. Drugs that are bound to plasma proteins are pharmacologically inactive because the large size of the complex keeps them in the bloodstream and prevents them from reaching the sites of action, metabolism, and excretion. Only the free, or *unbound*, portion of a drug is able to diffuse into tissues, interact with receptors, and produce physiologic effects; it is also only this portion that can be metabolized and excreted. The same proportions of bound and free drug are maintained in the blood at all times. Thus as the free drug acts on receptor sites or is metabolized, the decrease in the serum drug level causes some of the bound drug to be released from protein to maintain the ratio between bound and free drug.

When a drug leaves the bloodstream, it may become bound to tissues other than those with active receptor sites. The more lipid-soluble drugs have a high affinity for adipose tissue, which serves as a repository site for these agents. Because there is a relatively low level of blood circulation to fat tissues, the more lipid-soluble drugs tend to stay in the body much longer. Equilibrium is established between the repository site (i.e., lipid tissue) and the circulation so that as the **drug blood level** drops as a result of binding at the sites of physiologic activity, metabolism, or excretion, more drug is released from the lipid tissue. By contrast, if more drug is given, a new equilibrium is established among the blood, the receptor sites, the lipid tissue repository sites, and the metabolic and excretory sites.

Distribution may be general or selective. Some drugs cannot pass through certain types of cell membranes, such as the blood-brain barrier (i.e., the central nervous system) or the placental barrier (i.e., the placenta), whereas other types of drugs readily pass into these tissues. The distribution process is very important because the amount of drug that actually gets to the receptor sites determines the extent of pharmacologic activity. If little of the drug actually reaches and binds to the receptor sites, the response will be minimal.

Metabolism

Metabolism is the process whereby the body inactivates drugs. The enzyme systems of the liver are the primary sites for the metabolism of drugs, but other tissues and organs (e.g., white blood cells, GI tract, lungs) metabolize certain drugs to a minor extent. Genetic, environmental, and physiologic factors are involved in the regulation of drug metabolism reactions. The most important factors for the conversion of drugs to their metabolites are genetic variations of enzyme systems, the concurrent use of other drugs, exposure to environmental pollutants, concurrent illnesses, and age. (For more information, see Chapter 3.)

Excretion

The elimination of drug metabolites and, in some cases, of the active drug itself from the body is called **excretion**. The two primary routes of excretion are through the GI tract into the feces and through the renal tubules into the urine. Other routes of excretion include evaporation through the skin, exhalation from the lungs, and secretion into saliva and breast milk.

Because the kidneys are major organs of drug excretion, the nurse should review the patient's chart for the results of urinalysis and renal function tests. A patient with renal failure often has an increase in the action and duration of a drug if the dosage and frequency of administration are not adjusted to allow for the patient's reduced renal function.

Fig. 2.2 shows a schematic review of the ADME process of an oral medication. It is important to note how little of the active ingredient actually reaches the receptor sites for action.

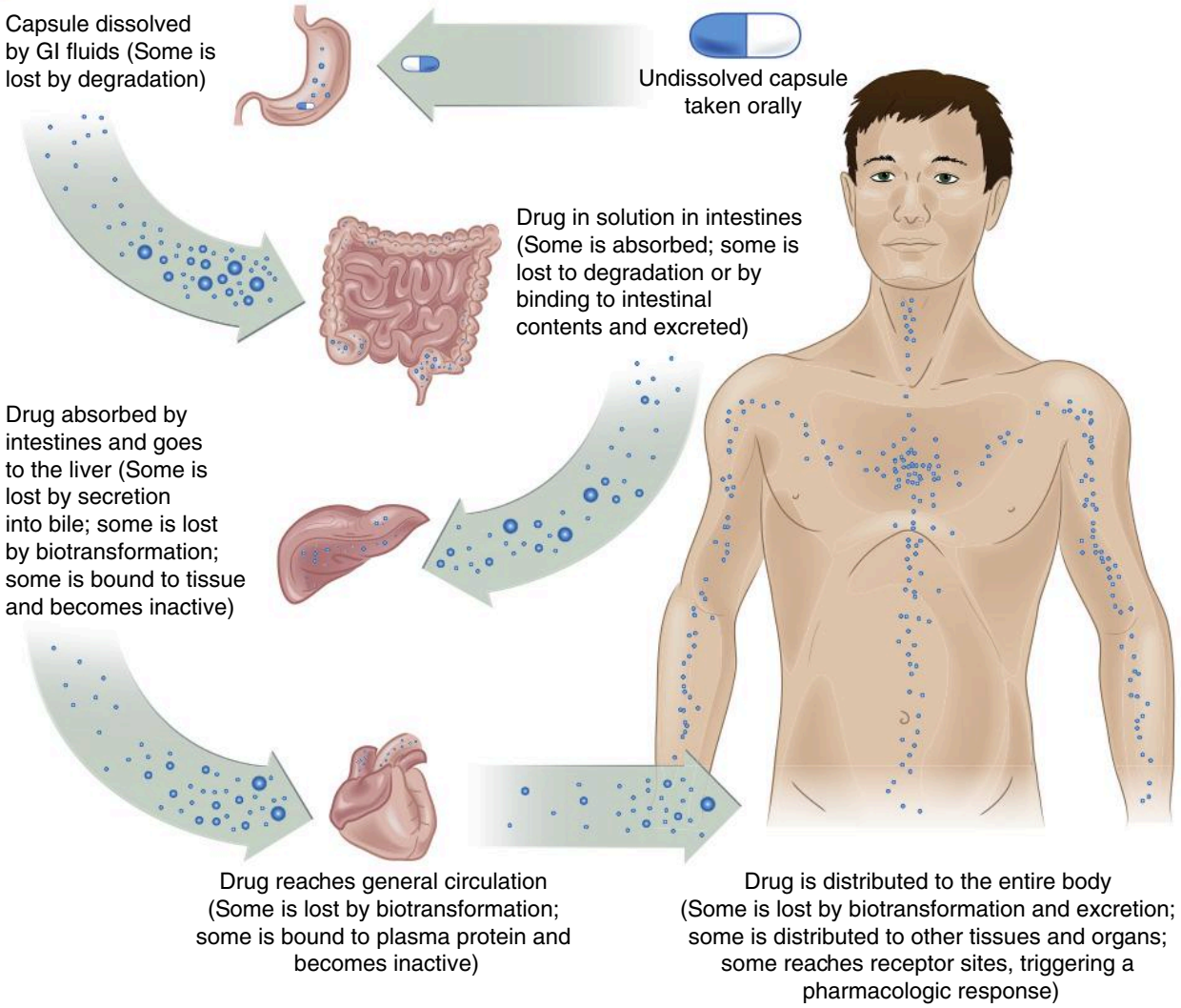

Fig. 2.2 Factors that modify the quantity of drug that reaches a site of action after a single oral dose. *GI*, Gastrointestinal.

HALF-LIFE

Drugs are eliminated from the body by means of metabolism and excretion. A measure of the time required for elimination is the half-life. The **half-life** is defined as the amount of time required for 50% of the drug to be eliminated from the body. For example, if a patient is given 100 mg of a drug that has a half-life of 12 hours, the following would be observed:

TIME (HOURS)	HALF-LIFE	DRUG REMAINING IN BODY (%)
0	—	100 mg (100)
12	1	50 mg (50)
24	2	25 mg (25)
36	3	12.5 mg (12.5)
48	4	6.25 mg (6.25)
60	5	3.12 mg (3.12)

Note that as each 12-hour period (i.e., one half-life) passes, the amount remaining is 50% of what was there 12 hours earlier. After six half-lives, more than 98% of the drug has been eliminated from the body.

The half-life is determined by an individual's ability to metabolize and excrete a particular drug. Because most patients metabolize and excrete a particular drug at approximately the same rate, the approximate half-lives of most drugs are now known. When the half-life of a drug is known, dosages and frequency of administration can be calculated. Drugs with long half-lives (e.g., digoxin, with a half-life of 36 hours) need to be administered only once daily, whereas drugs with short half-lives (e.g., aspirin, with a half-life of 5 hours) need to be administered every 4 to 6 hours to maintain therapeutic activity. For patients who have impaired hepatic or renal function, the half-life may become considerably longer because of their reduced ability to metabolize or excrete the drug. For example, digoxin has a half-life of about 36 hours in a patient with normal renal function; however, it has a half-life of about 105 hours in a patient with complete renal failure. Monitoring diagnostic tests that measure renal or hepatic function is important. Whenever laboratory data reflect impairment of

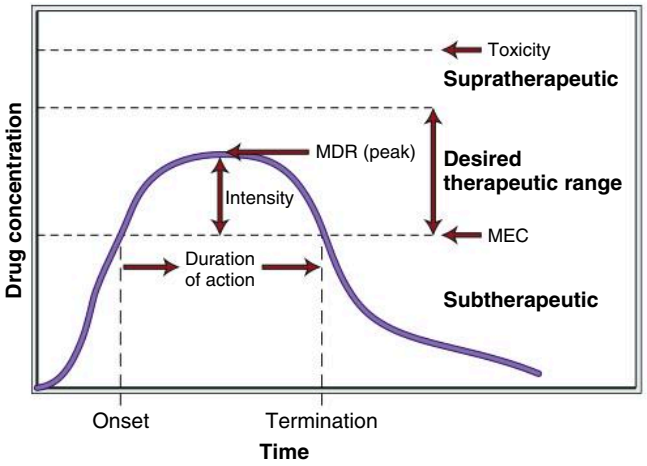

Fig. 2.3 A time-response curve, which is also known as a *drug concentration–time profile*, demonstrates the relationship between the administration of a drug and the patient's response. If the drug level does not reach the minimum effective concentration *(MEC)*, there will be no pharmacologic effect. If the peak level exceeds the toxicity threshold, toxic effects will result. The optimal drug concentration is in the middle of the therapeutic range. *MDR*, Maximum drug response (peak effect).

either function, the nurse should notify the healthcare provider.

DRUG ACTIONS

All drug actions have an onset, peak, and duration of action. The **onset of action** is when the concentration of a drug at the site of action is sufficient to start a physiologic (pharmacologic) response. Many factors—such as the route of administration and the rates of absorption, distribution, and binding to receptor sites—affect the onset of action. In general, increasing the dose of the drug hastens the onset of action by shortening the time required to achieve the necessary concentration of drug at the target site. **Peak action** is the time at which the drug reaches the highest concentrations on the target receptor sites, thereby inducing the maximal pharmacologic response for the dose given. The **duration of action** is how long the drug has a pharmacologic effect. The onset, peak, and duration of action of a drug are often illustrated by a time-response curve, which is also known as a drug concentration–time profile (Fig. 2.3). A time-response curve demonstrates the relationship between the administration of a drug and the associated response. If the drug level does not reach the minimum effective concentration, there will be no pharmacologic effect. If the peak level exceeds the toxicity threshold, toxic effects will result. Generally, the drug concentration is targeted to be in the middle of this range, between the minimum effective response and the toxic response; this is referred to as the *therapeutic range.*

DRUG BLOOD LEVEL

When a drug is circulating in the blood, a blood sample may be drawn and assayed to determine the amount of drug present. This is known as a *drug blood level.* It is important for certain drugs (e.g., anticonvulsants, aminoglycoside antibiotics) to be measured to ensure that the drug blood level is within the therapeutic range. If the drug blood level is low, the dosage must be increased, or the medicine must be administered more frequently. If the drug blood level is too high, the patient may develop signs of toxicity; in this case, the dosage must be reduced or the medicine administered less frequently.

ADVERSE EFFECTS OF DRUGS

No drug has a single action. When a drug enters a patient and is then absorbed and distributed, the **desired action** (i.e., the expected response) usually occurs. However, all drugs have the potential to affect more than one body system simultaneously, thereby producing responses that are known as **side effects** or **common adverse effects**, which are mild, or **serious adverse effects**, which can lead to toxicity. The World Health Organization's definition of an adverse drug reaction (ADR) is "any noxious, unintended, and undesired effect of a drug, which occurs at dosages used in humans for prophylaxis, diagnosis, or therapy." A more common definition is as follows: "Right drug, right dose, right patient, bad effect." ADRs should not be confused with medication errors or adverse drug events (ADEs), which are defined as "an injury resulting from medical intervention related to a drug." (For more information, see Chapter 6.)

Recent studies have indicated the following:

- ADRs may be responsible for more than 100,000 deaths among hospitalized patients per year, which makes them one of the top six leading causes of death in the United States.
- An average of 6% of hospitalized patients experience a significant ADR at some point during their hospitalizations.
- Between 5% and 9% of hospitalization costs are attributable to ADRs.
- The most commonly seen ADRs are rash, nausea, itching, thrombocytopenia, vomiting, hyperglycemia, and diarrhea.
- The classes of medicines that account for the largest number of ADRs are antibiotics, cardiovascular medicines, cancer chemotherapy agents, analgesics, and antiinflammatory agents.

Most ADEs are predictable because of the pharmacologic effects of a drug, and patients should be monitored so that dosages can be adjusted to allow for the maximum therapeutic benefits with a minimum of adverse effects. As described in Units III through X of this text, each drug has a series of parameters (e.g., therapeutic actions to expect, adverse effects, probable drug interactions) that should be monitored by the nurse, primary healthcare provider, pharmacist, and patient to optimize therapy while reducing the possibility of serious adverse effects.

Accurate and appropriate drug-drug interaction information must be available to prescribers, and continual attention is currently focused on this issue. Further

population-based studies still need to be conducted to meet federal initiatives to promote the meaningful use of information technologies and to integrate knowledge databases with clinical decision systems. Ideally, clinical decision systems and the databases of drug interactions that interface with them help the prescriber to identify and avoid potential medication interactions.

All hospitals have internal mechanisms for reporting suspected ADRs, and healthcare providers should not hesitate to report possible reactions. By monitoring and tracking the occurrences of ADRs, clinical protocols and improved patient screening will reduce the frequency of recurrence. The US Food and Drug Administration's MedWatch program is also available for the voluntary reporting of adverse events. (For more information, see MedWatch on Evolve.)

Idiosyncratic Reaction

Two other types of drug actions are much more unpredictable: idiosyncratic reactions and allergic reactions. An **idiosyncratic reaction** occurs when something unusual or abnormal happens when a drug is first administered. The patient usually demonstrates an unexpectedly strong response to the action of the drug. This type of reaction is generally the result of a patient's inability to metabolize a drug because of a genetic deficiency of certain enzymes. Fortunately, this type of reaction is rare.

Allergic Reaction

Allergic reactions, which are also known as *hypersensitivity reactions,* occur in about 6% to 10% of patients who are taking medications. Allergic reactions occur among patients who have previously been exposed to a drug and whose immune systems have developed antibodies to the drug. On reexposure to the drug, the antibodies cause a reaction; this reaction is most commonly seen as raised, irregularly shaped patches on the skin known as *hives,* which cause severe itching, known as *urticaria.*

Occasionally, a patient has a severe, life-threatening reaction that causes respiratory distress and cardiovascular collapse; this is known as an *anaphylactic reaction.* This condition is a medical emergency, and it must be treated immediately. Fortunately, anaphylactic reactions occur much less often than the more mild urticarial reactions.

If a patient has a mild reaction, it should be understood as a warning to not take the medication again. The patient is much more likely to have an anaphylactic reaction during their next exposure to the drug. Patients should receive information about the drug name and be instructed to tell healthcare providers that they have had such reactions and that they must not receive the drug again. In addition, patients should wear a medical alert bracelet or necklace that explains the allergy.

DRUG INTERACTIONS

A **drug interaction** is said to occur when the action of one drug is altered or changed by the action of another drug. Drug interactions are elicited in two ways: (1) by agents that, when combined, *increase* the actions of one or both drugs; and (2) by agents that, when combined, *decrease* the effectiveness of one or both drugs. Some drug interactions are beneficial, such as the use of caffeine, a central nervous system stimulant, with an antihistamine, a central nervous system depressant. The stimulatory effects of the caffeine counteract the drowsiness caused by the antihistamine without eliminating the antihistaminic effects. The mechanisms of drug interactions can be categorized as those that change the absorption, distribution, metabolism, or excretion of a drug and those that enhance the pharmacologic effect of a drug.

CHANGES IN ABSORPTION

Most drug interactions that change absorption take place in the GI tract, usually the stomach. Examples of this type of interaction include the following:

- Antacids inhibit the dissolution of ketoconazole tablets by increasing the gastric pH. The interaction is managed by giving the antacid at least 2 hours after ketoconazole administration.
- Aluminum-containing antacids inhibit the absorption of tetracycline. Aluminum salts form an insoluble chemical complex with tetracycline. The interaction is managed by separating the administration of tetracycline and antacids by 3 to 4 hours.

CHANGES IN DISTRIBUTION

Drug interactions that cause a change in distribution usually affect the binding of a drug to an inactive site (e.g., circulating plasma albumin, muscle protein). When a drug is absorbed into the blood, it is usually transported throughout the body bound to plasma proteins. It often binds to other proteins, such as those in muscle. A drug that is highly bound (e.g., >90% bound) to a protein-binding site may be displaced by another drug that has a higher affinity for that binding site. Significant interactions can take place this way because little displacement is required to have a major impact. Remember, only the **unbound drug** is pharmacologically active. If a drug is 90% bound to a protein, then 10% of the drug is providing the physiologic effect. If another drug is administered with a stronger affinity for the protein-binding site and it displaces just 5% of the bound drug, there is now 15% unbound for physiologic activity; this is the equivalent of a 50% increase in dosage (i.e., from 10% to 15% active drug). For example, the anticoagulant action of warfarin is increased by administration with furosemide, which is a loop diuretic. Furosemide displaces warfarin from albumin-binding sites, thereby increasing the amount of unbound anticoagulant. This interaction is managed by decreasing the warfarin dosage.

CHANGES IN METABOLISM

Drug interactions usually result from a change in metabolism that involves inhibiting or inducing (stimulating)

the enzymes that metabolize a drug. Medicines known to bind to enzymes and to slow the metabolism of other drugs include verapamil, ketoconazole, amiodarone, cimetidine, and erythromycin. Serum drug levels usually increase as a result of inhibited metabolism when these drugs are given concurrently, and the dosages of the inhibited drugs usually must be reduced to prevent toxicity. For example, erythromycin inhibits the metabolism of theophylline; therefore the dose of theophylline must be reduced on the basis of theophylline serum levels and signs of toxicity. Because erythromycin (an antibiotic) is usually administered only in short courses, the theophylline dosage usually needs to be increased when the erythromycin is discontinued.

Common drugs that bind to enzymes and increase the metabolism of other drugs (enzyme inducers) are phenobarbital, carbamazepine, rifampin, and phenytoin. Rapidly metabolized drugs include doxycycline, warfarin, metronidazole, theophylline, and verapamil. When administered with enzyme inducers, the dosages of the more rapidly metabolized drugs should generally be increased to provide therapeutic activity. The patient must be monitored closely for adverse effects. For example, if a woman who is taking oral contraceptives (see Chapter 40) requires a course of rifampin antimicrobial therapy, the rifampin will induce the enzymes that metabolize both the progesterone and estrogen components of the contraceptive, thereby causing an increased incidence of menstrual abnormalities and reduced effectiveness of conception control. This interaction is managed by advising the patient to use an additional form of contraception while she is receiving rifampin therapy. Adverse effects may also occur if an enzyme inducer is discontinued. The metabolism of the induced drug then decelerates, leading to accumulation and toxicity if the dosage is not reduced.

CHANGES IN EXCRETION

Drug interactions that cause a change in excretion usually act in the kidney tubules by changing the pH to enhance or inhibit excretion. The classic example of altered urine pH is the combination of acetazolamide (which elevates urine pH) and quinidine. The alkaline urine produced by acetazolamide causes quinidine to be reabsorbed in the renal tubules, which potentially increases the physiologic and toxic effects of quinidine. The frequent monitoring of quinidine serum levels and assessments for signs of quinidine toxicity are used as guides for reducing quinidine dosage.

DRUGS THAT ENHANCE THE PHARMACOLOGIC EFFECTS OF OTHER DRUGS

Major drug interactions also occur between drugs. This may occur when one drug enhances the physiologic effects of another drug. Alcohol and sedative-hypnotic agents both cause sedation, but when used together can cause significant central nervous system depression. Another drug interaction that can have serious consequences is the interaction between aminoglycoside antibiotics (gentamicin, tobramycin) and a neuromuscular blocking agent such as pancuronium. When used together, the antibiotic increases the neuromuscular blockade, prolonging return to normal respirations and recovery time. Table 2.2 defines the terminology related to drug-drug interactions.

Because it is impossible to memorize all possible drug interactions, the nurse must check for drug interactions when they are suspected. The nurse must take the time to consult drug resource books and pharmacists to ensure that a patient who is receiving multiple medications does not experience unanticipated drug interactions.

Table 2.2 Terminology Related to Drug-Drug Interactions

TERM	DEFINITION	EXAMPLE
Additive effect	Two drugs with similar actions are taken for an increased effect.	hydrocodone + acetaminophen = added analgesic effect
Synergistic effect	The combined effect of two drugs is greater than the sum of the effect of each drug given together.	aspirin + codeine = much greater analgesic effect
Antagonistic effect	One drug interferes with the action of another.	tetracycline + antacid = decreased absorption of the tetracycline
Displacement	The displacement of the first drug from protein-binding sites (i.e., bound drugs are inactive) by a second drug increases the activity of the first drug because more unbound drug is available.	warfarin + valproic acid = increased anticoagulant effect
Interference	The first drug inhibits the metabolism or excretion of the second drug, thereby causing increased activity of the second drug.	probenecid + ampicillin = prolonged antibacterial activity of ampicillin because probenecid blocks the renal excretion of ampicillin
Incompatibility	The first drug is chemically incompatible with the second drug, thereby causing deterioration when the drugs are mixed in the same syringe or solution or are administered together at the same site. Signs include haziness, formation of a precipitate, or a change in the color of the solution when the drugs are mixed.	ampicillin + gentamicin = ampicillin inactivates gentamicin

Clinical Judgment and Next-Generation NCLEX® Examination-Style Questions

Key Points

- The most common routes of drug administration are the enteral, parenteral, and percutaneous routes.
- The half-life of a drug is defined as the amount of time required for 50% of the drug to be eliminated from the body.
- After administration, all drugs go through five stages: *l*iberation, *a*bsorption, *d*istribution, *m*etabolism, and *e*xcretion (LADME). The enzyme systems of the liver are the primary sites for the metabolism of drugs, but other tissues and organs (e.g., white blood cells, GI tract, lungs) metabolize certain drugs to a minor extent.
- When a drug enters a patient and is absorbed and distributed, the desired action usually occurs. However, all drugs have the potential to affect more than one body system simultaneously, causing common adverse effects, which are generally mild, or serious adverse effects, which can be more severe and lead to toxicity.
- Drug interactions are elicited in two ways: (1) by agents that, when combined, *increase* the actions of one or both drugs; and (2) by agents that, when combined, *decrease* the effectiveness of one or both of the drugs.
- The mechanisms of drug interactions can be categorized as those that change the absorption, distribution, metabolism, or excretion of a drug and those that enhance the pharmacologic effect of a drug.

Additional Learning Resources

SG Go to your Study Guide for additional Review Questions for the NCLEX® Examination, Critical Thinking Clinical Situations, and other learning activities to help you master this chapter content.

Go to your Evolve website (https://evolve.elsevier.com/Willihnganz) for additional online resources.

Clinical Judgment and Next-Generation NCLEX® Examination-Style Questions

The following questions are typical of the NCLEX exam and include both NGN (Next Generation) and traditional questions. See Chapter 1 for further information regarding question types and formats.

1. A nurse is reviewing the drug route for an order written to be given via nasogastric tube and understands that this means that the drug will be administered by which route?

1. Enteral
2. Parenteral
3. Percutaneous
4. Intramuscular

Objective: Identify common drug administration routes.
NCLEX test item: Multiple choice
Cognitive skill: Knowledge

2. A patient takes 50 mg of a drug that has a half-life of 12 hours. What percentage of the dose remains in the body 36 hours after the drug is administered?

1. 50 mg (100%)
2. 25 mg (50%)
3. 12.5 mg (25%)
4. 6.25 mg (12.5%)

Objective: Identify the meaning and significance of the term half-life when used in relation to drug therapy.
NCLEX test item: Multiple choice
Cognitive skill: Comprehension

3. The nurse reviews the patient's charts for laboratory tests that relate to how well the patient's organ systems are working because drug metabolism is influenced by certain body systems.

Choose the most likely options for the information missing from the sentence below by selecting from the lists of options provided.

Metabolism is the process that deactivates drugs; sites for metabolism of drugs are _____1_____ and _____1_____ and _____1_____, and factors that influence these drug metabolism reactions are _____2_____ and _____2_____.

OPTIONS FOR 1	OPTIONS FOR 2
kidneys	exercise tolerance
white blood cells	environmental pollutants
GI tract	repository sites
liver	concurrent use of other drugs
heart	receptor sites

Objective: Describe the process of how a drug is metabolized in the body.
NGN test item: Cloze
Cognitive skill: Recognize cues

4. When an antihypertensive drug causes a drop in blood pressure to the normal range, what is this effect called?

1. Antagonistic effect
2. Desired therapeutic effect
3. Side effect
4. Additive effect

Objective: Compare and contrast the following terms that are used in relationship to medications: desired action, common adverse effects, serious adverse effects, allergic reactions, and idiosyncratic reactions.
NCLEX test item: Multiple choice
Cognitive skill: Understanding

5. The nurse noticed that, after administering an antibiotic ampicillin in the patient's IV line, the solution in the tubing started to turn milky and hazy after injecting another drug in the same tubing. The precipitate that was created meant the nurse needed to do what next? *(Select all that apply.)*

1. Recognize that the two drugs are incompatible and notify the healthcare providers.
2. Flush the line still connected to the patient until the precipitate is gone.
3. Stop the infusion, disconnect the IV line, flush the precipitate out, and reconnect the line.
4. Request that the drugs be placed on different schedules so that they are not administered at the same time.
5. Recognize that the two drugs are having a synergistic effect and notify the healthcare providers.

Objective: Differentiate among the terms: additive effect, synergistic effect, antagonistic effect, displacement, interference, and incompatibility.
NCLEX test item: Multiple response
Cognitive skill: Application

6. A patient is experiencing a rash over their torso and legs accompanied by severe itching after receiving an antibiotic for an ear infection. What does the nurse suspect is happening? *Select all that apply.*

1. The patient is having an idiosyncratic reaction.
2. The patient is having an antagonistic effect.
3. The patient is having an allergic reaction.
4. The patient is having a common adverse effect.
5. The patient is having the desired effect.
6. The patient is having a serious adverse effect.
7. The patient is having an anaphylactic reaction.

Objective: Compare and contrast the following terms that are used in relationship to medications: desired actions, common adverse effects, serious adverse effects, allergic reactions, and idiosyncratic reactions.
NGN test item: Extended multiple response
Cognitive skill: Recognize cues

7. When a patient who was prescribed warfarin and valproic acid begins experiencing an increased effect of warfarin (bruising on arms, bleeding gums), what is this known as?

1. Synergistic effect
2. Antagonistic effect
3. Idiosyncratic effect
4. Displacement effect

Objective: Compare and contrast the following terms that are used in relationship to medications: desired action, common adverse effects, serious adverse effects, allergic reactions, and idiosyncratic reactions.
NCLEX test item: Multiple choice
Cognitive skill: Knowledge

8. The nurse is aware that a patient who has an increased metabolic rate (e.g., hyperthyroidism) generally requires what type of dosage?

1. Normal dosage
2. Lower-than-normal dosage
3. Higher-than-normal dosage
4. A dosage that is based on the patient's thyroid function levels

Objective: Identify one way in which alternatives in metabolism create drug interactions.
NCLEX test item: Multiple choice
Cognitive skill: Comprehension

9. The nurse studied the terms for drug interactions and recognized that there are medications that will create an antagonistic effect when given together.

Choose the most likely option for the information missing from the statements below by selecting from the list of options provided.

An example of the drug interaction that causes an antagonistic effect is between ____1____ and ____2____ in which there is a decrease in the absorption of the second drug.

OPTIONS FOR 1	OPTIONS FOR 2
antacid	codeine
warfarin	ampicillin
probenecid	tetracycline
aspirin	valproic acid

Objective: Differentiate among the following terms: additive effect, synergistic effect, antagonistic effect, displacement, interference, and incompatibility.
NGN test item: Cloze
Cognitive skill: Analysis cues

10. The nurse is aware of enzymes that affect metabolism and therefore affect drug actions that are caused by alterations in enzyme activity.

Indicate with an arrow (up or down) whether the reaction by the enzyme activity will increase or decrease metabolism of a drug.

ENZYME ACTIVITY	CHANGE IN DRUG ACTION CAUSED BY ALTERED METABOLISM
Enzyme inhibitors	
Enzyme inducers	
Enzyme enhancers	
Enzyme metabolizers	

Objective: Identify one way in which alternatives in metabolism create drug interactions.
NGN test item: Extended Drag and Drop
Cognitive skill: Recognize cues

11. The nurse reviews terms used to describe the therapeutic effects of drugs and knows they include the additive effect and the synergistic effect.

Choose the most likely option for the information missing from the statements below by selecting from the list of options provided.

An example of a synergistic effect is one that is caused by the combination of ____1____ and ____2____, which increases the therapeutic analgesic effect of the drugs.

OPTIONS FOR 1	OPTIONS FOR 2
antacid	codeine
warfarin	ampicillin
probenecid	tetracycline
aspirin	valproic acid

Objective: Differentiate among the following terms: additive effect, synergistic effect, antagonistic effect, displacement, interference, and incompatibility.
NGN test item: Cloze
Cognitive skill: Analysis cues

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