2. Antacids, antibiotics, antihypertensives, diuretics, and laxatives are examples of drugs that are categorized by which factor?
   1. Nonprescription status
   2. Body system
   3. Chemical action
   4. Clinical indication

3. During which stage of the process of new drug development does testing on humans occur?
   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

4. 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 statement(s)? *(Select all that apply.)*
   1. "One of the two names is the trade name of the drug, and the other is the generic name."
   2. "When drugs are developed, the company that discovered the drug first gets to name it. After a period of time, the drug can be produced by other companies, and it then gets a generic name."
   3. "Lopressor is the generic name, and metoprolol is the brand name."
   4. "Generally, the generic form of the drug is cheaper."
   5. "The two names are used to determine whether the drug is a Schedule III drug or a Schedule V drug."

5. Which electronic database(s) provide(s) drug information for health care providers? *(Select all that apply.)*
   1. Lexi-Comp
   2. CINAHL
   3. Medline
   4. DailyMed
   5. Health on the Net

6. A nurse was teaching a patient from Canada the names of her medications and reviewed the differences between Canadian names. Which statement indicates 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 name and the brand name are the only names used in Canada."

chapter

2

Basic Principles of Drug Action and Drug Interactions

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Objectives

1. Identify common drug administration routes.
2. Explain the potential problems associated with drug absorption.
3. Describe nursing interventions that can enhance drug absorption.
4. Describe the mechanisms of drug distribution.
5. Describe how the body inactivates drugs.
6. Identify the meaning and significance of the term *half-life* when it is used in relation to drug therapy.

Key Terms

receptors (rē-SĔP-tĕrz) (p. 12)
pharmacodynamics (făr-mă-kō-dī-NĂM-īks) (p. 12)
agonists (ĂG-ō-nĭsts) (p. 12)
antagonists (ăn-TĂG-ō-nĭsts) (p. 12)
partial agonists (PĂR-shŭl ĂG-ō-nĭsts) (p. 12)
enteral (ĔN-tĕr-ăl) (p. 12)
parenteral (pă-RĔN-tĕr-ăl) (p. 12)
percutaneous (pĕr-kū-TĀ-nē-ŭs) (p. 12)
pharmacokinetics (făr-mă-kō-kĭ-NĔT-īks) (p. 13)
absorption (ăb-sŏrp-shŭn) (p. 13)
distribution (dis-trib-byü-shan) (p. 13)
drug blood level (p. 14)
metabolism (mĕ-TĂ-bō-lĭ-sm) (p. 14)
excretion (ĕks-KRĒ-shŭn) (p. 14)
half-life (p. 14)

BASIC PRINCIPLES RELATED TO DRUG THERAPY

DRUG RESPONSES IN THE BODY

Drugs do not create new responses but rather alter existing physiologic activity. 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 with the baseline data by the physician, the nurse, and the pharmacist to evaluate the effectiveness of the drug therapy.

DRUG INTERACTIONS IN THE BODY

Drugs interact with the body 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 (Figure 2-1, *A*). 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* (Figure 2-1, *B*). Drugs that attach to a receptor but do not stimulate a response are called *antagonists* (Figure 2-1, *C*). Drugs that interact with a receptor to stimulate a response but inhibit other responses are called *partial agonists* (Figure 2-1, *D*).

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, intramuscular, or intravenous injection. The **percutaneous** route involves drugs being absorbed through the skin and mucus 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: liberation, *a*bsorption, *d*istribution, *m*etabolism, and *e*xcretion (ADME). After liberation from the dosage form, each drug has its own unique ADME characteristics. The study of

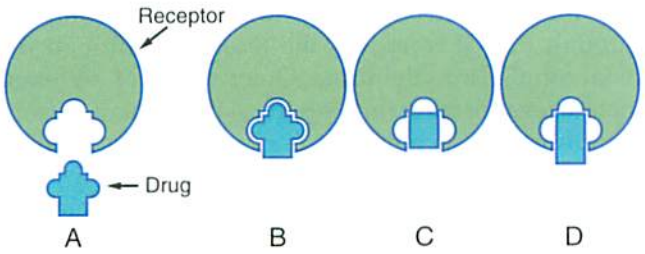


FIGURE 2-1 **A,** Drugs act by forming chemical bonds with specific receptor sites, similar to a key and lock. **B,** The better the fit, the better the response. Drugs with complete attachment and response are called *agonists*. **C,** Drugs that attach but that do not elicit a response are called *antagonists*. **D,** Drugs that attach and elicit a small response but that also block other responses are called *partial agonists*.

the mathematic 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-oz] 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. Subcutaneous (subcut) injections have the slowest absorption rate, especially if peripheral circulation is impaired. Intramuscular (IM) injections are more rapidly absorbed because of greater blood flow per unit weight of muscle as compared with subcutaneous 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 intravenous (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 drugs are 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. An 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.

Figure 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.

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

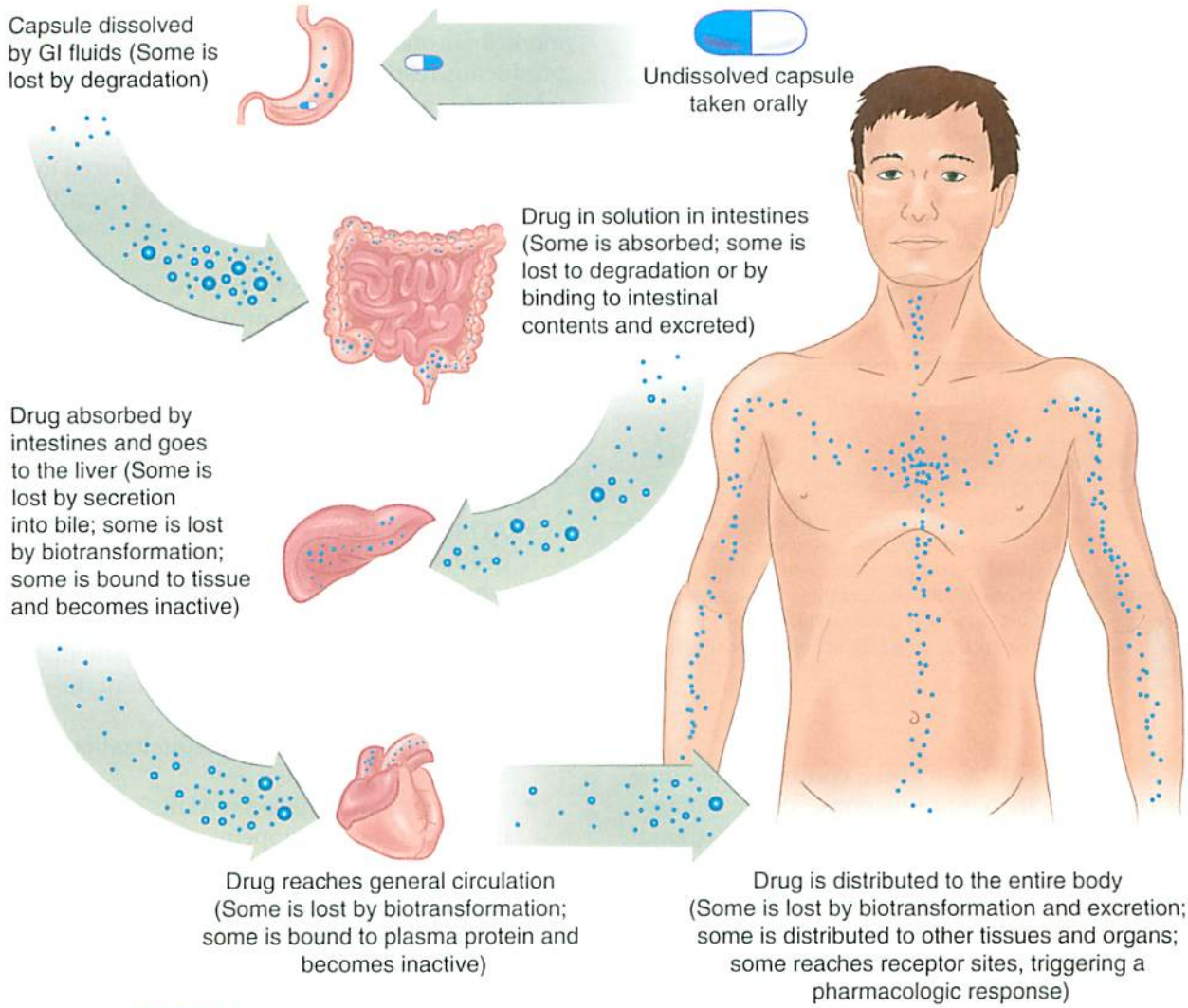


FIGURE 2-2 Factors that modify the quantity of drug that reaches a site of action after a single oral dose.

data reflect impairment of either function, the nurse should notify the physician.

DRUG ACTIONS

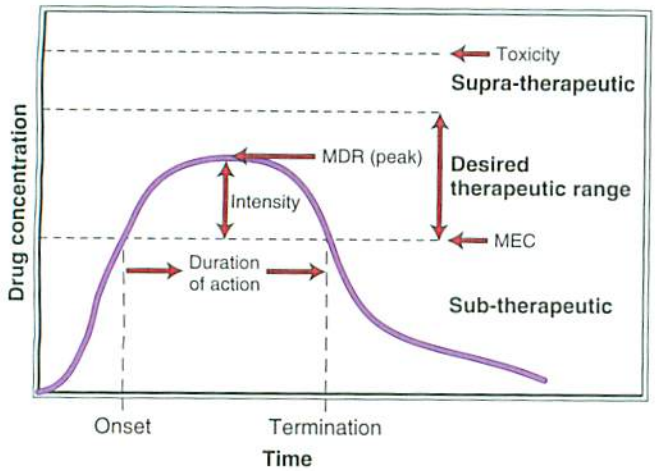
Objectives

7. Compare and contrast the following terms that are used in relationship to medications: *desired action, side effects, adverse effects, allergic reactions,* and *idiosyncratic reactions.*
8. Identify what drug interactions are, and give an example.

Key Terms

onset of action (p. 15)
peak action (p. 15)
duration of action (p. 15)
desired action (p. 16)
side effects (p. 16)
adverse effects (ĂD-vŭrs ĕf-FĔCTS) (p. 16)
toxicity (tŏk-SĬS-ĭ-tē) (p. 16)
idiosyncratic reaction (ĭd-ē-ō-sĭn-KRĂT-ĭk rē-ĂK-shŭn) (p. 17)
allergic reactions (ă-LŬR-jĭk) (p. 17)

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, the rate 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,



MEC = Minimum effective concentration
MDR = Maximum drug response (peak effect)

FIGURE 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, 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.

which is also known as a drug concentration–time profile (Figure 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. (See Appendix C for therapeutic blood levels for selected medicines.)

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*, which are mild, or *adverse effects*, which can be less severe but usually less common. When adverse effects are severe, the reaction is sometimes referred to as *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 7.)

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 anti-inflammatory agents.
- Among the 1.6 million residents of nursing homes in the United States, drug-related injuries are estimated to occur at a rate of 350,000 events per year, and more than half may be preventable. There may be as many as 20,000 life-threatening or fatal ADEs per year among nursing-home residents; of these, 80% may be preventable.

Most adverse drug effects 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 Unit III 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, physician, 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 (Hines et al, 2011).

All hospitals have internal mechanisms for reporting suspected ADRs, and health professionals 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 U.S. Food and Drug Administration's MedWatch program is also available for the voluntary reporting of adverse events. (For more information, see Appendix E.)

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. Upon re-exposure 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 his or her next exposure to the drug. Patients should receive information about the drug name and be instructed to tell health care practitioners 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

Objectives

9. Differentiate among the terms *additive effect, synergistic effect, antagonistic effect, displacement, interference,* and *incompatibility.*
10. Explain how a bound drug becomes unbound.
11. Identify one way in which alterations in metabolism create drug interactions.

Key Terms

drug interaction (p. 17)
unbound drug (ŭn-BOWND) (p. 18)
additive effect (ĂD-ĭ-tĭv) (p. 18)
synergistic effect (sĭn-ĕr-JĬS-tĭk) (p. 18)
antagonistic effect (ăn-tăg-ŏ-NĬST-ĭk) (p. 18)
displacement (dĭs-PLĀS-mĕnt) (p. 18)
interference (ĭn-tŭr-FĒR-ĕns) (p. 18)
incompatibility (ĭn-kŏm-păt-ĭ-BĬL-ĭ-tē) (p. 18)

A **drug interaction** is said to occur when the action of one drug is altered 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 of the 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 alter the absorption, distribution, metabolism, or excretion of a drug and those that enhance the pharmacologic effect of a drug.

ALTERATION OF ABSORPTION

Most drug interactions that alter 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.

ALTERATION OF DISTRIBUTION

Drug interactions that cause an alteration 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 the 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 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.

ALTERATION OF METABOLISM

Drug interactions usually result from an alteration 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, chloramphenicol, 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 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 an enzyme that increases its metabolism of the drug (enzyme inducers) are phenobarbital, carbamazepine, rifampin, and phenytoin. Rapidly metabolized drugs include disopyramide, doxycycline, griseofulvin, warfarin, metronidazole, mexiletine, quinidine, theophylline, and verapamil. When administered with enzyme inducers, the dosage of the more rapidly metabolized drug should generally be increased to provide therapeutic activity. The patient must be monitored closely for adverse effects, especially if the enzyme inducer is discontinued. The metabolism of the induced drug decelerates, thus leading to accumulation and toxicity if the dosage is not reduced. For example, if a woman who is taking oral contraceptives (e.g., Ortho-Novum [norethindrone, ethinyl estradiol], Lo/Ovral [ethinyl estradiol, norgestrel]) 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

Table 2-1 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

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.

ALTERATION OF EXCRETION

Drugs that interact by altering excretion usually act in the kidney tubules by altering the pH to enhance or inhibit excretion. The classic example of altered urine pH is with 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 with drugs that enhance the physiologic effects of other drugs (e.g., those that cause central nervous system depression, such as sedative-hypnotic agents and alcohol) or the potentiation of neuromuscular blockade between an aminoglycoside antibiotic and a neuromuscular blocking agent such as pancuronium. Table 2-1 defines 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.

Get Ready for the NCLEX® Examination!

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 to master this chapter's content.

evolve Go to your Evolve Web site (http://evolve.elsevier.com/Clayton) for the following FREE learning resources:

- Animations
- Appendices
- Drug dosage calculators
- Drugs@FDA (a catalog of FDA-approved drug products)
- Gold Standard Patient Teaching Handouts in English and Spanish
- Interactive Drug Flashcards
- Interactive Review Questions for the NCLEX® Examination and more!

Review Questions for the NCLEX® Examination

1. 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%)

2. What is the portion of a drug that is pharmacologically active called?
   1. Protein-bound drug
   2. Unbound drug
   3. Drug tolerance level
   4. Incompatibility factor

3. A person 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 his or her thyroid function levels

4. Drugs that are injected under the skin into the subcutaneous tissue are considered to be delivered by which route?
   1. Enteral
   2. Parenteral
   3. Percutaneous
   4. Inhalation

5. If the patient has been prescribed two drugs that have resulted in an increased effect of one drug. What is this called?
   1. Synergistic effect
   2. Antagonistic effect
   3. Idiosyncratic effect
   4. Displacement

6. The patient has received an insulin injection. During which phase does the nurse expect the action of the drug to be greatest?
   1. Onset
   2. Duration
   3. Peak
   4. Liberation

chapter 3

Drug Action Across the Life Span

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Objectives

1. Explain the impact of the placebo effect and nocebo effect.
2. Identify the importance of drug dependence and drug accumulation.
3. Discuss the effects of age on drug absorption, distribution, metabolism, and excretion.
4. Explain the gender-specific considerations of drug absorption, distribution, metabolism, and excretion.
5. List the definitions of the use-in-pregnancy categories A, B, C, D, and X.
6. Discuss the impact of pregnancy and breastfeeding on drug absorption, distribution, metabolism, and excretion.
7. Discuss the role of genetics and its influence on drug action.

Key Terms

gender-specific medicine (JĔN-dŭr spĕ-SĬ-fĭk) (p. 21)
placebo effect (plă-SĒ-bō ĕf-FĔKT) (p. 21)
nocebo effect (nō-SĒ-bō) (p. 21)
placebo (plă-SĒ-bō) (p. 21)
tolerance (TŎL-ŭr-ŭns) (p. 21)
drug dependence (dē-PĒN-dĕns) (p. 22)
drug accumulation (ă-kyū-myū-LĀ-shŭn) (p. 22)
carcinogenicity (kăr-sĭn-ō-jĕn-ĬS-ĭ-tē) (p. 22)
passive diffusion (PĂ-sĭv dĭ-FYŪ-shŭn) (p. 22)
hydrolysis (hī-DRŎ-lĭ-sĭs) (p. 23)
intestinal transit (ĭn-TĔS-tĭ-năl TRĂN-sĭt) (p. 23)
protein binding (PRŌ-tēn BĪN-dĭng) (p. 24)
drug metabolism (mĕ-TĂ-bō-lĭ-sm) (p. 24)
metabolites (mĕ-TĂB-ō-līts) (p. 24)
therapeutic drug monitoring (thĕr-ă-PYŪ-tĭk) (p. 25)
polypharmacy (pŏl-e-FĂR-mă-sē) (p. 28)
teratogens (tĕr-ĂT-ō-jĕnz) (p. 30)
genetics (jĭ-NĔT-ĭks) (p. 32)
genome (JĒ-nōm) (p. 32)
polymorphisms (pŏl-ē-MŎR-fĭz-ĭmz) (p. 32)
pharmacogenetics (făr-mă-k-ō-jĭ-NĔT-ĭks) (p. 32)

FACTORS THAT AFFECT DRUG THERAPY

Patients often say the following: "That drug really knocked me out!" or "That drug didn't touch the pain!" The effects of drugs are unexpectedly potent in some patients, whereas other patients show little response at the same dosage. In addition, some patients react differently to the same dosage of a drug that is administered at different times. Because of individual patient variation, exact responses to drug therapy are difficult to predict. The following factors have been identified as contributors to a variable response to drugs.

AGE

Infants and the very old tend to be the most sensitive to the effects of drugs. There are important differences with regard to the absorption, distribution, metabolism, and excretion of drugs in premature neonates, full-term newborns, and children. The aging process brings about changes in body composition and organ function that can affect the older patient's response to drug therapy. The age of the patient can have a significant impact on drug therapy. When discussing the effect of age on drug therapy, it is helpful to subdivide the population into the following categories:

Age	*Stage*
<38 wk gestation	Premature
0-1 mo	Newborn, neonate
1-24 mo	Infant, toddler
3-5 yr	Young child
6-12 yr	Older child
13-18 yr	Adolescent
19-54 yr	Adult
55-64 yr	Older adult
65-74 yr	Elderly
75-84 yr	The aged
85 yr or older	The very old

BODY WEIGHT

Considerably overweight patients may require an increase in dosage to attain the same therapeutic response as the general population. Conversely, patients who are underweight as compared with the general population tend to require lower dosages for the same therapeutic response. It is extremely important to obtain accurate heights and weights of patients, because the dosage of medicine may be calculated with the use of these parameters.

Most pediatric dosages are calculated by milligrams of drug per kilogram (mg/kg) of body weight to adjust for growth rate. The dosages of other medicines,