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Course Administered By:
J&D Educational Services, Inc
PO Box 130909
The Woodlands, Texas 77393-0909
Voice: 1-866-747-5545
Fax: 1-281-298-8335
www.jdeducation.com

BASIC CONCEPTS IN PHARMACOLOGY
FOR THE CERTIFIED PHARMACY TECHNICIAN
A Knowledge Based Course

By

Jeff Blackburn, C.Ph.T., MBA – Healthcare Administration

ACPE No. 0096-9999-12-008-H04-T

Release Date: 02/14/2012
Expiration Date: 02/14/2015

Total number of pharmacy continuing education hours: 4 hours (0.4 CEU’s)

Course Cost: $13.00.00 (to be paid at time of testing)
Average time to Complete: Approximately four hours including testing
Course Value: Four Contact Hours
Reading: 53 Pages
Final Exam: 40 Questions
Completion Requirements: Answer 70% of questions correctly. Eval.
STATEMENT OF NEED

Pharmacology is the science of the effects of drugs and other chemicals on biological systems, from the molecular and cellular levels through to patient studies. The science of pharmacology is at the forefront of modern medicine, designing, developing and testing drugs that have potential to alleviate and in some cases cure, the diseases that afflict humans.

As pharmacy technicians, it is important that we understand the basic concepts of pharmacology in order to not only serve our patients better to help participate in the ever present struggle against medication errors.

OBJECTIVES

At the end of this course, the reader will be able to meet the following objectives:

1. Discuss why the knowledge of basic pharmacology is important for successful patient outcomes.
2. Differentiate between efficacy and potency.
3. Identify the more common pharmacokinetic concepts.
4. Describe the methods for controlling drug effects.
5. Discuss the administration of pharmacologic agents.
6. List some of the common dosage forms and routes of administration.
**Introduction**

The role of the pharmacy technician in today’s pharmacy is both challenging and rewarding. Technicians are asked to perform many critical tasks. It is extremely important that they perform these tasks in the correct way, and they must be well versed in basic pharmaceutical concepts. One of the best approaches is to learn drugs is by their class. New drugs will be introduced during your lifetime, so it is necessary to develop a flexible framework for drug information.

You cannot possibly learn everything about every drug available. Although many pharmacy technicians are able to memorize an incredible amount of useful and useless information, there is a limit to what even the best technicians can learn. Therefore, you must try to organize the material in a way that minimizes the amount of information you have to memorize. You need to get the most bang for your buck, or most facts learned for each hour of time spent. Usually this means grouping drugs and making associations.

This course is designed to help students develop a commitment to the pharmacy field with the hope that, as pharmacy technicians, they will be challenged by this constantly changing field and motivated to learn more about the body and the drugs that heal and make patients’ lives more comfortable.

**Pharmacology**

The goal of drug therapy is to produce a response in the body that results in the cure or control of specific disease or condition. Drugs work via a series of processes, which can be described in the terms of pharmacokinetics. Pharmacokinetic studies reveal how drugs work in the body and provide critical insight for predicting the effects of each specific drug. An understanding of these processes enables the development of safe and effective treatments for various diseases.

**Receptors**

To maintain homeostasis\(^1\) within the body, it is essential that the body’s cells have the ability to communicate with each other. One of the ways that cells communicate is through the action of chemical messengers. These messengers, produced by cells, are sent out into the extra-cellular fluids of the body. Histamine, prostaglandin, and bradykinin are some important endogenous (i.e., originating from within the body) chemical messengers.

Once the messenger has been released it can diffuse throughout the extra-cellular fluid to reach its “target cell.” The target cell is recognized and communicated with via specific protein molecules present on the surface of or within the cell. These molecules are called

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\(^1\) the tendency of a system, especially the physiological system of higher animals, to maintain internal stability, owing to the coordinated response of its parts to any situation or stimulus that would tend to disturb its normal condition or function.
receptors. A receptor is a molecule on the surface of or within a cell that recognizes and
binds with specific molecules, producing some effect in the cell.

The various cell types within the body differ with regard to the types of receptors they
contain, and only certain cell types possess the receptor required for combination with a
particular chemical messenger. To bind with a specific cell type, the messenger must
have a chemical structure which is complementary to the structure of that cell’s receptors.
This property of a receptor site is known as specificity. For example, the cells involved
in immune responses have receptors that are highly specific to bacteria, viruses, and some
cancer cells. Receptors mediate many important bodily functions such as blood clotting
and smooth muscle contraction, and play an important role in the body’s protection
against injury and infection.

The strength by which a particular messenger binds to the receptor site is referred to as its
affinity for the site. Affinity is an important concept for understanding how drugs work
in the body.

**Mechanisms of Drug Action**

Drugs often act like the chemical messengers described above to exert powerful and
specific actions in the body. Some drugs bind to a particular receptor and trigger the
cell’s response in a similar way to the body’s own chemical messenger. These drugs are
termed agonists.

When two drugs have an affinity for a particular receptor, they will compete for available
receptor sites. The relative number of receptors occupied by each drug will depend on
the relative concentrations of each drug as well as the relative affinities of the receptor
site for each drug. When two drugs try to bind to the same receptor, site antagonism
occurs. Increasing concentration of the agonist will increase the biological response until
there are no more receptors for the agonist to bind or a maximal response has been
reached.

Some drugs produce their effects by interacting with chemically nonspecific membrane
lipids. Their effectiveness is related to lipid solubility and does not depend on receptor
sites. Examples of drugs that work this way are the volatile anesthetic agents.

Drugs can also combine with other proteins – such as enzymes, transport proteins, and
with nucleic acids – rather than receptors. Some antidepressants work this way by
blocking the uptake of serotonin by nerve terminals.

Other drugs act without any direct interaction with the cell. For example, drugs can work
through an osmotic effect. Mannitol is such a drug. It interferes osmotically with water
re-absorption by the kidneys.
**Efficacy and Potency**

Efficacy and potency are terms that technicians sometimes confuse. These terms are used for comparisons between drugs. Efficacy is the maximal response a drug can produce. Potency is a measure of the dose that is required to produce a response.

For example, one drug (drug A) produces complete eradication of premature ventricular contractions (PVCs) at a dose of 10mg. A second dose (drug B) produces complete eradication of PVCs at a dose of 20mg. Therefore, both drugs have the same efficacy (complete eradication of PVCs), but drug A is more potent than drug B. It takes less of drug A to produce the same effect. A third drug (drug C) can reduce the PVCs by only 60%, and it takes a dose of 50mg to achieve that effect. Therefore, drug C has less efficacy and less potency in the reduction of PVCs compared with both drug A and drug B.

Potency is often expressed as the dose of a drug required to achieve 50% of the desired therapeutic effect. This is the ED$_{50}$ (effective dose).

**Therapeutic Index**

Therapeutic index is a measure of drug safety. A drug with a higher therapeutic index is safer than one with a lower therapeutic index. That statement is true no matter what textbook you consult. However, the definition of therapeutic index may vary depending on who you ask. Usually,

\[
\text{Therapeutic index} = \frac{\text{LD}_{50}}{\text{ED}_{50}}
\]

The lethal dose (LD$_{50}$) is the dose that kills 50% of the animals that receive it. Sometimes the TD$_{50}$ is used in place of the LD$_{50}$. The TD$_{50}$ is the dose that is toxic in 50% of the animals that receive it. Death is the ultimate toxicity.

The therapeutic index is sometimes confused with the therapeutic window. The therapeutic window is the range of plasma concentration of a drug that will elicit the desired response in a population of patients.

**Pharmacokinetics**

Pharmacokinetics is the mathematical description of the rate and extent of uptake, distribution, and elimination of drugs in the body. Don’t’ let the word mathematical scare you. I include the formula for completeness, but no math is required for this course. What is important is that the reader understands the concepts surrounding the entry, distribution, and clearance of drugs in the body.
Medications are given to produce a response that results in cure, control, or prevention of a specific disease. The study of pharmacokinetics enables researchers to understand how a drug works within the body to affect both normal physiology and disease. Pharmacokinetics describes the action of drugs in the body over a period of time. As such, it can be conceived of as a series of processes which produce specific effects.

**Important Pharmacokinetic Parameters**

Most of the concepts discussed below are presented in more detail later in the course. However, it is important to get a “big picture” look at pharmacokinetics first.

An understanding of the pharmacokinetic processes enables researchers to make determinations regarding how a particular drug should be administered to the patients to obtain a specific response. Safe and effective drug therapy requires that drugs be delivered to their target sites in concentrations within a range that will treat the disease state for which it is intended without toxicity.

A dose is the quantity of a drug administered at one time. As greater doses of a drug are given, a greater response will be noted until a point is reached when no improved clinical response occurs with increased dosage. This is called the ceiling effect. Increased dosage beyond the ceiling effect may result in side effects, toxicity, or even death.

Dosages are fairly universal from patient to patient. In some cases, however, dosage must be individualized to the patient because of variables such as age, size, weight, sex, race, nutritional state, pregnancy, as well as other drugs the patient may be taking. A determination of individual patient dose and dosing intervals can be made, if necessary, based on the testing of drug concentration in body fluids such as blood, plasma, and urine. Testing of these fluids over specified time intervals provides an indication of how the patient is metabolizing the drug.

Typically, only a portion of the dose administered becomes biologically active in the body. The fraction of the administered dose that is available to the target tissue is an expression of the drug’s bioavailability. Drugs taken orally must pass through the intestinal wall and traverse the liver before reaching systemic sites. This process is referred to as the first pass effect. If a drug which is absorbed from the GI tract is metabolized by the liver to a great extent before it reaches the systemic circulation (first-pass effect), oral bioavailability will be decreased. Some drugs have such a substantial first-pass effect that their use is essentially limited to the parenteral route (i.e., injections).

The therapeutic window of serum concentrations for a particular drug should provide the optimum probability of achieving the desired response with the least probability of toxicity. A defined therapeutic range provides the best chance for successful therapy. Some patients may require concentrations of drug below or above the therapeutic range.

Doses and dosing intervals are determined by clinical trials but may need to be adjusted on an individual basis. This is done based on a blood sample and is particularly
beneficial for attaining the desired concentration for a drug with a narrow therapeutic range. When the amount of drug in a patient’s blood gives the desired response, it is said to be at the therapeutic level. The length of time a drug is at this level is referred to as its duration of action.

The time required to achieve therapeutic levels of a drug can be shortened by the administration of a loading dose – and amount of drug that will bring the blood concentration rapidly to a therapeutic level. Loading of the drug may be accomplished by the administration of a single loading dose. Alternatively, if a large single dose poses a risk of toxicity, loading can be accomplished by the administration of the loading amount in a series of doses. Maintenance-doses are then given to keep the drug at a therapeutic level. The volume of distribution, which describes the relationship between the blood concentration attained and the dose of the drug given, is important for prescribing the loading dose; whereas clearance, the removal of a drug from a specific volume of blood per unit of time is important for calculating the maintenance dose.

The time necessary for the body to eliminate half of the drug in circulation at any time is the half-life, written $T_{1/2}$. The longer the half-life, the longer the drug action. It takes about five to seven half-lives to consider the drug “removed” from the body – meaning that less than 3% remains. If the $T_{1/2}$ of a drug is two hours, then the drug would be gone in ten to fourteen hours. If the $T_{1/2}$ is thirty hours, then it would take 150 to 210 hours, or six to nine days, to eliminate the drug. A drug with a long half-life may produce effects for days or even weeks after being discontinued.

**Pharmacokinetic Processes**

Each drug’s pharmacokinetics can be described in terms of four processes of interaction with the body. These processes are absorption, distribution, metabolism, and elimination. An understanding of these processes provides an important framework for researchers who are responsible for the development of drugs.

**Absorption**

Absorption describes the process whereby a drug enters the circulatory system. The absorption of a drug depends on its route of administration, solubility, and other physical properties. The solubility of the drug refers to its ability to dissolve in body fluids (e.g., blood). The form of the drug is an important factor in controlling solubility. For example, drugs in liquid solution are already dissolved so they are absorbed more readily than those in capsule form.

The most common route of administration is the oral route. Other routes include intramuscular, subcutaneous, rectal, sublingual, transdermal, inhalation, and epicutaneous (topical) routes. Intravenous and intra-arterial administration (directly into systemic blood circulation) do not require absorption, as the drug is immediately available.
There are several useful routes of drug administration, but almost all require that the drug cross a biological membrane to reach its site of action. Drugs cross membranes by **passive diffusion** or **active transport**.

This statement is somewhat simplified, but it provides a useful starting point. Passive diffusion requires a concentration gradient across the membrane. The vast majority of drugs gain access to their site of action by this method. Water-soluble drugs can penetrate the cell membrane through aqueous channels. More commonly lipid-soluble drugs just move through the membrane.

When oral medication is not given as a solution, its rate of absorption is slowed by the time necessary for the tablet or capsule to release the drug (dissolution) and for the drug to dissolve in the gastrointestinal (GI) tract. Disintegration and dissolution depend on the physical properties of the drug and its dosage form. Factors affecting dissolution include the chemistry of the drug, the surface area of its particulates, as well as manufacturing variables. Some drugs interact with certain gastric contents, such as food. This effect subsequently reduces the amount of drug available for absorption.

The small intestine is the primary site of absorption because of its large surface area. When drugs are given orally, the degree of GI motility also affects absorption. The faster the rate of gastric emptying, the more rapid the absorption rate.

In the small intestine, the drug must cross the cell membrane of the epithelial cells. Membranes are composed of lipids, proteins, and carbohydrates. Pores are small openings or empty spaces in this membrane through which low-weight molecules pass freely. Lipid soluble molecules, small hydrophilic molecules, and ions readily pass through this barrier. Some drugs may be metabolized by enzyme action within the epithelial cell before they reach systemic blood.

**Bioavailability** is the amount of drug that is absorbed after administration by route X compared with the amount of drug that is absorbed after intravenous (IV) administration, where X is any route of drug administration other than IV.

Example: Suppose your pharmacy is involved in a clinical trial. The compound your pharmacy is testing is called “NewDrug.” NewDrug is administered orally and blood tests determine that only 65% of the oral dose reaches the circulation. Compared with intravenous (IV) administration where 100% of the dose reaches circulation, the bioavailability of NewDrug is 0.65% or 65%. In the case of hypothetical NewDrug, the pharmacy staff might discover that some of the drug is inactivated by the acid in the stomach. The manufacturer redesigns the pill with a coating that is stable in acid but dissolves in the more basic pH of the small intestine. This could help increase the bioavailability of NewDrug.

\[
\text{Bioavailability} = \frac{\text{AUC}_{\text{oral}}}{\text{AUC}_{\text{IV}}}
\]
Distribution

Distribution is the process by which a drug moves from the bloodstream into other body fluids and tissues and ultimately to its sites of action, the receptors. Blood flow is the rate-limiting factor for distribution of a drug. Three additional factors also affect the rate and degree of distribution.

1. **Binding Plasma to Proteins.** The biological activity of a drug is related to the concentration of “free” drug in circulation. The protein-bound portion of the drug is restricted from reaching its site of action and is essentially inactive. Once saturation binding occurs, the unbound drug increases and is available to be distributed to its site of action. This competition increases the plasma concentration of the free drug, which remains unbound and active. Disease states can also affect protein binding. Renal failure, for example, may result in a loss of plasma proteins (with less available for binding) or in the accumulation of metabolic wastes that could potentially displace some bound drugs. Liver disease may also result in fewer plasma proteins to transport drugs.

2. **Binding Cellular Constituents.** Drugs can also bind to other tissues besides blood plasma. This type of binding usually occurs when the drug has an affinity for some cellular constituent.

3. **Blood-Brain Barrier.** The capillaries in the central nervous system (CNS) are enveloped by glial cell, which present a barrier to many water-soluble compounds though they are permeable to lipid-soluble substances. This barrier prevents many substances from entering the cerebrospinal fluid from the blood. Therefore, many drugs cannot get to the CNS because they are unable to pass through the blood-brain barrier. However, pathologic states such as inflammation will reduce this resistance and the barrier becomes more permeable. For example, while general anesthetics penetrate this barrier with ease, penicillin cannot penetrate the CNS unless the meninges are swollen.

Metabolism

Metabolism is a process by which drugs are converted to compounds and then excreted through metabolic pathways. These pathways are the routes for a number of processes. Through oxidation, electrons are lost and oxygen is added to a molecule. In the reduction pathway, electrons are gained and oxygen is lost. In conjugation, drug molecules combine with a highly water-soluble compound. In hydrolysis, adding water cleaves a compound, the hydroxyl group being incorporated into one portion and the hydrogen atom into another.

Orally administered drugs are absorbed from the gastrointestinal (GI) tract. The blood from the GI tract then travels through the liver, the great chemical plant in the body. Many drugs that undergo liver metabolism will be extensively metabolized during this
passage from the GI tract to the body. This effect of liver metabolism is called the **first-pass effect**.

In general, metabolism converts drugs to more water-soluble (less lipid-soluble) forms. Once in a more water-soluble state, drug metabolites may be more easily excreted by the liver and kidneys.

Many factors can alter metabolism and elimination. If given together, two drugs may decrease or enhance the metabolism of each other. Some drugs decrease the metabolism of other drugs by competitive or complete inhibition of a particular drug-metabolizing enzyme. Other drugs enhance drug metabolism by induction of these same enzyme systems. Disease states, age and genetic predisposition all affect the way the body metabolizes drugs.

Enzymes in the cell’s endoplasmic reticular membrane convert drugs from fat-soluble to water-soluble. These enzymes exist and play a major role in metabolism of endogenous substances (i.e., steroids, fat-soluble vitamins, and fatty acids). They are responsible for the metabolism of most drugs as well as toxins such as those in tobacco smoke, charcoal-broiled meat, polychlorinated biphenyls (PCBs), herbicides, and general combustion by-products. The enzymes convert lipophilic substances into more readily excreted water-soluble metabolites. Enzyme levels may be hyper-stimulated, resulting in excessively rapid metabolism of drugs, or hypo-stimulated, increasing a compound’s toxicity.

Two processes, induction and inhibition, can control specific enzymes:

1. **Induction.** The concentration of a particular enzyme can be affected by some drugs, foods, and smoking. Drugs that increase these enzymes can decrease the pharmacologic response to other agents (e.g., Phenobarbital increases the metabolism of warfarin) or to themselves (e.g., some barbiturates stimulate self-metabolism).

2. **Inhibition.** Some agents can slow or block enzyme activity, which impairs the metabolism of drugs and may increase their concentration and toxic or pharmacological effects. An example is cimetidine.

**Elimination**

Elimination occurs primarily in the kidney and the bowel, but other routes exist. Drugs may be exhaled by the lungs or excreted in perspiration, saliva, and breast milk. The elimination rate of a drug from a specific volume of blood per unit of time is referred to as it clearance.

Clearance is a term that indicates the rate at which a drug is cleared from the body. It is defined as the volume of plasma from which all drug is removed in a given time. Thus, the units of clearance are given in volume per unit of time.
Clearance is an odd term, mostly because of the units used to report it. It is not intuitive. Let’s try another hypothetical example as a way to remember the units.

Suppose we have a 10 liter (10-L) aquarium that contains 10,000 mg of “crud.” The concentration is 1 mg/ml. Clearance is 1 L/h (h = hour). In other words, the aquarium filter and pump clear 1 L of water in an hour. At the end of the first hour, 1000 mg of crud has been removed from the aquarium (1000 mL of 1 mg/mL). The aquarium thus has 9000 mg of crud remaining, for a concentration of 0.9 mg/mL. At the end of the second hour, 900 mg of crud has been removed (1000 mL of 0.9 mg/mL). The aquarium now has 8100 mg of crud remaining, for a concentration of 0.81 mg/mL. The process continues forever. Notice that the time to clear this particular aquarium is not 10 hours. It would take 10 hours (10 L at 1 L/h) if the clean water was pumped into another container. In the case of clearance in the aquarium, however, the clean water is returned to the tank and dilutes the remaining crud. The same principle holds true for clearance of a drug from the human body.

A more official definition is the following equation:

\[
\text{Clearance} = \frac{\text{Rate of removal of drug (mg/min)}}{\text{Plasma concentration of drug (mg/min)}}
\]

Notice that this equation gives you units of milliliters per minute (mL/min) or volume per unit of time.

Total body clearance is the sum of the clearances from the various organs, involved in drug metabolism and elimination.

**Volume Distribution**

Volume of distribution (\(V_D\)) is a calculation of the apparent volume in which a drug is dissolved. It assumes that a drug is evenly distributed and that metabolism or elimination has not taken place. In reality, it does not correspond to any real volume:

\[
\text{Volume of distribution (V}_D\text{)} = \frac{\text{Dose(mg)}}{\text{Plasma concentration (mg/mL)}}
\]

The equation is very easy to remember. Suppose you take 1000 mg of sugar and dissolve it into a beaker of water. After it has dissolved, you take a sample of water (let’s say 10 mL) and determine the concentration of sugar in that sample (for example, 1 mg/mL). From this finding you can calculate the volume of water in which the sugar was dissolved as follows:

\[
1\text{mg/mL} = 1000 \text{mg/volume of water}
\]
Thus,

\[
\frac{1000\text{mg}}{1\text{mg/mL}} = 1000\text{mL}
\]

In this case the volume was 1000 mL, or 1. If you keep the units straight, the equation does not need to be memorized.

The volume of distribution is rather large. The only explanation is that the drug is hiding someplace in the body where it is not recorded by the measurement of plasma concentration. The drug could be lipid soluble or stored in fat, or it could be bound to plasma proteins. As this example shows, the volume of distribution is a hypothetical volume and not a real volume.

**First-Order Kinetics**

The order of a reaction refers to the way in which the concentration of drug influences the rate of a chemical reaction. For most drugs, only the first-order and zero-order are important.

Most drugs disappear from the blood by processes (absorption, elimination) that are dependent on the level of concentration of the drug (how much, what strength). With first-order elimination, a constant percentage of the drug is lost per unit of time.

For first order kinetics, the half-life is constant. The half-life \( t_{1/2} \) is the period of time required for the concentration of a drug to decrease by one half.

**Zero-Order Kinetics**

Drugs that saturate routes of elimination disappear from the blood in ways that are not dependent on the level of concentration, which is called zero-order kinetics. The half-life is not constant for zero-order reactions. Zero-order kinetics is also known as nonlinear or dose-dependent kinetics.

You will see the terms zero-order and dose-dependent used interchangeably in the medical literature. The term dose-dependent refers to drugs that are first-order at lower doses and switch to zero-order at higher doses (often in the therapeutic range). Therefore, the kinetics of these drugs are dose-dependent. Nonlinear refers to the fact that drugs with zero-order kinetics do not show a linear relationship between drug dose and plasma concentration.

**Steady-State Concentration**

Rarely are drugs given as a single dose. Normally repeated doses are given and sometimes drugs are given as a continuous intravenous (IV) infusion. When a drug is given as a continuous infusion it will increase in concentration in the blood until the rate
of elimination is equal to the infusion rate. At this point the amount going in per unit time is equal to the amount going out. The plasma concentration at this point is called the concentration at steady-state, or $C_{SS}$.

Let’s consider a patient who has no drug in his system. You start an IV infusion at 100 mg/kg. At first the plasma level will be low and the infusion rate will be greater than the elimination rate. The plasma level will rise relatively quickly. Remember that the elimination rate is proportional to the plasma concentration level of the drug (aquarium example), so as the concentration rises so does the elimination rate. As the elimination rate increases with the increasing plasma concentration, the rate of increase in the plasma level will slow. At steady-state, the infusion rate and the elimination rate are equal.

For an IV infusion,

$$C_{SS}m = \frac{\text{Infusion rate (mg/min)}}{\text{Clearance (mL/min)}}$$

There is also a concentration at steady state for repeated doses. Sometimes this is called an average concentration ($C_{AVG}$). With multiple dosing schedules, we normally assume that early doses of the drug do not affect the pharmacokinetics of subsequent doses. Generally, we also give equal doses at equal time intervals.

**Time Needed to Reach Steady-State**

The time needed to reach steady state depends only on the half-life of the drug. Ninety percent of steady state is reached in 3.3 half-lives.

There is a good bit of math behind these numbers, which you can read about elsewhere if you want. The bottom line is that during each half-life, 50% of the change from the starting point to concentration steady state ($C_{SS}$) is achieved.

After one half-life, we will gain 50% of the steady state ($C_{SS}$). We have 50% of the distance remaining. In the next half-life, we will gain 50% of this remaining distance, or ½ of 50%, which is 25%. So after two half-lives, we will be 75% of the way to steady state. If you repeat this several times, you can generate the table below. Notice that after five half lives, we are still approaching steady state.

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<th>No. of $t_{1/2}$</th>
<th>% $C_{SS}$</th>
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<td>4</td>
<td>94</td>
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<td>97</td>
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</table>
When asked the question, how long does it take to get the steady state, some sources accept 3.3 half-lives (90% of $C_{SS}$), whereas others use 4-half-lives (94% of $C_{SS}$), and still others accept 5 half-lives (97% $C_{SS}$).

**Loading Dose**

If the half-life of a drug is relatively long, such as 6 days for digoxin, it will take quite a long time for the drug concentration to reach steady state (about four times the half-life). For digoxin, this would take over 3 weeks. Sometimes the patient cannot wait that long for the therapeutic effect to occur. In these instances a loading dose is used.

A single dose of a drug can be given that will result in the desired plasma concentration. This dose is called a loading dose, if followed by repeated doses or a continuous infusion that will maintain the plasma concentration at the desired level (termed maintenance doses).

**Pharmacokinetic Modeling**

Studies on drug absorption, distribution, metabolism, and elimination have advanced the concept that the body may be considered as consisting of different compartments. In the simplest form, a drug passes from one compartment to another in direct proportion to its concentration gradient.

Pharmacokinetic modeling is a method of describing the process of absorption, distribution, metabolism, and elimination of a drug within the body. For some drugs, elimination is a zero-order process; that is, a fixed quantity of drug is eliminated per unit of time. The best example is alcohol. For the majority of drugs, elimination is said to be “first-order.” That is, a constant fraction of remaining drug is eliminated per unit of time. Two pharmacokinetic models, based on the compartment theory, have been developed. In the one-compartment model, the drug is distributed into blood volume. This model assumes an instantaneous and homogenous distribution of drugs throughout the body. In the two-compartment model, the drug is distributed into blood volume, and then into body tissue. This more complex model better describes the distribution of many drugs.

**DRUG EFFECTS**

The pharmacokinetic models described above provide critical insight for predicting the effects of each specific drug. Some effects are beneficial, while others can be detrimental or dangerous. Just as each person is different, each person’s reaction to a drug may be different. Thus, each patient must be monitored closely to ensure that his response to the drug he is taking is appropriate.
**Beneficial Responses**

The desired action of a drug in the treatment of a particular disease state or symptom is referred to as a therapeutic effect. The therapeutic effect is the action for which the drug is prescribed. Drugs can act locally or they can act on the body as a whole. A local effect is confined to a specific part of the body. A systemic effect, on the other hand, has a generalized, all-inclusive effect on the entire body.

Sometimes drugs are prescribed to prevent the occurrence of an infection or disease. In this case, the drug effect is referred to as prophylaxis. Patients who will be undergoing surgery will, in some cases, be administered prophylactic drugs, which will work to prevent the occurrence of infections.

In selecting a drug for an individual patient, the healthcare practitioner considers its approved uses and situations in which it should or should not be given. The indications for a drug are the diseases, symptoms, and conditions for which the drug is known to be of benefit. The contraindications are the diseases, symptoms, and conditions in which the drug will not be beneficial and may indeed do harm.

Side effects are secondary response to a drug other than the primary therapeutic effect for which the drug was intended. Drugs can on occasion be prescribed for their side effects.

**Harmful Responses**

*Allergic Responses*

An allergic reaction is a local or general immune response. In essence, an allergy is an instance of the immune system overreacting to an otherwise harmless substance. The first exposure to an allergen generally gives little or no observable response. Rather, what is critical about the initial exposure is the resulting “memory storage” which characterizes active immunity. Thus, upon re-exposure, the body recognizes (“remembers”) the antigen and responds with a more potent antibody response. This response can elicit a range of reactions from uncomfortable to life threatening. Some responses start within minutes of exposure; others may be delayed. Exposure to the allergen may be mild, moderate, or in some cases, even cause death.

Anaphylactic reactions are severe allergic responses resulting in immediate life-threatening respiratory distress, usually followed by vascular collapse and shock and accompanied by hives. Idiosyncratic reactions are unusual or unexpected responses to a drug, unrelated to the dose given.

*Drug Dependence, Addiction, Abuse, and Tolerance*

Drug dependence describes a state in which a person’s body has adapted physiologically and psychologically to a drug and cannot function without it. Dependence should not be confused with addiction, which is a dependence characterized by perceived need to take a
drug to attain the psychological and physical effects of mood-altering substances. One sign of addiction is a decrease in psychological well-being and social or vocational functioning. Patients who are being treated for various disease states may become dependent on medications, without exhibiting the signs of addiction. Drug abuse is the use of a drug for purposes other than those prescribed and/or in amounts that were not directed. It is generally thought of as experimental or recreational use of a substance that may have adverse effects. Abusive use of drugs can be, but is not always, linked to addiction.

After a patient has been taking a drug over a significant period of time, he or she may begin to develop a decreased response to the drug. This decrease in response to the effects of a drug due to its continued administration is referred to as tolerance. As tolerance develops, there may be a need to increase the dosage of the drug in order to maintain a constant response.

**Drug Interaction**

Another reaction to drugs involves that of interaction. In this case, one drug alters the action of another. Foods, alcohol, and nicotine can also interact with drugs. A system of enzymes tagged as cytochrome P-450 has been identified as the factor that contributes to many drug interactions. Cytochrome P-450 plays a key role in the oxidative biotransformation of drugs.

It is important that the physician and pharmacist have a complete list of all drugs – prescription and over-the-counter – that a patient is taking so that potential interactions can be recognized and appropriately handled. The pharmacy technician should routinely ask the patient for this information.

The table below describes a number of common drug relationships:

<table>
<thead>
<tr>
<th>Drug Relationship</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addition</td>
<td>The combined effect of two drugs. It is equal to the sum of the effects of each drug taken alone.</td>
</tr>
<tr>
<td>Antagonism</td>
<td>The action of one drug negates the action of a second drug.</td>
</tr>
<tr>
<td>Potentiation</td>
<td>An effect that occurs when a drug increases or prolongs the action of another drug, and the total effect is greater than the sum of the effects of each drug used alone. If one drug prescribed alone cannot get the desired effect, another drug can be prescribed to increase the first drug’s potency. The term is used when a drug has little or no action when given alone and the second drug increases the potency of the first drug.</td>
</tr>
</tbody>
</table>
**Synergism**

The joint action of drugs in which their combined effect is more intense or longer in duration than the sum of their individual effects. Drugs that work synergistically are usually prescribed together.

---

**ADMINISTRATION OF PHARMACOLOGIC AGENTS**

All of the information listed in this section should be review for any certified pharmacy technician. So why include it? One of the purposes of continuing education is to review concepts and information that you may not have thought about since your certification test. Also, as most of us work in a specific practice setting, we may forget certain practices that are more common to one practice setting versus another. For example, if you are an IV technician in a home infusion or hospital setting, you may see physician orders dozens of times a day, but may not review new prescriptions for oral medications as often as a technician within the retail setting. Conversely, a technician within a retail setting may not have to interpret parenteral routes of administration on an everyday basis. It is our hope that each person taking this course will reaffirm a few concepts that they may have forgotten.

**Dispensing Pharmacologically Agents**

Pharmacy technicians play a key role in the dispensing of pharmacologic agents. This role requires a thorough understanding of the components of the drug prescription and the responsibilities of pharmaceutical personnel. The prescription includes all the information necessary for the pharmacist to fill the prescription with the correct dosing form and for the patient to take the medication correctly. Two age groups of patients, elderly and pediatric, have special needs to be considered in dispensing drugs.

**The Drug Prescription**

A prescription is an order written by a physician to be filled by a pharmacist indicating the medication the patient needs. The prescription should contain:

- Patient’s name
- The date the prescription was written
- The inscription, which states the name of the drug, dose, and quantities of the ingredients.
- The signa, often referred to as the sig, which gives directions to be included on the label for the patient to follow in taking the medication
- An indication of the number of refills allowed, or “no refills” if that is the case
- The signature (handwritten, not stamped) and address of the prescribing physician
- Indication whether generic substitution is permitted
The DEA number of the prescribing physician must be on the prescription, if it is for the dispensing of a controlled substance. Pharmacy technicians should always double check a prescription for accuracy and to ensure that all of the legal requirements have been met. The label on the medication container given to the patient must include the patient’s name, date written, inscription, signa, number of refills, expiration date, the physician’s name, and the phone number and address of the pharmacy.

To fill the prescription safely, the pharmacy technician should be familiar with common abbreviations used in prescriptions, listed in the table below:

<table>
<thead>
<tr>
<th>Abbreviations</th>
<th>Translation</th>
<th>Abbreviation</th>
<th>Translation</th>
</tr>
</thead>
<tbody>
<tr>
<td>ac</td>
<td>Before meals</td>
<td>NKA</td>
<td>No known allergy</td>
</tr>
<tr>
<td>AD</td>
<td>Right ear</td>
<td>npo</td>
<td>Nothing by mouth</td>
</tr>
<tr>
<td>AS</td>
<td>Left ear</td>
<td>OD</td>
<td>Right eye</td>
</tr>
<tr>
<td>AU</td>
<td>Both ears</td>
<td>OS</td>
<td>Left eye</td>
</tr>
<tr>
<td>Bid</td>
<td>Twice a day</td>
<td>OU</td>
<td>Both eyes</td>
</tr>
<tr>
<td>C</td>
<td>With</td>
<td>pc</td>
<td>After meals</td>
</tr>
<tr>
<td>cap</td>
<td>Capsule</td>
<td>po</td>
<td>By mouth</td>
</tr>
<tr>
<td>cc</td>
<td>Cubic centimeter</td>
<td>Prn</td>
<td>As needed</td>
</tr>
<tr>
<td>DAW</td>
<td>Dispense as written</td>
<td>q</td>
<td>Every</td>
</tr>
<tr>
<td>D/C</td>
<td>Discontinue</td>
<td>qd</td>
<td>Every day</td>
</tr>
<tr>
<td>g</td>
<td>Gram</td>
<td>qh</td>
<td>Every hour</td>
</tr>
<tr>
<td>gr</td>
<td>Grain</td>
<td>q2h</td>
<td>Every 2 hours</td>
</tr>
<tr>
<td>gtt</td>
<td>drop</td>
<td>qid</td>
<td>Four times a day</td>
</tr>
<tr>
<td>hs</td>
<td>At bedtime</td>
<td>qs</td>
<td>A sufficient qty</td>
</tr>
<tr>
<td>ID</td>
<td>Intradermal</td>
<td>sig</td>
<td>Write on label</td>
</tr>
<tr>
<td>IM</td>
<td>Intramuscular</td>
<td>tab</td>
<td>Tablet</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenously</td>
<td>ss</td>
<td>One half</td>
</tr>
<tr>
<td>L</td>
<td>Liter</td>
<td>stat</td>
<td>Immediately</td>
</tr>
<tr>
<td>mcg</td>
<td>Microgram</td>
<td>syr</td>
<td>Syrup</td>
</tr>
<tr>
<td>mEq</td>
<td>Millequivalent</td>
<td>tab</td>
<td>Tablet</td>
</tr>
<tr>
<td>min</td>
<td>Minute</td>
<td>Tid</td>
<td>3 times daily</td>
</tr>
<tr>
<td>mL</td>
<td>milliter</td>
<td>Ud</td>
<td>As directed</td>
</tr>
</tbody>
</table>

While these abbreviations are standard usage for physicians, pharmacists, and their technicians, the instructions to the patient are spelled out in full and as simply as possible to ensure proper use of the medication. Most pharmacies provide the patient an information sheet with additional details regarding the proper way to take the medication (especially in regard to food intake), possible side effects, and situations in which the prescribing physician should be consulted. Limiting the number of refills allowed without another physician consultation is a way to prevent the patient from encountering severe side effects or addiction from overuse of the medication.
Five “Rights” for Correct Drug Administration

There are five “rights” of medication administration that offer useful guidelines when filling prescriptions for patient medications. These concepts have been widely used to avoid medication errors. A drug misadventure occurs whenever these are not followed correctly. The five rights are overviewed below:

- **Right Patient.** Always verify the patient’s name before dispensing medication.

- **Right Drug.** Always check the medication against the original prescription and the patient’s disease state. The medication label contains important information about the drug that will be dispensed to the patient.

- **Right Strength.** Check the original prescription for this information and pay attention to the age of the patient. Pediatric or elderly patients can easily get the wrong dose.

- **Right Route.** Check that the physician’s order agrees with the drug’s specified route of administration. Many medications can be given by a variety of routes and the route of administration can affect the medication’s absorption.

- **Right Time.** Check the prescription to determine the appropriate time for the medication to be administered. Some medications must be taken on an empty stomach (one hour before or two hours after a meal) while others should be taken with food. Sometimes a certain time span is needed between doses to maintain a therapeutically effective blood level.

Dosage Forms and Routes of Administration

There are many different forms into which a medicinal agent may be placed for the convenient and efficacious treatment of disease. The route and dosage form are determined by many factors. Among these are the disease being treated, the area of the body which the drug needs to reach, and the chemical composition of the drug itself. Each drug has its own characteristics related to absorption, distribution, metabolism, and elimination. Drugs are prepared for administration by every conceivable route. There are three routes of administration: oral, parenteral, and topical. The table below lists a few examples of these:

<table>
<thead>
<tr>
<th>Dosage Routes</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral (by mouth)</td>
<td>Swallowed&lt;br&gt;SUBLINGUAL (under the tongue)&lt;br&gt;BUCCAL (dissolves in the cheek)</td>
</tr>
<tr>
<td>Parenteral (injection through the veins, ect. for rapid entry of the drug into the circulatory system)</td>
<td>IV (vein)&lt;br&gt;INTRARTERIAL (artery)&lt;br&gt;INTRANCARDIAC (heart)</td>
</tr>
</tbody>
</table>
Medications are available in a variety of forms, and frequently a single drug will be available in a number of different forms. Examples of the common drug forms associated with the three administration routes are overviewed in the table below:

**Common Dosage Forms**

<table>
<thead>
<tr>
<th>Route</th>
<th>Primary Dosage Forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Tablets, Capsules, Solutions, Syrups, Elixirs, Suspensions, Magmas, Gels, Powders, Trouches/lozenges</td>
</tr>
<tr>
<td>Parenteral</td>
<td>Solutions, Suspensions</td>
</tr>
<tr>
<td>Topical</td>
<td>Ointments, Creams, Pastes, Powders, Aerosols, Lotions, Transdermal patches, Sprays, Inhalants, Suppositories, Enemas, Emulsions, Sponges</td>
</tr>
</tbody>
</table>
The age and condition of the patient often determine the dosage form that will be used. Pediatric and geriatric populations frequently have special needs. These two groups often need liquid dosage forms. Convenience may also play a role in the selection of the appropriate dosage forms. It has also been found that drugs with distinctive sizes, shapes and colors are inherently easier to identify. Dosage forms that reduce the frequency of administration without sacrifice of efficacy are often advantageous and facilitate patient compliance.

*Oral Routes*

The oral route is the most economical and most convenient way to give medications. The term oral means that the medication is given by mouth in either solid form, as a tablet or capsule, or in liquid form, as a solution or syrup. Once the medication enters the mouth, it must be swallowed to reach the stomach. Then it must pass to the point of absorption, most commonly the small intestine, although some medications are absorbed in the stomach.

This process takes time and is affected by several factors including the presence of food (which slows the process) or digestive disorders. It is important to refer to a reliable drug reference guide to determine if the medication should be given with or without food and whether any specific assessments should be done before dispensing it.

Sublingual (under the tongue) and buccal (between the cheek and gum) routes of administration are used when a rapid action is desired, or when a drug is specifically designed to be easily absorbed into blood vessels. The medication enters the bloodstream directly from the richly vascularized mucous membrane of the mouth and produces its effects more quickly than drugs that are swallowed. This dosage form cannot obtain the same effect if swallowed.

When taking medication by the sublingual route, the patient should hold the tablet under the tongue until it is completely absorbed. For buccal administration, the patient should place the tablet between the cheek and gums, close the mouth, and hold the tablet there until it is absorbed. It is important to remind the patient not to drink water or swallow excessively until the tablet is completely absorbed.

*Parenteral Routes*

Medications that are injected directly into the tissues of the body do not pass through the liver before entering the bloodstream. Avoiding this “first pass effect” prevents medications from being inactivated by the liver. Drugs may be injected into:

- A muscle: intramuscular
- A vein: intravenous
- The skin: intradermal
- The tissue beneath the skin: subcutaneous
- The spinal column
Drugs such as insulin are inactive in digestive juices, so swallowing them would be ineffective.

Parenteral routes also offer the potential for quick absorption of injected medication into the bloodstream and a rapid effect (especially for the intravenous route). Disadvantages include pain during administration and the possibility of infection since the skin is punctured. Also, once the medication is injected, there is no way to retrieve it if an error has been made.

**Topical Routes**

Topical medications are applied to the surface of the skin or mucous membranes. The desired effect can be local or systemic. Other topical routes are inhalation, ophthalmic, otic, nasal, and rectal.

The inhalation route delivers medications to the respiratory system. These medications are intended to produce one or more of the following effects. They are intended to alter the condition of the mucous membranes, alter the character of the secretions in the respiratory system, and treat diseases and infections of the respiratory tract.

Administration of medications via the ophthalmic route includes the instillation of a cream or ointment or placing of drops of a liquid preparation into the conjunctival sac of the eye.

A drug preparation for otic route is a drug that is used locally to treat inflammation or infection of the external ear canal or to remove excess cerumen (wax) or foreign objects from the canal. Eardrops come in solutions and suspensions. If the patient has a tube in the ear, a suspension rather than a solution should be used.

Medications can be administered into the nose by instillation or spray

Medications that are administered by the rectal route are most commonly in suppository form and enemas. Suppositories are rounded, soft pieces of easily melted glycerin. They dissolve at body temperature and release the medication to be absorbed through the walls of the large intestine.

The prominent advantage to rectal administration is that the medication does not depend on the digestive system to be absorbed into the bloodstream. Therefore, it is frequently used to treat nausea and vomiting. Suppositories also can be used for local effect to treat constipation. Additionally, the rectal route is ideal for treating fever in infants and young children.

Medications given by the vaginal route can be used to treat local infections caused by either bacteria or fungi.
Factors that Influence Drug Effects

A variety of factors can influence the effects of drugs and may require dosage adjustment. Pediatric patients and the elderly may require less of a drug, because of their smaller size or inability of the liver to metabolize the medication adequately. In these instances, if the dosage is not decreased, it may have toxic effects on the patient. The physician can use a variety of formulas when prescribing medications for the elderly and pediatric patients.

Gender also needs to be considered when prescribing some medications, especially hormonal preparations, since men and women have different amounts of hormones.

Patients with specific diseases may be unable to absorb, metabolize, or excrete various medications. Impaired gastrointestinal functions may affect absorption, impaired liver function may affect metabolism, and impaired kidney function may affect elimination. Inadequate nutritional intake may also adversely affect the metabolism of drugs. Therefore, the patient’s disease condition must be evaluated before prescribing medications.

Other factors physicians consider when prescribing medications include psychological and genetic factors. The mental state of a patient can influence the body’s ability to release chemical substances needed to appropriately absorb or metabolize a drug. Genes can also control the release of chemicals and how the body absorbs or metabolizes various medications. Unfortunately, these factors are less predictable than age, gender, and disease condition. However, if the patient does not seem to be responding to a medication, these factors should be considered.

Immune responses should also be evaluated for all patients before medications are prescribed. Allergic response to medications should be documented in the medical record, and each time a new medication is dispensed, the pharmacy technician should ask whether the patient has had any additional allergic response in order to keep the records up to date.

Special Considerations in Elderly Patients

The elderly tend to have more chronic disease than the young. They use more drugs – both prescription and nonprescription. For some elderly patients, medication is often the difference between an independent ambulatory lifestyle and confinement in a long-term care facility. Many elderly individuals take three to four medications, three to four times daily; and four out of five in this age group have at least one chronic disease. As a result, geriatric medicine has emerged as a new and important medical specialty of the healthcare system. A listing of the drugs most often used by elderly patients is given in the table below. Pharmacy technicians should be familiar with both the brand and generic names of these drugs.
### Most-Commonly Used Agents for Elderly Patients

<table>
<thead>
<tr>
<th>Generic Name and Class</th>
<th>Brand Name</th>
<th>Dosage Form</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-steroidal Anti-Inflammatory Drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Tylenol</td>
<td>Tablet, caplet, liquid, chewable, suppository</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Bayer</td>
<td>Tablet, caplet, chewable</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Advil, Motrin</td>
<td>Tablet, caplet, gel caplet, oral suspension</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Aleve</td>
<td>Tablet, caplet</td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Prozac</td>
<td>Capsule, liquid, tablet</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Paxil</td>
<td>Capsule, oral solution, suspension, tablet</td>
</tr>
<tr>
<td>sertraline</td>
<td>Zoloft</td>
<td>Tablet, liquid</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuterol</td>
<td>Proventil</td>
<td>Tablet, aerosol, solution, syrup</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>Celebrex</td>
<td>Capsule</td>
</tr>
<tr>
<td>Clonidine</td>
<td>Catapres</td>
<td>Tablet, transdermal</td>
</tr>
<tr>
<td>Conjugated estrogen</td>
<td>Premarin</td>
<td>Tablet, IM, IV, cream</td>
</tr>
<tr>
<td>Digoxin (glycoside)</td>
<td>Lanoxin</td>
<td>Tablet, elixir, capsule, IV, IM</td>
</tr>
<tr>
<td>Furosemide</td>
<td>Lasix</td>
<td>Tablet, solution, IM, IV</td>
</tr>
<tr>
<td>Levothyroxin</td>
<td>Synthroid</td>
<td>Tablet, IV</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>Zestril</td>
<td>Tablet</td>
</tr>
<tr>
<td>Loratidine</td>
<td>Claritin</td>
<td>Tablet, syrup</td>
</tr>
<tr>
<td>Triamterene (HCTZ)</td>
<td>Dyazide, Maxzide</td>
<td>Capsule, tablet</td>
</tr>
<tr>
<td>Warfain</td>
<td>Coumadin</td>
<td>Tablet</td>
</tr>
<tr>
<td>zolpidiem</td>
<td>Ambien</td>
<td>Tablet</td>
</tr>
</tbody>
</table>

**Changes in Physiologic Function**

The concept of aging has traditionally been linked to declining mental function; however, physiologic changes do not occur equally or predictably in an individual patient. Successful aging is characterized by non-pathologic loss when compared with that of average persons in the same age group. Impaired aging represents pathologic physiologic changes.

These changes occur slowly or with increasing rapidity in a wide range of body systems.
- **Optic Changes.** As the lenses become less elastic, more dense, and yellow, visual acuity is compromised; this is often correctable with eyeglasses. Macular degeneration and cataracts become a problem, often necessitating surgery.

- **Auditory Changes.** Hearing loss occurs in all frequencies, but especially in the high ranges. Impairment of sound localization and loudness perception is a problem for many elderly patients. A delay in central processing of auditory messages results in an increase in the time it takes for the person to respond to a question.

- **Gastrointestinal Changes.** These changes create many problems, among them decreases in saliva production, esophageal motility, hydrochloric acid secretion, absorptive surface, and a reduction in the rate of gastric emptying. Constipation is a daily complaint; the elderly are often preoccupied with physiologic function. Overuse of stimulant laxatives is a significant problem for some elderly patients.

- **Pulmonary Changes.** Many elderly patients have chronic obstructive pulmonary disease (COPD). Aging brings on increased rigidity of the chest wall, decreased vital capacity (maximum intake and exhalation), decreased response to hypoxia (reduced oxygen in the blood), and hypercapnia (increased carbon dioxide in the blood). If an elderly patient also has cardiac disease, these conditions are further compromised.

- **Cardiovascular Changes.** Hypertension and coronary artery disease are major issues to address. Healthy persons at rest have little age-related loss of cardiac output; during exercise, however, cardiac responses needed to meet the increased oxygen demand are diminished. To compensate, the sympathetic nervous system releases more norepinephrine and epinephrine. As a result, a compensatory increase in stroke volume occurs, and cardiac output is maintained. In elderly patients with cardiac disease, these compensatory mechanisms are impaired, resulting in decreased output.

- **Urinary Changes.** These changes can result from a decrease in the number of functioning nephrons and in renal blood flow. The elderly have a higher incidence of renal insufficiency (reduced capacity to perform). Incontinence (inability to retain urine in the bladder) is often a problem, and diapers become a necessity. Instability of bladder muscle, overflow, and sphincter weakness are the causes. Diuretics, often necessary medications to treat an existing illness, may aggravate this condition. Urinary retention may be the result of prostatic hypertrophy, malignant states, stones, anticholinergic drug intake, and urinary tract infections.

- **Hormonal Changes.** Functional changes are a natural consequence of aging.
Compositional Body Changes. The proportion of total body weight composed of fat increases with age, while lean body mass and total body mass decrease. Albumin production decreases with aging, possibly as a result of poor nutrition, hepatic disorders, or other disease states. Loss in bone density (osteoporosis) causes some loss of height. Arthritis also takes its toll on the skeletal system.

Altered Drug Responses

Age-related changes in organ functions and body composition can alter the response to medication. These factors play in important part in selecting a drug and its dosage.

• Absorption Changes. Changes in GI function with aging may affect dissolution, enzymatic breakdown, and drug ionization. Reduction in the rate of gastric emptying may delay absorption of some drugs. For most, the rate and extent of absorption are determined by passive diffusion during contact with the surface area of the gut. Reduction in absorptive surface reduces absorption. GI fluids and GI motility also decrease.

• Distribution Changes. Alterations in body composition, such as protein binding (less protein, more free drug in plasma), affect distribution of drugs. If the drug is highly protein-bound, it may have enhanced pharmacologic or toxic effects in elderly patients. Other factors that affect distribution are decreases in total body water, lean body mass, and cardiac output.

• Elimination Changes. Metabolism occurs in the liver, and the kidneys are responsible for elimination. Both processes may be altered with aging, with serious effects on blood levels of a drug. Varying degrees of renal and hepatic dysfunction may be present, depending on the patient’s disease states, the drugs used, and the degree of successful aging.

• Metabolism Changes. During metabolism, a drug is transformed biochemically to a more water-soluble compound. Elderly patients may have impaired metabolism, therefore, decreasing clearance and allowing the drug to accumulate, sometimes reaching toxic levels. Normally, blood flow per minute decreases about 1% per year as an individual ages, beginning at about the age of 35 (40% from ages 35 to 75).

Older patients are more likely to have chronic disease requiring long term treatment. Many take from three to twelve medications, and they tend to have disproportionate number of adverse drug reactions (ADRs). Maintaining medication profiles is important in these cases.

Special Considerations in Pediatric Patients

Providing drug therapy to children presents a unique set of challenges. As they grow, children undergo profound physiologic changes that affect drug absorption, distribution,
metabolism, and elimination. Failure to understand these changes and their effects can lead to underestimating or overestimating drug dosage, with the resultant potential for failure of therapy, severe adverse reactions, or perhaps fatal toxicity.

Age may be the least reliable guide to drug administration in children because of the wide variation in the relationship between age and degree of organ-system development. Height better correlates with lean body mass than body weight. Body surface area may be the best measure because it correlates with all body parameter however, it is not easily determined. Body weight is most commonly used because of its ease of calculation. Children who are small for their age should receive conservative doses, but larger children may require a dose recommended for the next higher age bracket.

Dosing pediatric patients, can be a challenge. Pediatricians often prescribe an over-the-counter medication for a child without telling the parent how to dose the drug, or they forget, thinking the dosing instructions will be on the package. A caretaker may purchase the medication only to find the drug is intended for use in a older child and appropriate dosage information for a smaller child is not provided with the medication. The pharmacist may have to determine the child’s dose for the caretaker. The pharmacy technician should always refer these questions to the pharmacist. Many factors need to be considered before recommending a drug dosage that goes beyond the printed instructions on the box.

The following considerations are important when dosing children:

- Reevaluate all dosages at regular intervals.
- Be sure the dosage is appropriate for the child’s age. A dose appropriate for a neonate may not be so for a premature infant or a toddler.
- Always double-check all computations.

Natural Chemicals that Affect Drug Action and Response

The body naturally produces several chemicals that invariably affect the metabolism of drugs. Some important chemicals are histamine, prostaglandins, and bradykinin.

Histamine

Histamine is a decarboxylation product formed from the amino acid histidine. Stress and infections can increase histidine decarboxylase activity in some tissues. Histamine is widely distributed in body fluid and almost all organs. The highest concentration is in the lungs, but significant amounts are also found in the gut, liver, skin, and peripheral nerve trunks. Histamine is bound in the mast cells, where it is stored in large cytoplasmic granules.

When an antigen (a foreign substance) enters the body, it evokes a tissue response in the form of an antibody, which is synthesized specifically to combat the particular antigen. The complex reactions that follow are believed to trigger the release of histamine. It is
this body chemical that evokes the symptoms more commonly known as the allergic reaction: red watery eyes, sneezing, urticaria (hives), rash, and bronchiolar constriction. Gastric mucosal cells (particularly the acid-secreting parietal cells) also stimulate the secretion of histamine. Histamine may be released from the mast cells by the action of competing compounds (binding sites), the process of exocytosis, and leakage due to damage to the mast cells. The aggregation of migrating leukocytes in the affected tissue is part of the inflammatory response resulting from cell degeneration. The release of histamine is the body’s mobilization of a protective mechanism. Various physical and chemical stimuli, including certain chemical compounds and drugs and antigen-antibody reactions, can trigger this release. Histamine release is definitely involved in anaphylactic shock. It is a major mediator of allergic reactions like hay fever.

**Prostaglandins**

Prostaglandins (PGs) are mediators of several physiologic processes and are synthesized from arachidonic acid, a fatty acid. They are formed by intact tissues and cells, and by extracts. They produce diverse, complex pharmacologic actions in several body systems and metabolic pathways.

**Bradykinin**

Bradykinin is a polypeptide first discovered in urine. Researchers found that with IV administration, it would lower blood pressure. Bradykinin is formed from plasma alphaglobulin and causes contraction of intestinal, uterine, and bronchial smooth muscle. Aspirin and some NSAIDs can block this reaction. It causes arterial dilation that is offset by the pressor action of increased heart rate, increased permeability (edema), and increased lymph production. It stimulates autonomic ganglion cells in contact with sensory nerve endings, which causes pain. Aspirin and other anti-inflammatory drugs antagonize this action by inhibiting synthesis of PGs, which potentiates the pain-producing action of bradykinin.
Final Exam

1. __________ studies reveal how drugs work in the body and provide critical insight for predicting the effects of each specific drug.
   a. Sterile products
   b. Aseptic technique
   c. Pharmacokinetics
   d. Merchandising

2. __________ is an important endogenous chemical messenger.
   a. Histamine
   b. Prostaglandin
   c. Bradykin
   d. All of the above

3. A receptor is a molecule on the surface of or within a cell that recognizes and binds with specific molecules, producing some effect in the cell.
   a. True
   b. False

4. When two drugs try to bind to the same receptor, _________ occurs.
   a. Efficacy
   b. Potency
   c. Site antagonism
   d. Therapeutic Index

5. __________ is a measure of drug safety.
   a. Efficacy
   b. Potency
   c. Site antagonism
   d. Therapeutic Index

6. __________ is a measure of the dose that is required to produce a response.
   a. Efficacy
   b. Potency
   c. Site antagonism
   d. Therapeutic Index
Final Exam

7. ________________ is the maximal response a drug can produce.
   a. Efficacy
   b. Potency
   c. Site antagonism
   d. Therapeutic Index

8. A _____ is the quantity of drug administered at one time.
   a. Therapeutic window
   b. Dose
   c. Potency
   d. Therapeutic Index

9. Doses and dosing intervals are determined by clinical trials and should never be changed.
   a. True
   b. False

10. The time required to achieve therapeutic levels of a drug can be shortened by the administration of a ____________.
    a. Loading dose
    b. Half life dose
    c. Double dose
    d. Triple dose

11. ______________ describe the process whereby a drug enters the circulatory system.
    a. Metabolism
    b. Elimination
    c. Absorption
    d. Loading dose

12. Bioavailability is the amount of drug that is absorbed after administration by route X compared with the amount of drug that is absorbed after intravenous (IV) administration where X is any route of drug administration other than IV.
    a. True
    b. False
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13. _______________ is the process by which a drug moves from the blood stream into other body fluids and tissues and ultimately to its sites of action, the receptors.
   
   a. Metabolism  
   b. Elimination  
   c. Absorption  
   d. Distribution

14. _______________ is a process by which drugs are converted to compounds and then excreted through metabolic pathways.
   
   a. Metabolism  
   b. Elimination  
   c. Absorption  
   d. Distribution

15. Many drugs that undergo liver metabolism will be extensively metabolized during this passage from the GI tract to the body. This effect of liver metabolism is called:
   
   a. Elimination  
   b. Absorption  
   c. First-pass effect  
   d. Steady state concentration

16. In general, ___________ converts drugs to more water-soluble (less lipid-soluble) forms.
   
   a. Metabolism  
   b. Elimination  
   c. Absorption  
   d. Distribution

17. Elimination occurs primarily in the kidney and the bowel, but other routes exist.
   
   a. True  
   b. False

18. Total body clearance is the sum of the clearance from the various organs, involved in drug metabolism and elimination.
   
   a. True  
   b. False
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19. ___________ is a calculation of the apparent volume in which a drug is dissolved.
   a. Clearance
   b. Steady-state concentration
   c. First order kinetics
   d. Volume distribution

20. With ________ elimination, a constant percentage is lost per unit of time.
   a. First-Order
   b. Zero-Order
   c. Both A and B
   d. None of the above

21. ___________ _________ is also known as non-linear or dose-dependent or dose dependent kinetics.
   a. First-Order
   b. Zero-Order
   c. Both A and B
   d. None of the above

22. The term dose-dependent refers to drugs that are first-order at lower doses and switch to zero-order at higher doses.
   a. True
   b. False

23. When a drug is given as a continuous infusion it will increase in concentration in the blood until the rate of elimination is equal to the infusion rate. This is referred to as:
   a. Clearance
   b. Steady-state concentration
   c. First order kinetics
   d. Volume distribution
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24. The time needed to reach steady state depends only on the half-life of the drug. ___ percent of steady state is reached in 3.3 half-lives.
   a. 45   b. 50   c. 75   d. 90

25. A single dose of a drug that will result in the desired plasma concentration is called a ________.
   a. Loading dose   b. Steady-state concentration   c. First order kinetics   d. Volume distribution

26. Side effects are secondary responses to a drug other than the primary therapeutic effect for which the drug was intended.
   a. True   b. False

27. The first exposure to an allergen generally gives an immediate harmful response.
   a. True   b. False

28. __________ is a dependence characterized by perceived need to take a drug to attain the psychological and physical effects of mood-altering substances.

29. __________ describes a state in which a person’s body had adapted physiologically and psychologically to a drug and cannot function without it.
30. ___________ is a decrease in responses to the effects of a drug due to its continued administration.
   a. Dependence
   b. Addiction
   c. Abuse
   d. Tolerance

31. ___________ is a case when one drug alters the action of another.
   a. Dependence
   b. Addiction
   c. Drug interaction
   d. Tolerance

32. The age and condition of the patient should not be a factor in determining the dosage form to be used.
   a. True
   b. False

33. The _______ route is the most economical and convenient way to give medication.
   a. Oral
   b. Parenteral
   c. Topical
   d. All of the above

34. The _______ route has medications injected directly into the tissues of the body and do not pass through the liver before entering the bloodstream.
   a. Oral
   b. Parenteral
   c. Topical
   d. All of the above

35. Drugs such as insulin are inactive in digestive juices, so swallowing them would be ineffective.
   a. True
   b. False
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36. __________ routes are applied to the surface of the skin or mucous membranes.
   a. Oral
   b. Parenteral
   c. Topical
   d. All of the above

37. Medications can be administered into the nose by:
   a. Instillation
   b. Spray
   c. Both A and B
   d. None of the above

38. __________ is a polypeptide first discovered in urine.
   a. Histamine
   b. Prostaglandin
   c. Bradykinin
   d. None of the above

39. __________ is a decarboxylation product formed from the amino acid histidine.
   a. Histamine
   b. Prostaglandin
   c. Bradykinin
   d. None of the above

40. __________ are mediators of several physiologic processes and are synthesized from arachidonic acid, a fatty acid.
   a. Histamine
   b. Prostaglandin
   c. Bradykinin
   d. None of the above