EDITION 5

FOCUS ON NURSING PHARMACOLOGY

AMY M. KARCH

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FOCUS ON NURSING PHARMACOLOGY

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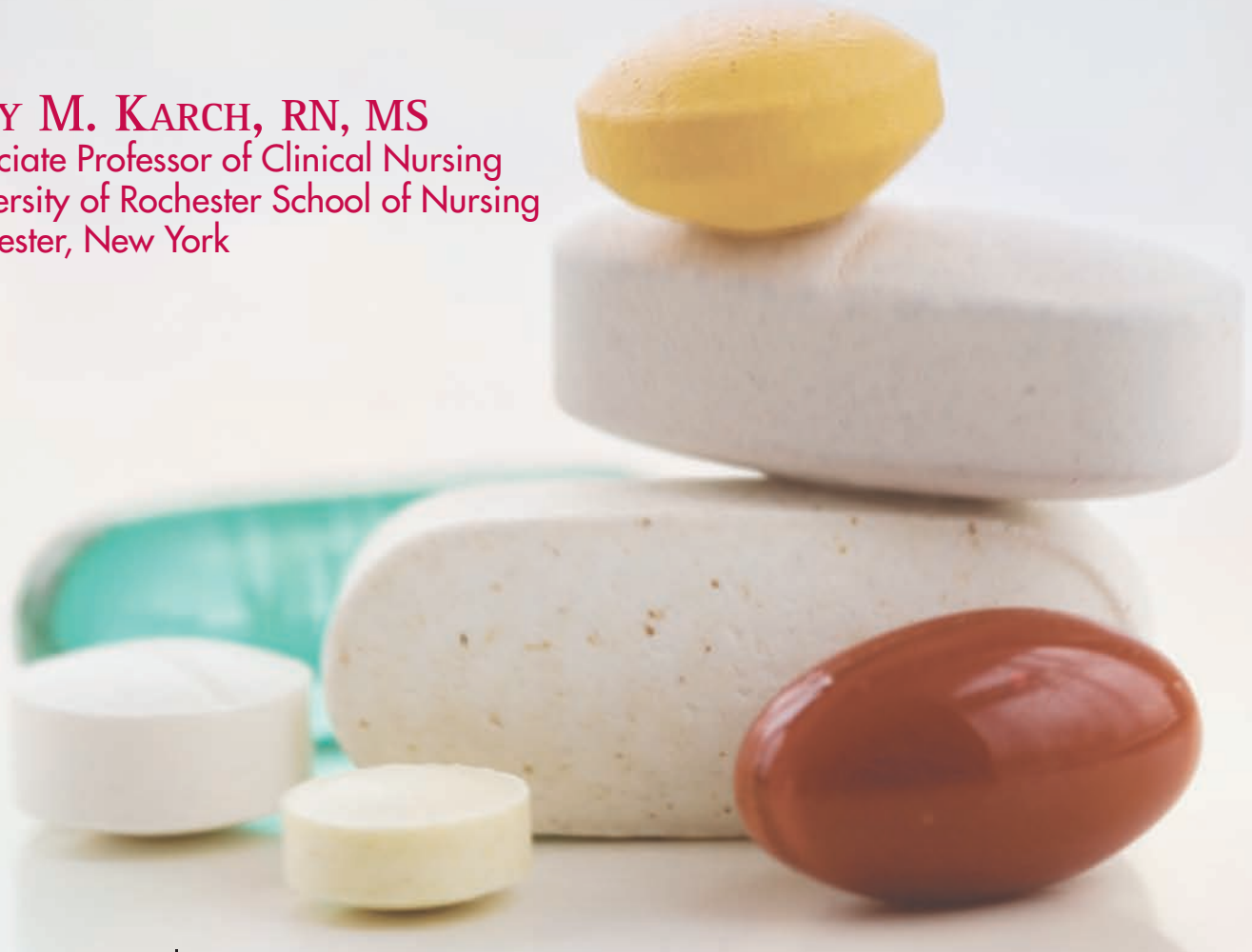

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Dedicated to the many wonderful men and women who are entering the nursing profession today, to the hard-working faculty who are teaching them the art and science of nursing, and to my family and colleagues, who have offered so much support, humor, and sunshine.

AMY M. KARCH

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Preface

Pharmacology is a difficult course to teach in a standard nursing curriculum, whether it be a diploma, associate, baccalaureate, or graduate program. Teachers are difficult to find, and time and money often dictate that the invaluable content of such a course be incorporated into other courses. As a result, the content is often lost. At the same time, changes in medical care delivery—more outpatient and home care, shorter hospital stays, and more self-care—have resulted in additional legal and professional responsibilities for nurses, making them more responsible for the safe and effective delivery of drug therapy.

Pharmacology should not be such a formidable obstacle in the nursing curriculum. The study of drug therapy incorporates physiology, pathophysiology, chemistry, and nursing fundamentals—subjects that are already taught in most schools. A textbook that approaches pharmacology as an understandable, teachable, and learnable subject would greatly facilitate the incorporation of this subject into nursing curricula. Yet many nursing pharmacology texts are large and burdensome, mainly because they need to cover not only the basic pharmacology, but also the particulars included in each area considered.

The fifth edition of *Focus on Nursing Pharmacology* is based on the premise that students first need to have a solid and clearly focused concept of the principles of drug therapy before they can easily grasp the myriad details associated with individual drugs.

Armed with a fundamental knowledge of pharmacology, the student can appreciate and use the specific details that are so readily available in the many annually updated and published nursing drug guides, such as *Lippincott's Nursing Drug Guide*.

With this goal in mind, *Focus on Nursing Pharmacology* provides a concise, user-friendly, and uncluttered text for the modern student. This difficult subject is presented in a streamlined, understandable, teachable, and learnable manner. Because this book is designed to be used in conjunction with a handbook of current drug information, it remains streamlined. This fifth edition of *Focus on Nursing Pharmacology* continues to emphasize "need-to-know" concepts.

The text reviews and integrates previously learned knowledge of physiology, chemistry, and nursing fundamentals into chapters focused on helping students conceptualize what is important to know about each group of drugs. Illustrations, sidebars, and tables sum up concepts to enhance learning. Special features further focus student learning on clinical application, critical thinking, patient safety, lifespan issues related to drug therapy, evidence-based practice, patient teaching, and case-study-based critical thinking exercises that incorporate nursing process principles. The text incorporates study materials that conclude each chapter. Check Your Understanding sections provide both new- and old-format National Council Licensure Examination (NCLEX)-style review questions, as well as study guide review questions to help the student master the material and prepare for the national licensing exam.

Focus on Teaching/Learning Activities

ThePoint (available at http://thepoint.lww.com/), a trademark of Wolters Kluwer Health, is a Web-based course and content management system that provides every resource instructors and students need in one easy-to-use site. ThePoint . . . where teaching, learning, and technology click!

Student Resources

Students can visit thePoint to access supplemental multimedia resources to enhance their learning experience, download content, upload assignments, and join an online study group. ThePoint offers a variety of free student resources, including NCLEX-Style Student Review Questions (over 1,200 NEW to this edition!), Watch and Learn video clips, Practice and Learn activities, an Alternate-Format NCLEX Tutorial, and a Spanish-English Audioglossary. It also has free journal articles related to topics discussed in the Focus on Safe Medication Administration boxes from the book. Also included are videos on preventing medication errors and three-dimensional animated depictions of pharmacology concepts. In addition, an online course is available that includes interactive activities.

Instructor Resources

Advanced technology and superior content combine at thePoint to allow instructors to design and deliver online and offline courses, maintain grades and class rosters, and communicate with students. In addition to housing the material from the Instructor's Resource DVD-ROM, thePoint also provides additional resources, including Pre-lecture Quizzes, PowerPoints with Guided Lecture Notes, Discussion Topics, Assignments, and over 1700 Test Generator questions—almost 1200 of which are brand new to this edition!

Organization

Focus on Nursing Pharmacology is organized following a "simple-to-complex" approach, much like the syllabus for a

basic nursing pharmacology course. Because students learn best "from the bottom up," the text is divided into distinct parts.

Part I begins with an overview of basic nursing pharmacology, including such new challenges as bioterrorism, street drugs, herbal therapies, and the information overload; each of the other parts begins with a review of the physiology of the system affected by the specific drugs being discussed. This review refreshes the information for the student and provides a quick and easy reference when he or she is reading about drug actions.

Part II of the text introduces the drug classes, starting with the chemotherapeutic agents—both antimicrobial and antineoplastic drugs. Because the effectiveness of these drugs depends on their interference with the most basic element of body physiology—the cell—students can easily understand the pharmacology of this class. Mastering the pharmacotherapeutic effects of this drug class helps the student to establish a firm grasp of the basic principles taught in Part I. Once the easiest pharmacological concepts are understood, the student is prepared to move on to the more challenging physiological and pharmacological concepts.

Part III focuses on drugs affecting the immune system because recent knowledge about the immune system has made it the cornerstone of modern therapy. All of the immune system drugs act in ways in which the immune system would act if it were able. Recent immunological research has contributed to a much greater understanding of this system, making it important to position information about drugs affecting this system close to the beginning of the text instead of at the end as has been the custom.

Parts IV and **V** of the text address drugs that affect the nervous system, the basic functioning system of the body. Following the discussion of the nervous system, and closely linked with it in **Part VI**, is the endocrine system. The sequence of these parts introduces students to the concept of control, teaches them about the interrelatedness of these two systems, and prepares them for understanding many aspects of shared physiological function and the inevitable linking of the two systems into one: the neuroendocrine system.

Parts VII, VIII, and **IX** discuss drugs affecting the reproductive, cardiovascular, and renal systems, respectively. The sequencing of cardiovascular and renal drugs is logical because most of the augmenting cardiovascular drugs (such as diuretics) affect the renal system.

Part X covers drugs that act on the respiratory system, which provides the link between the left and right ventricles of the heart.

Part XI addresses drugs acting on the gastrointestinal system. The gastrointestinal system stands on its own; it does not share any actions with any other system.

Text Features

The features in this text are skillfully designed to support the text discussion, encouraging the student to look at the whole patient and to focus on the essential information that is important to learn about each drug class. Important features in the fifth edition focus on incorporating basic nursing skills, patient safety, critical thinking, and application of the material learned to the clinical scenario, helping the student to understand the pharmacology material.

Special Elements and Learning Aids

Each chapter opens with a list of learning objectives for that chapter, helping the student to understand what the key learning points will be. A list of featured drugs and a glossary of key terms are also found on the opening chapter page. Key points appear periodically throughout each chapter to summarize important concepts. The text of each chapter ends with a summary of important concepts. This is followed by a series of review exercises, Check Your Understanding, which includes NCLEX-style questions in the new format to focus student learning on the seminal information presented in the chapter.

- In the *Nursing Considerations* section of each chapter, *italics* highlight the *rationale* for each nursing intervention, helping the student to apply the information in a clinical situation. Elsewhere in the text, the rationale is consistently provided for therapeutic drug actions, contraindications, and adverse effects.
- In the *Drug List* at the beginning of each chapter, a special icon appears next to the drug that is considered the prototype drug of each class. In each chapter, *prototype summary* boxes spotlight need to know information for each prototype drug.
- *Drugs in Focus* tables clearly summarize and identify the drugs within a class, highlighting them by generic and trade names, usual dosage, and indications. The icon appears in these tables next to each drug that is considered to be the prototype for its specific class.
- *Web Links* alert the student to electronic sources of drug information and sources of drug therapy information for specific diseases.
- *Focus on Safe Medication Administration* boxes present important safety information to help keep the patient safe, prevent medication errors, and increase the therapeutic effectiveness of the drugs.
- *Focus on the Evidence* boxes compile information based on research to identify the best nursing practices associated with specific drug therapy.
- *Focus on Herbal and Alternative Therapies* displays highlight known interactions with specific herbs or alternative therapies that could affect the actions of the drugs being discussed.
- *Focus on Calculations* reviews are designed to help the student hone calculation and measurement skills while learning about the drugs for which doses might need to be calculated.
- *Focus on Drug Therapy Across the Lifespan* boxes concisely summarize points to consider when using the drugs of each class with children, adults, and the elderly.

- *Focus on Gender Considerations* and *Focus on Cultural Considerations* discussions encourage the student to think about cultural awareness and to consider the patient as a unique individual with a special set of characteristics that not only influences variations in drug effectiveness, but also could influence a patient's perspective on drug therapy.
- *Critical Thinking Scenarios* tie each chapter's content together by presenting clinical scenarios about a patient using a particular drug from the class being discussed. Included in the case study are hints to guide critical thinking about the case and a discussion of *drug- and nondrug-related nursing considerations* for that particular patient and situation. Most important, the case study provides a *plan of nursing care* specifically developed for that patient and specifically based on the nursing process. The care plan is followed by a checklist of *patient teaching points* designed for the patient presented in the case study. This approach helps the student to see how assessment and the collected data are applied in the clinical situation.
- *Check Your Understanding* sections present NCLEX-style questions, including alternate format questions, to help the student prepare for that exam. Other questions and activities in this section are designed to help students test their knowledge of the information that has been learned in the chapter.

To the Student Using This Text

As you begin your study of pharmacology, don't be overwhelmed or confused by all of the details. The study of drugs fits perfectly into your study of the human body—anatomy, physiology, chemistry, nutrition, psychology, and sociology. Approach the study of pharmacology from the perspective of putting all of the pieces together; this can be not only fun, but also challenging! Work to understand the concepts, and all of the details will fall into place and be easy to remember and apply to the clinical situation. This understanding will help you in creating the picture of the whole patient as you are learning to provide comprehensive nursing care. This text is designed to help you accomplish all of this in a simple and concise manner. Good luck!

Amy M. Karch, RN, MS

Acknowledgments

I would like to thank the various people who have worked so hard to make this book a reality, especially the many students and colleagues who have for so long pushed for a pharmacology book that was straightforward and user-friendly and who have taken the time to make suggestions to improve each edition. Thanks also to my summer team—Patrick Hopkins, Rebecca Tucker, Melanie Bobry, and Kathy Rideout—who brought a fresh approach to pharmacology and teaching with the humor that is so necessary to keep teaching a joy; to Ginny Hanchett for the wonderful opportunity to take on new challenges; to Hilarie Surrena, my acquisitions editor at Lippincott Williams & Wilkins; to Helene Caprari, my amazing development editor, who had the vision and helped to make it reality; to Amy Giuffi, who got the word out; to Victoria White, Joan Wendt, and Karin Duffield, who saw it all come together; to Indu Jawwad, who worked with us to produce the finished product; to Tim, Jyoti, Mark, Tracey, Cortney, Bryan, and Kathryn, who continue to thrive and grow and have become the wonderful, supportive people in my life; to the new generation—Vikas, Nisha, Logan, and Jack—who have returned the sunshine and joy of learning to our lives; and lastly to Hayley and Brodie, whose happily wagging tails never fail to bring smiles and help to keep everything in perspective.

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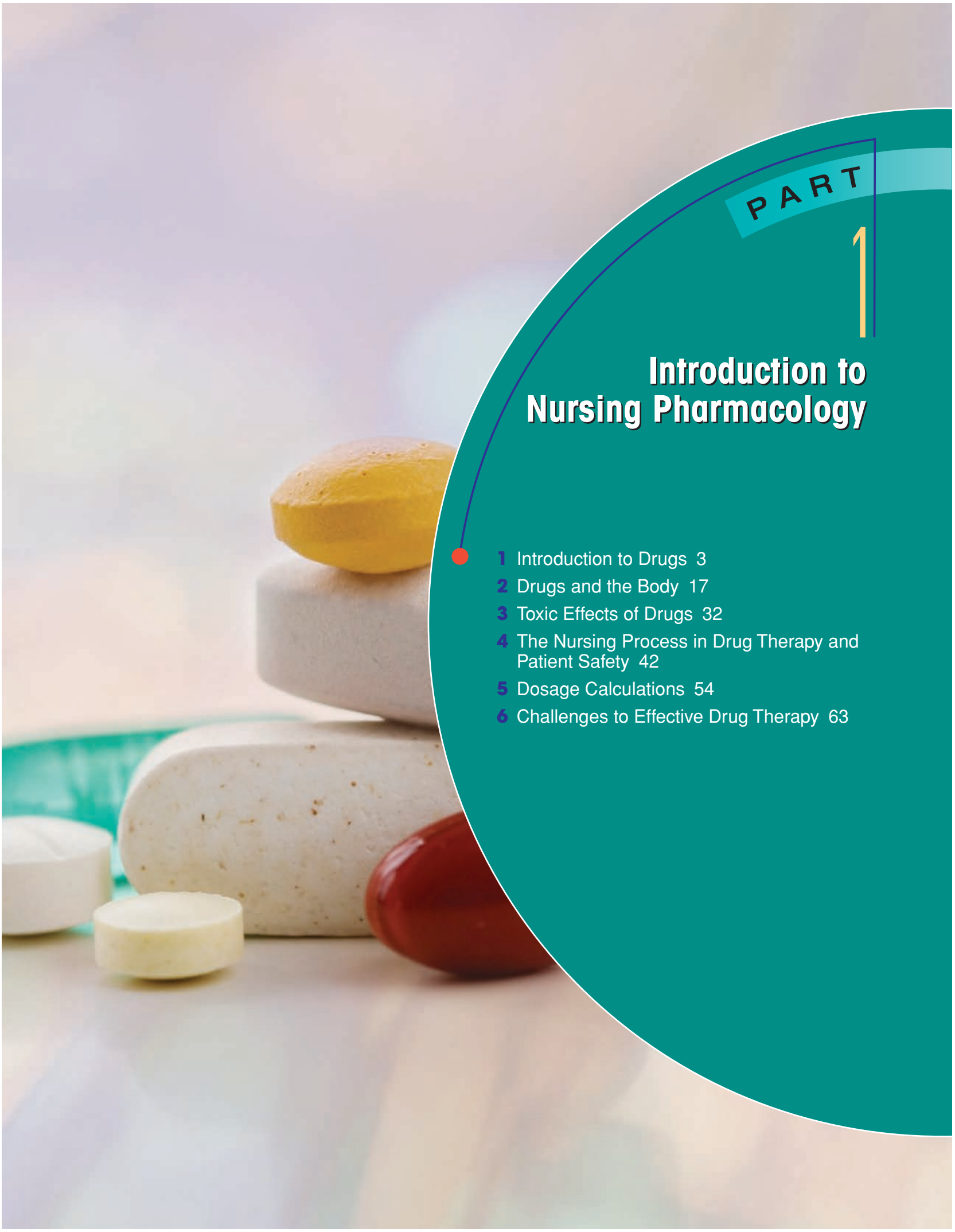

PART 1

Introduction to Nursing Pharmacology

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Introduction to Drugs

1

Learning Objectives

Upon completion of this chapter, you will be able to:

1. Define the word pharmacology.
2. Outline the steps involved in developing and approving a new drug in the United States.
3. Describe the federal controls on drugs that have abuse potential.
4. Differentiate between generic and brand-name drugs, over-the-counter and prescription drugs.
5. Explain the benefits and risks associated with the use of over-the-counter drugs.

Glossary of Key Terms

adverse effects: drug effects that are not the desired therapeutic effects; may be unpleasant or even dangerous
brand name: name given to a drug by the pharmaceutical company that developed it; also called a trade name
chemical name: name that reflects the chemical structure of a drug
drugs: chemicals that are introduced into the body to bring about some sort of change
Food and Drug Administration (FDA): federal agency responsible for the regulation and enforcement of drug evaluation and distribution policies
generic drugs: drugs sold by their chemical name; not brand (or trade) name products
generic name: the original designation that a drug is given when the drug company that developed it applies for the approval process
genetic engineering: process of altering DNA, usually of bacteria, to produce a chemical to be used as a drug
orphan drugs: drugs that have been discovered but would not be profitable for a drug company to develop; usually drugs that would treat only a small number of people; these orphans can be adopted by drug companies to develop
over-the-counter (OTC) drugs: drugs that are available without a prescription for self-treatment of a variety of complaints; deemed to be safe when used as directed
pharmacology: the study of the biological effects of chemicals
pharmacotherapeutics: clinical pharmacology—the branch of pharmacology that deals with drugs; chemicals that are used in medicine for the treatment, prevention, and diagnosis of disease in humans
phase I study: a pilot study of a potential drug done with a small number of selected, healthy human volunteers
phase II study: a clinical study of a proposed drug by selected physicians using actual patients who have the disorder the drug is designed to treat; patients must provide informed consent
phase III study: use of a proposed drug on a wide scale in the clinical setting with patients who have the disease the drug is thought to treat
phase IV study: continual evaluation of a drug after it has been released for marketing
preclinical trials: initial trial of a chemical thought to have therapeutic potential; uses laboratory animals, not human subjects
teratogenic: having adverse effects on the fetus

The human body works through a complicated series of chemical reactions and processes. **Pharmacology** is the study of the biological effects of chemicals. **Drugs** are chemicals that are introduced into the body to cause some sort of change. When drugs are administered, the body begins a sequence of processes designed to handle the new chemicals. These processes, which involve breaking down and eliminating the drugs, in turn affect the body's complex series of chemical reactions. In clinical practice, health care providers focus on how chemicals act on living organisms.

Nurses deal with **pharmacotherapeutics,** or clinical pharmacology, the branch of pharmacology that uses drugs to

treat, prevent, and diagnose disease. Clinical pharmacology addresses two key concerns: the drug's effects on the body, and the body's response to the drug.

For many reasons, understanding how drugs act on the body to cause changes and applying that knowledge in the clinical setting are important aspects of nursing practice. For instance, patients today often follow complicated drug regimens and receive potentially toxic drugs. Many also manage their care at home. A drug can have many effects, and the nurse must know which ones may occur when a particular drug is administered. Some drug effects are therapeutic, or helpful, but others are undesirable or potentially dangerous. These negative effects are called **adverse effects.** (See Chapter 3 for a detailed discussion of adverse effects.)

The nurse is in a unique position regarding drug therapy because nursing responsibilities include the following:

- Administering drugs
- Assessing drug effects
- Intervening to make the drug regimen more tolerable
- Providing patient teaching about drugs and the drug regimen
- Monitoring the overall patient care plan to prevent medication errors

Knowing how drugs work makes these tasks easier to handle, thus enhancing the effectiveness of drug therapy.

This text is designed to provide the pharmacological basis for understanding drug therapy. The physiology of a body system and the related actions of many drugs on that system are presented in a way that allows clear understanding of how drugs work and what to anticipate when giving a particular type of drug.

Thousands of drugs are available for use, and it is impossible to memorize all of the individual differences among drugs in a class. This text addresses *general* drug information. The nurse can refer to *Lippincott's Nursing Drug Guide* (*LNDG*) or to another drug guide to obtain the *specific* details required for safe and effective drug administration. Drug details are changing constantly. The practicing nurse must be knowledgeable about these changes and rely on an up-to-date and comprehensive drug guide in the clinical setting.

A section related to nursing considerations for patients receiving particular drugs will be found in each chapter of this book. This includes assessment points, nursing diagnoses to consider, and implementation or particular interventions that should be considered, and evaluation points will provide a guide for using the nursing process to effectively incorporate drug therapy into patient care. This information can be used to develop an individual nursing care plan for your patient. The monographs in *LNDG* (Table 1.1) can be used to provide the specific information that you need to plan care for each particular drug you might be giving. The various sections of each drug monograph (Figure 1.1) can provide information to help in the development of patient teaching guides and drug cards for reference in the clinical setting. The Patient Drug Sheet: Oral Linezolid (Figure 1.2) is an example of how this information can be used to develop a patient teaching guide.

The CD-ROM in the front this book contains patient teaching guides for all of the drugs found in *LNDG*. The nurse can use this text as a resource for basic concepts of pharmacology and a nursing drug guide as an easy-to-use reference in the clinical setting.

SOURCES OF DRUGS

Drugs are available from varied sources, both natural and synthetic. Natural sources include plants, animals, and inorganic compounds.

Natural Sources

Chemicals that might prove useful as drugs can come from many natural sources, such as plants, animals, or inorganic compounds. To become a drug, a chemical must have a demonstrated therapeutic value or efficacy without severe toxicity or damaging properties.

Plants

Plants and plant parts have been used as medicines since prehistoric times. Even today, plants are an important source of chemicals that are developed into drugs. For example, digitalis products used to treat cardiac disorders and various opiates used for sedation are still derived from plants. Table 1.2 provides examples of drugs derived from plant sources.

Drugs also may be processed using a synthetic version of the active chemical found in a plant. An example of this type of drug is dronabinol (*Marinol*), which contains the active ingredient delta-9-tetrahydrocannabinol found in marijuana. This drug helps to prevent nausea and vomiting in cancer patients but does not have all of the adverse effects that occur when the marijuana leaf is smoked. Marijuana leaf is a controlled substance with high abuse potential and has no legal or accepted medical use. The synthetic version of the active ingredient allows for an accepted form to achieve the desired therapeutic effect in cancer patients.

Ingestion of a plant-derived food can sometimes lead to a drug effect. For instance, the body converts natural licorice to a false aldosterone—a hormone found in the body—resulting in fluid retention and hypokalemia or low serum potassium levels if large amounts of licorice are eaten. However, people seldom think of licorice as a drug.

Finally, plants have become the main component of the growing alternative therapy movement. Chapter 6 discusses the alternative therapy movement and its impact on today's drug regimens.

TABLE 1.1 Sample Nursing Care Plan From *Lippincott's Nursing Drug Guide* for a Patient Receiving Oral Linezolid

ASSESSMENT	NURSING DIAGNOSIS	IMPLEMENTATION	EVALUATION
History (contraindications/cautions) Hypertension Hyperthyroidism Blood dyscrasias Hepatic dysfunction Pheochromocytoma Phenylketonuria Carcinoid syndrome Pregnancy Lactation Known allergy to: linezolid **Medication History** (possible drug–drug interactions) Pseudoephedrine SSRIs MAOIs Antiplatelet drugs **Diet History** (possible drug–food interactions) Foods high in tyramine **Physical Assessment** (screen for contraindications and to establish a baseline for evaluating effects and adverse effects) Local: Culture site of infection CNS: Affect, reflexes, orientation CV: P, BP, peripheral perfusion GI: Bowel sounds, liver evaluation Skin: Color, lesions Hematologic: CBC with differential, liver function tests	Potential for imbalanced nutrition, less than body requirements, related to GI effects Potential for pain related to GI effects, headache Ineffective tissue perfusion related to bone marrow effects Deficient knowledge related to drug therapy	Safe and appropriate administration of drug: Culture infection site to ensure appropriate use of drug Provision of safety and comfort measures: • Monitor BP periodically • Monitor platelet counts before and periodically during therapy • Alleviation of GI upset • Ready access to bathroom facilities • Nutritional consult • Safety provisions if dizziness and CNS effects occur • Avoidance of tyramine-rich foods Patient teaching regarding: Drug Side effects to anticipate Warnings Reactions to report Support and encouragement to cope with disease, high cost of therapy, and side effects Provision of emergency and life-support measures in cases of acute hypersensitivity	Monitor for therapeutic effects of drug: resolution of infection. If resolution does not occur, reculture site. Monitor for adverse effects of drug: • GI upset—nausea, vomiting, diarrhea • Liver function changes • Pseudomembranous colitis • Blood dyscrasias—changes in platelet counts • Fever • Rash • Sweating • Photosensitivity • Acute hypersensitivity reactions Evaluate effectiveness of patient teaching program: patient can name drug, dose of drug, use of drug, adverse effects to expect, reactions to report Evaluate effectiveness of comfort and safety measures Monitor for drug–drug, drug–food interactions as appropriate Evaluate effectiveness of life-support measures if needed

Animal Products

Animal products are used to replace human chemicals that fail to be produced because of disease or genetic problems. Until recently, insulin for treating diabetes was obtained exclusively from the pancreas of cows and pigs. Now **genetic engineering**—the process of altering DNA—permits scientists to produce human insulin by altering *Escherichia coli* bacteria, making insulin a better product without some of the impurities that come with animal products.

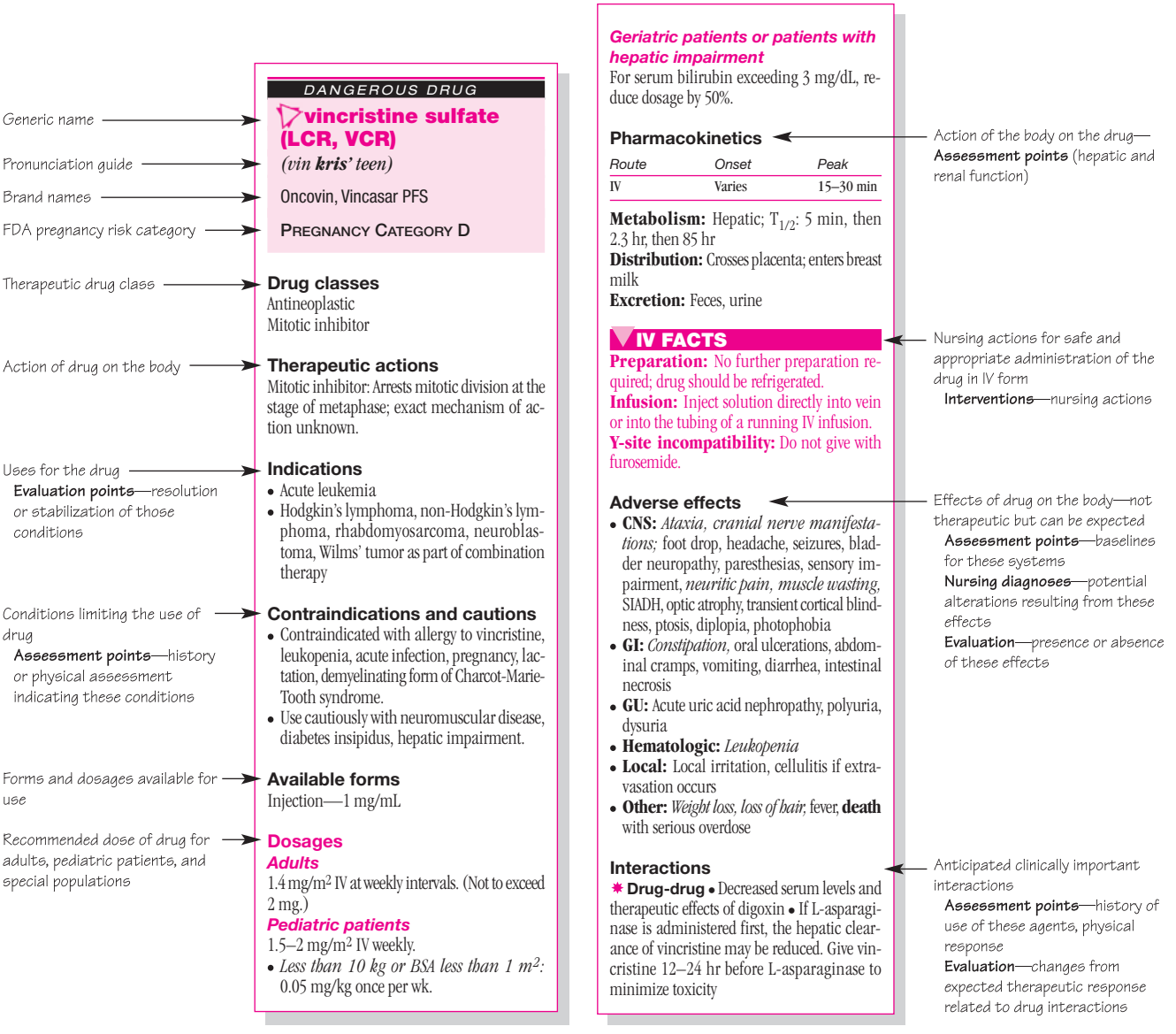
Thyroid drugs and growth hormone preparations also may be obtained from animal thyroid and hypothalamic tissues. Many of these preparations are now created synthetically, however, and the synthetic preparations are considered to be purer and safer than preparations derived from animals.

Inorganic Compounds

Salts of various chemical elements can have therapeutic effects in the human body. Aluminum, fluoride, iron, and even gold are used to treat various conditions. The effects of these elements usually were discovered accidentally when a cause–effect relationship was observed. Table 1.3 shows examples of some elements used for their therapeutic benefit.

Synthetic Sources

Today, many drugs are developed synthetically after chemicals in plants, animals, or the environment have been tested and found to have therapeutic activity. Scientists use genetic engineering to alter bacteria to produce chemicals that are therapeutic and effective. Other technical advances allow scientists to alter a chemical with proven therapeutic effectiveness to make it better. Sometimes, a small change in a chemical's structure can make that chemical more useful as a drug—more potent, more stable, less toxic. These technological advances have led to the development of



● FIGURE 1.1 Example of a drug monograph from *Lippincott's Nursing Drug Guide*.

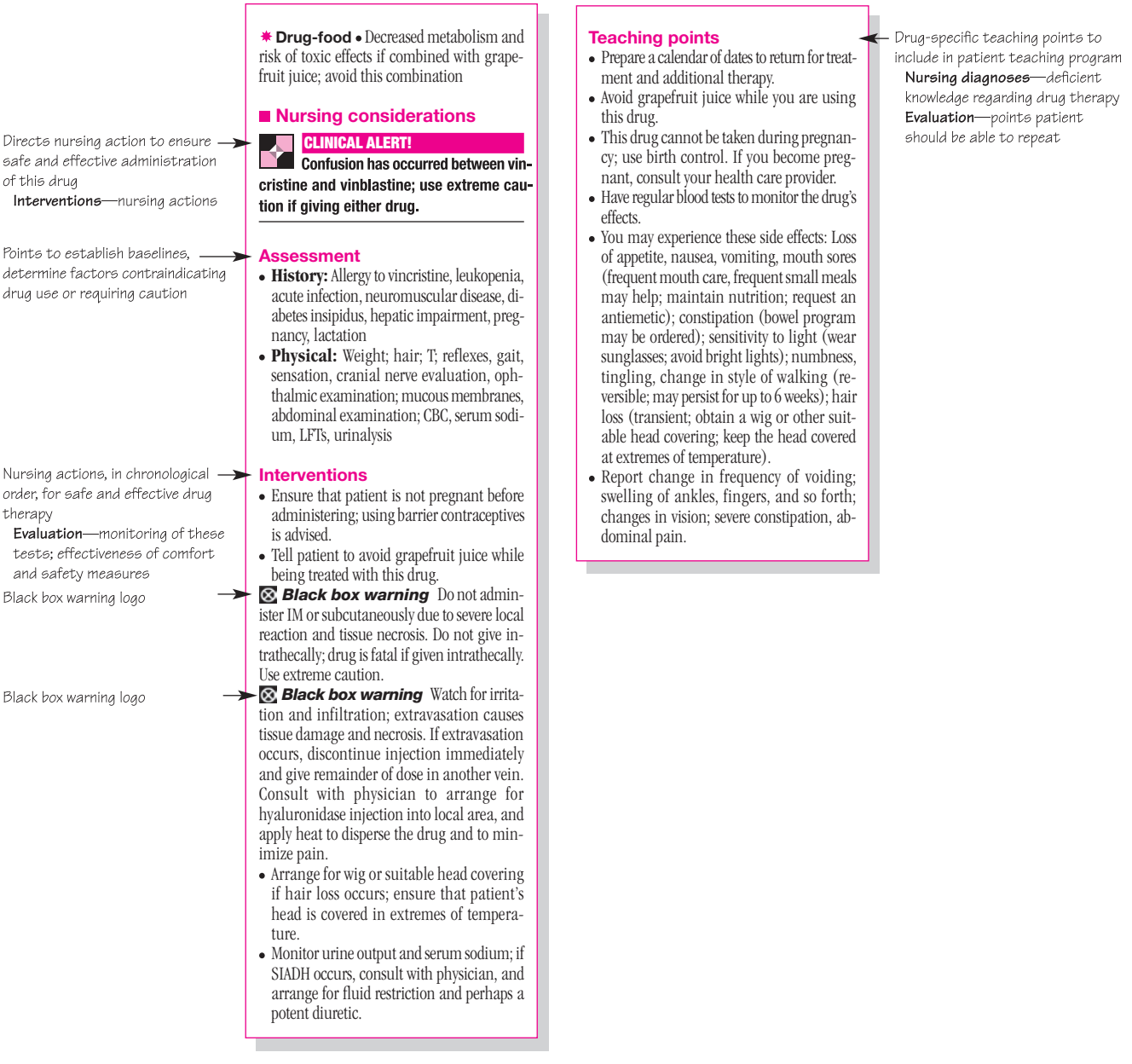
groups of similar drugs, all of which are derived from an original prototype, but each of which has slightly different properties, making a particular drug more desirable in a specific situation. Throughout this book, the icon (P) will be used to designate those drugs of a class that are considered the prototype of the class, the original drug in the class, or the drug that has emerged as the most effective. For example, the cephalosporins are a large group of antibiotics derived from the same chemical structure. Alterations in the chemical rings or attachments to that structure make it possible for some of these drugs to be absorbed orally, whereas others must be given parenterally. Some of these drugs cause severe toxic effects (e.g., renal toxicity), but others do not.

KEY POINTS

- Clinical pharmacology is the study of drugs used to treat, diagnose, or prevent a disease.
- Drugs are chemicals that are introduced into the body and affect the body's chemical processes.
- Drugs can come from plants, foods, animals, salts of inorganic compounds, or synthetic sources.

DRUG EVALUATION

After a chemical that might have therapeutic value is identified, it must undergo a series of scientific tests to evaluate its actual therapeutic and toxic effects. This process is tightly



● FIGURE 1.1 *Continued*

controlled by the U.S. **Food and Drug Administration (FDA),** an agency of the U.S. Department of Health and Human Services that regulates the development and sale of drugs. FDA-regulated tests are designed to ensure the safety and reliability of any drug approved in this country. For every 100,000 chemicals that are identified as being potential drugs, only about 5 end up being marketed. Before receiving final FDA approval to be marketed to the public, drugs must pass through several stages of development. These include preclinical trials and phase I, II, and III studies. The drugs listed in this book have been through rigorous testing and are approved for sale to the public, either with or without a prescription from a health care provider.

Preclinical Trials

In **preclinical trials,** chemicals that may have therapeutic value are tested on laboratory animals for two main purposes: (1) to determine whether they have the presumed effects in living tissue, and (2) to evaluate any adverse effects. Animal testing is important because unique biological differences can cause very different reactions to the chemical. These differences

Patient Drug Sheet: Oral Linezolid

Patient's Name: Mr. Kors
Prescriber's Name: J. Smith, ANP
Phone Number: 555-555-5555

Instructions:

1. The name of your drug is *linezolid*; the brand name is *Zyvox*. This drug is an antibiotic that is being used to treat your *pneumonia*. This drug is very specific in its action and is only indicated for your particular infection. Take the full course of your drug. Do not share this drug with other people or save tablets for future use.
2. The dose of the drug that has been prescribed for you is: *600 mg* (*1 tablet*).
3. The drug should be taken *once every 12 hours*. The best time for you to take this drug will be *8:00 in the morning and 8:00 in the evening*. Do not skip any doses. Do not take two doses at once if you forget a dose. If you miss a dose, take the dose as soon as you remember and then again in 12 hours.
4. The drug can be taken with food if GI upset is a problem. Avoid foods that are rich in tyramine (list is below) while you are taking this drug.
5. The following side effects may occur:
   Nausea, vomiting, abdominal pain (taking the drug with food and eating frequent small meals may help).
   Diarrhea (ensure ready access to bathroom facilities). Notify your health care provider if this becomes severe.
6. Do not take this drug with over-the-counter drugs or herbal remedies without first checking with your health care provider. Many of these agents can cause problems with your drug.
7. Tell any nurse, physician, or dentist who is taking care of you that you are on this drug.
8. Keep this and all medications out of the reach of children.

Notify your health care provider if any of the following occur:
Rash, severe GI problems, bloody or excessive diarrhea, weakness, tremors, increased bleeding or bruising, anxiety.

Foods high in tyramine to avoid: Aged cheeses, avocados, bananas, beer, bologna, caffeinated beverages, chocolate, liver, over-ripe fruit, pepperoni, pickled fish, red wine, salami, smoked fish, yeast, yogurt.

FIGURE 1.2 Example of a patient teaching sheet from *Lippincott's Nursing Drug Guide*.

can be found only in living organisms, so computer-generated models alone are often inadequate.

At the end of the preclinical trials, some chemicals are discarded for the following reasons:

- The chemical lacks therapeutic activity when used with living animals.

TABLE 1.2 Drugs Derived From Plants

PLANT	PRODUCT
Ricinus communis	Seed
	Oil
	Castor oil (*Neolid*)
Digitalis purpurea (foxglove plant)	Leaves
	Dried leaves
	Digitalis leaf
Papaver somniferum (poppy plant)	Unripe capsule
	Juice
	Opium (paregoric)
	Morphine (*Roxanol*)
	Codeine
	Papaverine (*Pavabid*)

TABLE 1.3 Elements Used for Their Therapeutic Effects

ELEMENT	THERAPEUTIC USE
Aluminum	Antacid to decrease gastric acidity
	Management of hyperphosphatemia
	Prevention of the formation of phosphate urinary stones
Fluorine (as fluoride)	Prevention of dental cavities
	Prevention of osteoporosis
Gold	Treatment of rheumatoid arthritis
Iron	Treatment of iron deficiency anemia

- The chemical is too toxic to living animals to be worth the risk of developing into a drug.
- The chemical is highly **teratogenic** (causing adverse effects to the fetus).
- The safety margins are so small that the chemical would not be useful in the clinical setting.

Some chemicals, however, are found to have therapeutic effects and reasonable safety margins. This means that the chemicals are therapeutic at doses that are reasonably different from doses that cause toxic effects. Such chemicals will pass the preclinical trials and advance to phase I studies.

Phase I Studies

A **phase I study** uses human volunteers to test the drugs. These studies are more tightly controlled than preclinical trials and are performed by specially trained clinical investigators. The volunteers are fully informed of possible risks and may be paid for their participation. Usually, the volunteers are healthy, young men. Women are not good candidates for phase I studies because the chemicals may exert unknown and harmful effects on a woman's ova, and too much risk is involved in taking a drug that might destroy or alter the ova. Women do not make new ova after birth. Men produce sperm daily, so there is less potential for complete destruction or alteration of the sperm.

Some chemicals are therapeutic in other animals but have no effects in humans. Investigators in phase I studies scrutinize the drugs being tested for effects in humans. They also look for adverse effects and toxicity. At the end of phase I studies, many chemicals are dropped from the process for the following reasons:

- They lack therapeutic effect in humans.
- They cause unacceptable adverse effects.
- They are highly teratogenic.
- They are too toxic.

Some chemicals move to the next stage of testing despite undesirable effects. For example, the antihypertensive drug minoxidil (*Loniten*) was found to effectively treat malignant hypertension, but it caused unusual hair growth on the palms and other body areas. However, because it was so much more

effective for treating malignant hypertension at the time of its development than any other antihypertensive drug, it proceeded to phase II studies. (Now, its hair-growing effect has been channeled for therapeutic use into various hair-growth preparations such as *Rogaine*.)

Phase II Studies

A **phase II study** allows clinical investigators to try out the drug in patients who have the disease that the drug is designed to treat. Patients are told about the possible benefits of the drug and are invited to participate in the study. Those who consent to participate are fully informed about possible risks and are monitored very closely, often at no charge to them, to evaluate the drug's effects. Usually, phase II studies are performed at various sites across the country—in hospitals, clinics, and doctors' offices—and are monitored by representatives of the pharmaceutical company studying the drug. At the end of phase II studies, a drug may be removed from further investigation for the following reasons:

- It is less effective than anticipated.
- It is too toxic when used with patients.
- It produces unacceptable adverse effects.
- It has a low benefit-to-risk ratio, meaning that the therapeutic benefit it provides does not outweigh the risk of potential adverse effects that it causes.
- It is no more effective than other drugs already on the market, making the cost of continued research and production less attractive to the drug company.

A drug that continues to show promise as a therapeutic agent receives additional scrutiny in phase III studies.

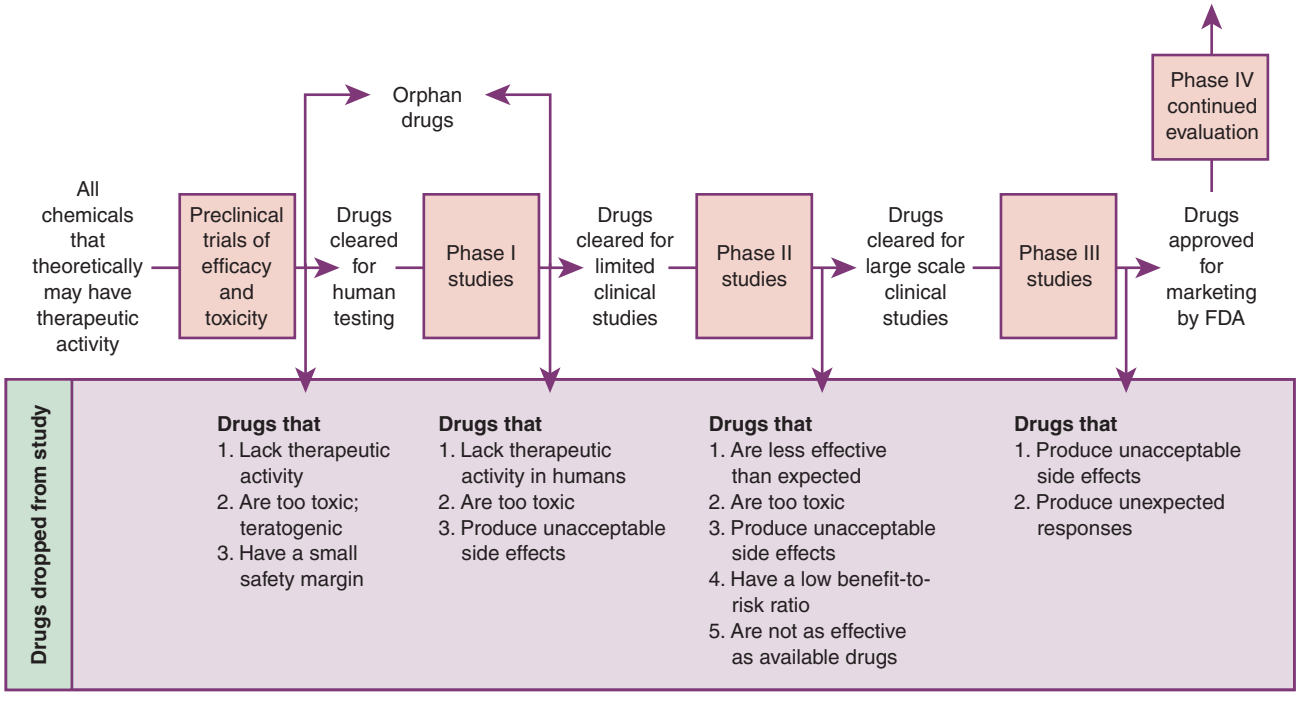
Phase III Studies

A **phase III study** involves use of the drug in a vast clinical market. Prescribers are informed of all the known reactions to the drug and precautions required for its safe use. Prescribers observe patients very closely, monitoring them for any adverse effects. Sometimes, prescribers ask patients to keep journals and record any symptoms they experience. Prescribers then evaluate the reported effects to determine whether they are caused by the disease or by the drug. This information is collected by the drug company that is developing the drug and is shared with the FDA. When a drug is used widely, totally unexpected responses may occur. A drug that produces unacceptable adverse effects or unforeseen reactions is usually removed from further study by the drug company. In some cases, the FDA may have to request that a drug be removed from the market.

Food and Drug Administration Approval

Drugs that finish phase III studies are evaluated by the FDA, which relies on committees of experts familiar with the specialty area in which the drugs will be used. Only those drugs that receive FDA committee approval may be marketed. Figure 1.3 recaps the various phases of drug development discussed.

An approved drug is given a **brand name** (trade name) by the pharmaceutical company that developed it. The **generic name** of a drug is the original designation that the drug was given when the drug company applied for the approval process. **Chemical names** are names that reflect the chemical structure of a drug. Some drugs are known by all three names. It can be confusing to study drugs when so many different



● FIGURE 1.3 Phases of drug development.

TABLE 1.4 Comparison of Generic, Chemical, and Brand Names of Drugs

levothyroxine sodium	←	**generic name**	→	colfosceril palmitate
L-thyroxine, T_4	←	**chemical name**	→	dipalmitoylphosphatidylcholine
Eltroxin, Levothroid, Synthroid	←	**brand names**	→	*Exosurf Neonatal*

names are used for the same compound. In this text, the generic and chemical names always appear in straight print, and the brand name is always italicized (e.g., minoxidil [*Rogaine*]). Table 1.4 compares examples of drug names.

The entire drug development and approval process can take 5 to 6 years, resulting in a so-called drug lag in the United States. In some instances, a drug that is available in another country may not become available here for years. The FDA regards public safety as primary in drug approval, so the process remains strict; however, it can be accelerated in certain instances involving the treatment of deadly diseases. For example, some drugs (e.g., delavirdine [*Rescriptor*] and efavirenz [*Sustiva*]) that were thought to offer a benefit to patients with acquired immune deficiency syndrome (AIDS), a potentially fatal immune disorder, were pushed through because of the progressive nature of AIDS and the lack of a cure. All literature associated with these drugs indicates that long-term effects and other information about the drug may not yet be known.

In addition to the drug lag issue, there also are concerns about the high cost of drug approval. In 2004, *Fortune* magazine did a study that found that the estimated cost of taking a chemical from discovery to marketing as a drug was about $802 million. Because of this kind of financial investment, pharmaceutical companies are unwilling to risk approval of a drug that might cause serious problems and prompt lawsuits.

Phase IV Studies

After a drug is approved for marketing, it enters a phase of continual evaluation, or **phase IV study.** Prescribers are obligated to report to the FDA any untoward or unexpected adverse effects associated with drugs they are using, and the FDA continually evaluates this information. Some drugs cause unexpected effects that are not seen until wide distribution occurs. Sometimes, those effects are therapeutic. For example, patients taking the antiparkinsonism drug amantadine (*Symmetrel*) were found to have fewer cases of influenza than other patients, leading to the discovery that amantadine is an effective antiviral agent.

In other instances, the unexpected effects are dangerous. In 1997, the diet drug dexfenfluramine (*Redux*) was removed from the market only months after its release because patients taking it developed serious heart problems In 2004, the drug company Merck withdrew its cyclooxygenase-2 (Cox-2) specific nonsteroidal anti-inflammatory drug rofecoxib (*Vioxx*) from the market when postmarketing studies seemed to show a significant increase in cardiovascular mortality in patients who were taking the drug. These problems were not seen in any of the premarketing studies of the drug. The effects were only seen with a much wider use of the drug after it had been marketed.

KEY POINTS

- The FDA carefully regulates the testing and approval of all drugs in this country.
- To be approved for marketing, a drug must pass through animal testing, testing on healthy humans, selected testing on people with the disease being treated, and then broad testing on people with the disease being treated.

LEGAL REGULATION OF DRUGS

The FDA regulates the development and sale of drugs. Local laws further regulate the distribution and administration of drugs. In most cases, the strictest law is the one that prevails. Nurses should become familiar with the rules and regulations in the area in which they practice. These regulations can vary from state to state, and even within a state.

Over the years, the FDA has become more powerful, usually in response to a drug disaster affecting many people. In the 1930s, the drug "elixir of sulfanilamide" was distributed in a vehicle of ethylene glycol that had never been tested in humans. It turned out that ethylene glycol is toxic to humans, and hundreds of people died and many others became very ill. This led to the Federal Food, Drug and Cosmetic Act of 1938, which gave the FDA power to enforce standards for testing drug toxicity and monitoring labeling.

In the 1960s, the drug thalidomide (*Thalomid*) was used as a sleeping aid by pregnant women, resulting in the birth of many babies with limb deformities. The public outcry resulted in the Kefauver-Harris Act of 1962, which gave the FDA regulatory control over the testing and evaluating of drugs and set standards for efficacy and safety.

Other laws have given the FDA control over monitoring of potentially addictive drugs and responsibility for monitoring, to some extent, the sale of drugs that are available without prescription. Table 1.5 provides a summary of these laws.

Safety During Pregnancy

As part of the standards for testing and safety, the FDA requires that each new drug be assigned to a pregnancy category (Box 1.1). The categories indicate a drug's potential or actual teratogenic effects, thus offering guidelines for use of

TABLE 1.5 Federal Legislation Affecting the Clinical Use of Drugs

YEAR ENACTED	LAW	IMPACT
1906	Pure Food and Drug Act	Prevented the marketing of adulterated drugs; required labeling to eliminate false or misleading claims
1938	Federal Food, Drug and Cosmetic Act	Mandated tests for drug toxicity and provided means for recall of drugs; established procedures for introducing new drugs; gave FDA the power of enforcement
1951	Durham-Humphrey Amendment	Tightened control of certain drugs; specified drugs to be labeled "may not be distributed without a prescription"
1962	Kefauver-Harris Act	Tightened control over the quality of drugs; gave FDA regulatory power over the procedure of drug investigations; stated that efficacy as well as safety of drugs had to be established
1970	Controlled Substances Act	Defined drug abuse and classified drugs as to their potential for abuse; provided strict controls over the distribution, storage, and use of these drugs
1983	Orphan Drug Act	Provided incentives for the development of orphan drugs for treatment of rare diseases

BOX 1.1 FDA Pregnancy Categories

The Food and Drug Administration (FDA) has established five categories to indicate the potential for a systemically absorbed drug to cause birth defects. The key differentiation among the categories rests on the degree (reliability) of documentation and the risk–benefit ratio.

Category A: Adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy, and there is no evidence of risk in later trimesters.

Category B: Animal studies have not demonstrated a risk to the fetus but there are no adequate studies in pregnant women, *or* animal studies have shown an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus during the first trimester of pregnancy, and there is no evidence of risk in later trimesters.

Category C: Animal studies have shown an adverse effect on the fetus but there are no adequate studies in humans; the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks, *or* there are no animal reproduction studies and no adequate studies in humans.

Category D: There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.

Category X: Studies in animals or humans demonstrate fetal abnormalities or adverse reaction; reports indicate evidence of fetal risk. The risk of use in a pregnant woman clearly outweighs any possible benefit.

Regardless of the designated Pregnancy Category or presumed safety, *no* drug should be administered during pregnancy unless it is clearly needed.

that particular drug in pregnancy. Research into the development of the human fetus, especially the nervous system, has led many health care providers to recommend that no drug should be used during pregnancy because of potential effects on the developing fetus. In cases in which a drug is needed, it is recommended that the drug of choice be one for which the benefit outweighs the potential risk.

Controlled Substances

The Controlled Substances Act of 1970 established categories for ranking of the abuse potential of various drugs. This same act gave control over the coding of drugs and the enforcement of these codes to the FDA and the Drug Enforcement Agency (DEA), a part of the U.S. Department of Justice. The FDA studies the drugs and determines their abuse potential; the DEA enforces their control. Drugs with abuse potential are called *controlled substances*. Box 1.2 contains descriptions of each category, or schedule.

The prescription, distribution, storage, and use of these drugs are closely monitored by the DEA in an attempt to decrease substance abuse of prescribed medications. Each prescriber has a DEA number, which allows the DEA to monitor prescription patterns and possible abuse. A nurse should be familiar with not only the DEA guidelines for controlled substances, but also the local policies and procedures, which might be even more rigorous.

Generic Drugs

When a drug receives approval for marketing from the FDA, the drug formula is given a time-limited patent, in much the same way as an invention is patented. The length of time for which the patent is good depends on the type of chemical involved. When the patent runs out on a brand-name drug, the drug can be produced by other manufacturers. **Generic drugs** are chemicals that are produced by companies involved solely in the manufacturing of drugs. Because they do not have the research, the advertising, or, sometimes, the quality control departments that pharmaceutical companies have, they can produce the generic drugs more cheaply. In the past, some quality-control problems were found with generic products. For example, the binders used in a generic drug might not be the same as those used in the brand-name product. As a result, the way the body breaks down and uses the generic drug may differ from that of the brand-name product. In that case, the bioavailability of the drug is different from that of the brand-name product.