The term pharmacology is derived from the Greek words “pharmakon,” meaning drugs, and “logos,” meaning science. Pharmacology dates back to ancient times when man used plants and roots to treat ailments. In more recent times, the United States Congress has passed regulations that require drug manufacturers to study and prove drugs are safe and effective before being approved, prescribed, and sold to the public.

Even with these studies, no drugs are perfectly safe. Although all drugs produce different side effects, the objective of drug therapy is to provide maximum benefits with minimal harm. Pharmacology concepts are used routinely in nursing practice (see Table 1). These concepts may be as simple as drug names and side effects, or as complex as pharmacokinetics or pharmacodynamics. This article will provide a practical review of pharmacokinetic and pharmacodynamic concepts.

Pharmacokinetics

Pharmacokinetic concepts come into play once a drug enters the body. They include the phases of absorption, distribution, metabolism, and excretion (Lilley, Harrington, & Snyder, 2007).

Absorption

Absorption is an important phase of pharmacokinetics and includes three aspects: 1) routes of administration, 2) methods of absorption, and 3) factors that affect the absorption process (Lilley et al., 2007). Routes of administration can be divided into three categories: enteral, parenteral, and other (non-enteral or parenteral) routes. The enteral route includes any route using the gastrointestinal tract – oral, sublingual, buccal, and rectal. The parenteral route entails intravenous, intramuscular, and subcutaneous administrations. The other route consists of inhalation, topical, transdermal, intranasal, intrathecal, intraventricular, and opthalmic (Lilley et al., 2007).

The three most common methods of absorption are passive absorption, active absorption, and pinocytosis. Passive absorption is also known as passive or simple diffusion. It is dependent on a concentration gradient and is...
Table 1. Definitions of Pharmacology Concepts

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>Absorption</td>
<td>The uptake of substance by a tissue, such as nutrients, though the wall of the gastrointestinal tract.</td>
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<td>Agonist</td>
<td>A drug or other chemical that can combine with a receptor on a cell to produce a physiologic reaction typical of a naturally occurring substance.</td>
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<td>Antagonist</td>
<td>A drug that counteracts the effect of another drug.</td>
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<td>Bioavailability</td>
<td>The fraction of an administered dose that reaches the systemic circulation.</td>
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<td>Clearance</td>
<td>A measure of how well a patient can metabolize or eliminate a drug per unit time.</td>
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<td>Creatinine clearance</td>
<td>A measure of the kidneys’ ability to eliminate creatinine from the body.</td>
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<td>Effective dose (ED50)</td>
<td>The dose required to produce a specific therapeutic response in 50% of the patients.</td>
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<tr>
<td>First-Pass</td>
<td>Drug removed from the blood or plasma following absorption from the gastrointestinal tract before reaching the systemic circulation.</td>
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<td>Glomerular filtration rate (GFR)</td>
<td>The volume of water filtered out of the plasma though glomerular capillary walls into Bowman's capsules per unit of time.</td>
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<td>Half-life</td>
<td>The time required for the plasma concentration to be reduced to one-half of the original value.</td>
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<tr>
<td>Lethal dose (LD50)</td>
<td>A dose that will produce a lethal toxicity in 50% of studied group. Data obtained from TD50.</td>
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<tr>
<td>Partial agonist</td>
<td>A drug that produces a weaker or less efficient response than an agonist.</td>
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<tr>
<td>Pharmacodynamics</td>
<td>The study of the biochemical and physiological interactions of drugs at their sites of activity.</td>
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<tr>
<td>Pharmacokinetics</td>
<td>The study of the absorption, distribution, metabolism, and excretion of a drug, and its metabolites in the body.</td>
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<tr>
<td>Pharmacology</td>
<td>The science of drugs, including their composition, uses, and effects.</td>
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<tr>
<td>Prodrug</td>
<td>An inactive drug dosage form that is converted to an active metabolite by various biochemical reactions once it is inside the body.</td>
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<tr>
<td>Receptor</td>
<td>A molecular structure or site on the surface or interior of a cell that binds with substances, such as hormones, antigens, drugs, or neurotransmitters.</td>
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<td>Steady state</td>
<td>Rate of drug administration is equal to the rate of drug elimination.</td>
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<tr>
<td>Toxicity dose (TD50)</td>
<td>A dose that will produce a given toxicity in 50% of the studied group.</td>
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<td>Therapeutic class</td>
<td>A group of drugs with similar mechanism of actions that treat the same disease state.</td>
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<tr>
<td>Therapeutic index</td>
<td>The ratio of the drug's LD50 to its ED50 and measures drug safety margins.</td>
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<tr>
<td>Volume of distribution</td>
<td>The apparent volume required to account for all the drug in the body in the same concentration as in the sample from the plasma.</td>
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the most important mechanism for drug absorption. In simple diffusion, particles move from an area of high concentration to an area of low concentration. There is no energy expenditure during this process, and drugs must be small, lipid or fat soluble, and non-ionized (no positive or negative charge) to cross the membranes. An acidic environment, such as the stomach, favors non-ionization of weak acids, such as aspirin. Therefore, aspirin is more efficiently absorbed in the stomach than in the intestine. In contrast, the intestine is a basic environment and would favor non-ionization of weak bases, such as diazepam, which is more efficiently absorbed in the intestine than in the stomach. The second method of absorption is active absorption, also known as active transport. Since this method requires energy, it is the opposite of passive diffusion, which means it moves particles from an area of low concentration to an area of high concentration. The third method is called pinocytosis. This process allows cells to carry the drug across their membrane by engulfing the drug particles (Adams, Holland, & Bostwick, 2008; Kee, Hayes, & McCutision, 2009).

Multiple factors affect absorption, including rate of dissolution, blood flow, and contact time. The rate of dissolution determines the rate of absorption. If the drug dis-
solves quickly, it will be absorbed, and the effects will be apparent in a short period of time. With a slow-dissolving drug, the drug must move from the stomach into the intestine, and the effects may not be seen for a longer period of time (Adams & Koch, 2010). This is a key concept with immediate or sustained release products, such as tolterodine (Detrol®/Dettrol LA®) or oxybutynin ( Ditropan®/Ditropan XL®), often used for an overactive bladder.

Blood flow impacts the rate of absorption. If an area has a high blood flow, there may be increased absorption from that site. The intestine has more blood flow than the stomach; therefore, more absorption may occur. Conversely, shock reduces blood flow to cutaneous tissue, and drug absorption may be decreased in that area (Adams & Koch, 2010). If a patient uses a drug in a patch form, such as oxybutynin (Oxytro®) or fentanyl (Duragesic®), and absorption increases, some side effects of toxicity may be seen. However, if blood flow is decreased, the medications may not work as well on these patients. Using higher doses or switching to another form of the medication may be needed to optimize the desired effect.

Contact time also affects absorption. If a drug is not in contact with absorption sites for a specific period of time, the drug will not be completely absorbed. For example, diarrhea occurs because the decreased transit time in the gastrointestinal tract can affect the absorption of drugs in the body. Drug-drug interactions and drug-food interactions may increase or decrease absorption of a drug (Sloan, 1992). One drug may bind or alter the properties of another drug. Specific drugs can react with a number of drugs, food, or alcohol, and can be affected by various diseases and conditions (Anastasio, Cornell, & Menscer, 1997; Kirk, 1995; Sloan, 1992; Yamnadeewong, Henann, Fazio, Lower, & Cassidy, 1995).

The bioavailability of a drug can be altered by drug form, metabolism, surface area, and food. If a drug is administered intravenously, it has a bioavailability of 100% because the drug is injected directly into a vein, and the body absorbs the entire drug. However, a drug administered orally has a bioavailability of less than 100% for two reasons: 1) absorption is reduced, or 2) the drug is absorbed by the intestine, transported by the portal vein to the liver, and is metabolized before reaching the systemic circulation. Since this decreases the amount of drug available to the systemic circulation, it is known as the first-pass effect. Surface area is a principle element because drugs are absorbed slower in the stomach, which has a smaller surface area. Conversely, drugs are absorbed faster in the intestine, which has a larger surface area. Some drugs are absorbed faster when taken with food, whereas other drugs may absorb better if taken on an empty stomach (Kee et al., 2009).

After drugs are absorbed into the bloodstream, they are distributed or transported through the body. Drugs are distributed into the plasma, extracellular fluid, total body water, and the blood-brain barrier. Drugs bound to plasma proteins, most commonly bound to albumin, are known as bound drugs, which are not pharmacologically active. Drugs that are not bound are known as free drugs, which are active and able to produce a pharmacological response. This is an important consideration in patients with hypoalbuneminemia. If a drug is highly protein bound and a patient has low albumin levels, more free drug would be available to the body, and the patient may experience toxic effects (Kee et al., 2009).

Distribution
Initially, drugs are distributed to the highest areas of blood flow, such as the heart, liver, kidney, and brain. Drugs are then distributed to areas with lower blood flow, such as muscles, skin, and fat. In these low-flow areas, it is difficult to obtain high drug concentrations, so different routes of administration may be needed. Some areas, such as bone, have a very poor blood supply and are difficult to obtain adequate drug concentrations. The blood-brain barrier is a barrier that inhibits many chemicals and drugs from exiting the blood. Most medications do not easily cross this barrier, making infections difficult to treat. With certain infections, such as meningitis, the blood-brain barrier becomes more permeable when inflamed and infections are more easily treated (Adams & Koch, 2010).

The volume of distribution is a term used to quantify the distribution of a medication between plasma and the rest of the body after oral or parenteral doses. A small volume of distribution and high blood concentration usually occur with highly water-soluble drugs. The high water content allows the drug to stay within the blood compartment. Water-soluble drugs that are highly protein bound are more strongly bound to proteins and are less likely to be absorbed into tissues, and thus, usually concentrated in the blood compartment. Atenolol (Tenomin®) is an example of a water-soluble drug. Conversely, a large volume of distribution and low blood concentration are seen with fat-soluble drugs. Fat-soluble drugs, such as diazepam (Valium®), are usually poorly bound to protein but are easily absorbed into tissue and distributed throughout the body. Because of this, they may be reabsorbed into the circulation from tissue (Adams & Koch, 2010).

Metabolism
Metabolism is primarily associated with termination of drug action. Metabolites often exhibit
lower pharmacologic activity and are more water soluble, and therefore, are more easily excreted (Kee et al., 2009). Pro-drugs have no pharmacological activity and must be metabolized to become active. Clopidogrel (Plavix®), an antiplatelet drug used for coronary artery disease, peripheral vascular disease, and cerebrovascular disease, is an example of a pro-drug. It undergoes rapid hydrolysis to its active form by the cytochrome P450 system (Savi et al., 1994).

The primary site of metabolism for drugs is the liver. The rate of metabolism is dependent on the blood flow. Other sites of metabolism include skin, lung, kidneys, and gastrointestinal tract. The most common drug metabolism action is performed by a large class of enzymes called microsomal enzymes, also known as the Cytochrome P-450 enzyme system (Adams & Koch, 2010). The metabolism capabilities of the liver can vary from patient to patient. Factors that can alter metabolism include genetics, diseases, and concurrent use of other drugs.

**Excretion**

Routes of drug excretion include urine, bile, feces, expired air, sweat, tears, saliva, and breast milk. Renal excretion of drugs is usually through glomerular filtration, proximal tubular secretion, and distal tubular reabsorption (Lilley et al., 2007). Urinary excretion is the primary route of excretion. Excretion can be affected by altering urinary pH. Acidification of urine increases the excretion of weak bases, such as diazepam. Alkaline urine can increase the excretion of weak acids, such as aspirin. This is important especially in cases of overdose of these medications (Kee et al., 2009).

The elimination half-life (t1/2) is a pharmacokinetic term that describes a drug’s duration of action. Drugs may have a half-life of minutes, hours, or days. The longer the half-life, the longer it takes for a drug to be excreted. It usually takes four to five half-lives for a drug to be at steady state. Therefore, if a drug is ingested and the half-life is 2 hours, then in about 10 hours the drug will be out of the body’s system (Adams & Koch, 2010; Kee et al., 2009).

Clearance depends on blood flow and the ability of the organ to remove the drug. Total body clearance is the sum of all the clearances in the body. This includes hepatic clearance, renal clearance, pulmonary clearance, and other organ clearances (Winter, 2004).

Renal disease can affect glomerular filtration rate (GFR), which may reduce the amount of drug that is excreted by the kidney and could produce toxic effects. Creatinine clearance is used to evaluate renal function in milliliters per minute and can be calculated by many equations, the most common being the Cockcroft-Gault equation (see Figure 1) (Winter, 2004).

**Side Effects/Adverse Effects**

Side effects are types of adverse effects that are predictable and may occur even at therapeutic doses. An adverse effect, however, is an undesirable and potentially harmful action caused by the administration of medications. The number of drugs a patient is taking increases the chance of an adverse effect or drug interaction. This risk is estimated to be 6% when two medications are taken, 50% with five medications, and almost 100% with eight or more concurrent medications (Adams & Koch, 2010; Terrie, 2004).

**Pharmacodynamics**

While pharmacokinetics relates to how the body changes the drug, pharmacodynamics refers to how a drug changes the body. Patients can respond very differently to drugs. This can be shown on a frequency distribution curve, which is a graphic representation of patients’ response to a drug action at different doses and usu-
ally looks like a bell curve. The median effective dose (ED50) is in the middle of the distribution curve and reflects the dose required to produce a specific therapeutic response in 50% of the patients. Studies from animal data provide information to determine the median lethal dose (LD50). Since the median lethal dose (LD50) cannot be determined experimentally in humans, a median toxicity dose (TD50) is of value for clinical practice. The TD50 is a dose that will produce a given toxicity in 50% of the studied group and is extrapolated from animal data and adverse drug effects that are recorded during the clinical trials. By using the median effective dose and the median lethal dose, the therapeutic index can be determined. With the therapeutic index, the higher the safety margin, the safer the drug. A drug with a low therapeutic index is associated with a narrow safety margin, whereby a drug with a high therapeutic index is associated with a large safety margin. Therefore, if a small medication error would occur, the consequences from the drug with a narrow safety margin could be toxic or lethal (Adams & Koch, 2010).

Plasma levels must be monitored in drugs that have narrow safety margins. The concentration is measured usually at two points by obtaining peak and trough blood levels. The peak level is the highest plasma concentration at a specific time, whereas the trough level is the lowest plasma concentration and measures the rate at which the drug is excreted (Kee et al., 2009). An example is gentamicin, an aminoglycoside antibiotic that may be used to treat urinary tract infections or urosepsis. Obtaining peak and trough levels are necessary to determine therapeutic response and prevent toxicity.

There are four ways to compare medications within a therapeutic class: potency, efficacy, safety, and cost. A more potent drug will produce an effect at a lower dose. The efficacy is the magnitude of maximal response that can be produced from a drug. If two drugs are compared, the drug with the highest maximal response is more efficacious (Adams & Koch, 2010). Safety would be determined based on side effects or toxicity. Cost is an important aspect; however, it is not the only issue when comparing medications in different classes.

Drugs produce their actions by activating or inhibiting receptors. Several possibilities may occur when a drug binds to a receptor, which includes agonists, partial agonists, and antagonists. An agonist activates a receptor and produces the same type of response as the endogenous substance. Compared with an agonist, a partial agonist produces a weaker or less efficient response. An antagonist competes with agonists for receptor binding sites (Adams & Koch, 2010).

Drug interactions can occur every day. Individual drugs may interact with other drugs, food, or laboratory tests. The occurrence of a drug interaction is more likely with polypharmacy. Drug interactions can either increase or decrease the actions of one or both of the involved drugs, which can either be beneficial or harmful (Adams & Koch, 2010).

Drug interactions can be categorized as additive, synergistic, antagonistic, and incompatibility. Additive effects can occur when two drugs with similar actions are given together and a combined summation response occurs (for example, a diuretic and a beta blocker—each drug decreases blood pressure, but together, they decrease blood pressure to a greater degree). Synergistic effect is when the effect of two drugs is greater than would be expected from adding the two individual drug responses. For example, Bactrim® combines trimethoprim and sulfamethoxazole. Together they work better against bacteria than either one by itself. An antagonistic effect is caused when adding a second drug results in a diminished response and can cancel out the effects of the first drug. This effect is seen frequently when a narcotic, such as morphine, is given, and the patient has respiratory depression. Naloxone (Narcan®) is given to antagonize or block the effects of morphine, thereby restoring respirations. Incompatibility usually involves parenteral drugs, and it occurs when two parenteral drugs or solutions are mixed together. The result is a chemical or physical reaction. The combination of the two drugs usually forms a precipitate, haziness color, or a temperature change occurs (Lilley et al., 2007) as in intravenous phenytoin (Dilantin®) and Dextrose 5% in Water (D5W). Phenytoin will usually precipitate out when mixed in D5W.

Conclusion

Pharmacokinetics and pharmacodynamics play a major role in drug efficacy and safety. As each individual’s response to drug therapy may be different, these two concepts can have a significant impact on patient outcomes. Nurses and health care providers should be aware of the pharmacokinetic and pharmacodynamic properties of the drugs they administer. Absorption, distribution, metabolism, and elimination of drugs are all important factors that define the body’s reactions to drugs once they enter the body and the impact of the drug on the body itself. Equally important is the mechanism by which the drug works, and the relationship between the drug concentration and the body’s response. Knowledge of side effects, adverse drug reactions, and monitoring parameters for drugs being administered are
crucial elements of the clinical practice of nursing. These factors can be used to ultimately help assess the therapeutic outcome of drug therapy. Utilization of these concepts can assist health care providers meet the objective of drug therapy, which is to provide maximum benefits with minimal harm.

References


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**Urologic Nursing Editorial Board Statements of Disclosure**

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