Pharmacology Training Course
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LESSON ASSIGNMENT

LESSON 1
Professional References in Pharmacy.

TEXT ASSIGNMENT
Paragraphs 1-1 through 1-6.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

1-1. Given a description of a reference used in a pharmacy and a list of pharmacy references, select the particular reference being described.

1-2. Given a description of a situation requiring the use of a pharmacy reference and a list of pharmacy references, select the reference most likely to contain the information required in that situation.

SUGGESTION
After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 1
PROFESSIONAL REFERENCES IN PHARMACY

Section I. GENERAL

1-1. CONSIDERATIONS INVOLVED IN SELECTING A REFERENCE

   a. At this point, you may already possess a strong background in pharmacology. However, if you do not take steps to maintain and expand your knowledge in pharmacology, you will quickly find yourself out-of-date in terms of drugs and drug therapy. Furthermore, no individual knows everything about every drug used in medicine. What happens when a drug-related question arises? What sources of drug information should be readily available in the pharmacy? Which reference should be consulted to find the answer to a specific question? These questions will be examined in this lesson.

   b. This lesson does not attempt to every available pharmaceutical reference. Instead, this lesson will focus on some references that are commonly used in the practical of pharmacy.

   c. Some references, by design, are tailored to meet the needs of those persons who have strong backgrounds in pharmacy, physiology, and/or medicine. Therefore, you should carefully select references that are written to a level comparable to your background and experience. An individual who lacks a technical background can become frustrated when reading a highly technical reference.

1-2. HUMAN SOURCES

   Use human sources of information. Most health care professionals are more than willing to share their knowledge and experience. Carefully identify those professionals who are willing to instruct you and/or answer your questions. Also, you should be willing to share your knowledge and experience with others.

Section II. PHARMACEUTICAL JOURNALS

1-3. OVERVIEW

   a. Journals serve as excellent sources of drug information. For the most part, the information contained in journals is up-to-date. Journals reflect the state of the art of that discipline at that point in time.
b. Some journals are designed to be read by many members of the medical community. Other journals are specifically written to meet the needs of the individuals who are directly involved with the field of pharmacy. Further, some journals are especially written for pharmacy personnel, who work in hospitals, while others are designed for those who work in retail.

c. As you know, there are many journals written for people who work in the medical field. Some journals are designed to be read by the members of many medical disciplines, while other journals focus on a particular job specialty (that is, nursing, pharmacy, or medical technology). Many journals are written to meet the needs of those in pharmacy practice. Some of these journals are especially written for pharmacy personnel who work in an inpatient setting, while other journals are designed for those who work in an outpatient environment.

d. To meet your individual needs, you should become familiar with some frequently used pharmacy journals, the type of information each contains, and the particular group(s) for whom the journal is written.

e. As you read a journal, do not limit yourself to the main articles. Letters to the editor, advertisements, and job announcements also provide information, which can be very helpful. For example, these parts of a journal can provide up-to-date information on new products, changes in old products, as well as short- and long-term trends in the state of the art of pharmacy practice.

1-4. SPECIFIC JOURNALS

a. **The American Journal of Health-Systems Pharmacists.** The American Journal of Health-Systems Pharmacists (AJHP) is an official publication of the American Society of Health-Systems Pharmacists. It is published on a twice monthly basis. As the name implies, this journal is tailored to pharmacy personnel who practice in a hospital setting. The AJHP can be read and understood by almost all-medical personnel who have a background in pharmacy. The AJHP contains information on drug therapy, new and innovative pharmacy practices, and other topics of particular interest to hospital pharmacy personnel.

b. **Hospital Pharmacy.** This journal is a monthly publication of the L. B. Lippincott Company. Although designed for hospital pharmacists, the journal's contents can be read and understood by medical personnel who have a background in pharmacy. Hospital Pharmacy contains information on innovative pharmacy procedures (that is, unit dose), drug therapies, and other topics of general interest. One section, "Medication Error Reports," provides a constant reminder of the types of medication errors that occur in a hospital.

c. **The American Journal of Intravenous Therapy.** The McMahon Publishing Company on a bimonthly basis publishes this journal. The journal is tailored toward those persons directly involved with the preparation and/or administration of intravenous
products. Therefore, it is particularly useful to the pharmacy personnel who work in the unit-dose/sterile product area. Experienced sterile product prepares should be able to read and understand this journal. Articles in this journal focus on the theoretical and practical considerations of intravenous therapy.

d. **American Pharmacy.** This journal is the official publication of the American Pharmaceutical Society. It is published on a monthly basis. It is especially designed for pharmacists who work in an outpatient environment, although the journal contains useful information for all pharmacy personnel. Articles in American Pharmacy cover a variety of pharmacy-related topics. For example, changes in drug laws, changes in drug therapies, and perspectives on the various aspects of health-care management are found in the journal.

e. **Clinical Pharmacology and Therapeutics.** This journal is the official publication of the American Society for Clinical Pharmacology and Therapeutics and the American Society for Pharmacology and Experimental Therapeutics. As the name implies, the journal is designed to communicate up-to-date drug information and research related to pharmacology to those medical personnel who have an in-depth background in pharmacology, therapeutics, and the basic sciences.

f. **The Journal of Clinical Pharmacology.** This journal is the official publication of the American College of Clinical Pharmacology. This publication is designed for those medical personnel who have an excellent background in pharmacology, therapeutics, and the basic sciences. Articles focus on clinical research pertaining to pharmacology.

**Section III. PHARMACEUTICAL TEXTS**

1-5. OVERVIEW

As with journals, many texts are available to pharmacy personnel. Some texts require a certain amount of background knowledge in physiology, anatomy, and/or pharmacology. It is important for you to recognize your background strengths and weaknesses before you begin to search for a text to answer a particular question. You should also be familiar with the subjects discussed in each of these texts. Being able to identify a text on your knowledge level, which can provide you with the answer you are seeking, can pay dividends in terms of saved time and reduced frustration.

1-6. SPECIFIC TEXTS

a. **The Physicians' Desk Reference.** The Physicians' Desk Reference (PDR) is published on an annual basis by the Medical Economics Company. The drug manufacturers, whose products are listed in the reference, prepare the information contained in the PDR. For the most part, the drug monographs in the PDR come
directly from the package inserts for the drugs. The publisher supplies periodic supplements to the text. The PDR is written primarily for physicians; however, many medical personnel have the background to use the reference. The PDR is divided into the following nine areas:

1. **The Manufacturers’ Index.** This section supplies information (that is, address and telephone number) on the manufacturers who supplied prescribing information for the PDR.

2. **The Product Name Index.** This section provides an alphabetical listing of the drug products by trade name and the page number where the drug product information may be located.

3. **The Product Classification Index.** This section of the PDR provides an alphabetical listing of the drug products by their therapeutic classifications. Page numbers for locating the drug products are provided for quick reference.

4. **The Generic and Chemical Name Index.** In this section, the products are categorized under generic and chemical name headings according to their principal components.

5. **The Product Identification Section.** This section of the PDR provides a pictorial display (by manufacturer) of capsules, tablets, and containers. This area can be used to identify products that one does not immediately recognize by appearance.

6. **The Product Information Section.** Manufacturer lists this alphabetical arrangement of over 2,500 pharmaceuticals. The drug products are fully described in the following areas: common names, generic compositions, chemical names, composition, action and uses, administration and dosage, contraindications, precautions, side effects, supplied, and other information concerning use.

7. **The Diagnostic Product Information Section.** The PDR focuses on the descriptions of diagnostic products. This section of PDR focuses on the descriptions of diagnostic products. The products are listed alphabetically.

8. **The Poison Control Centers Section.** This section contains a list of poison control centers and their emergency telephone numbers.

9. **The Guide to Management of Drug Overdose Section.** This section is located on the inside back cover of the PDR. The aim of this section is to provide the physician with useful information on the management of drug overdoses. Of course, any individual who is suspected to have ingested an overdose of medication should be taken to the nearest medical treatment facility for prompt attention and treatment.

b. **Remington’s Pharmaceutical Sciences.** Mack Publishing Company publishes this text. Although written for pharmacists, who work in any pharmacy setting,
the reference can be read, understood, and used by other medical/pharmacy personnel. Remington's deals with the theory and practice of the art of pharmacy. It provides essential information about drugs. Furthermore, the text is especially useful as an information source for the compounding of extemporaneous products.

c. **The Pharmacological Basis of Therapeutics.** Louis Goodman and Alfred Gilman wrote this text. This reference is written for medical personnel who have a strong background in physiology and pharmacology. Indeed, it is not written for a reader who has a weak or limited background in the sciences. The clinical application of drug knowledge is the aim of the text. The book is divided into major sections based upon therapeutic categories. Sections are subdivided into chapters that focus on specific drug uses. Each chapter has an excellent overview of the therapeutic area and a discussion of considerations pertinent to the topic being examined.

d. **American Medical Association Drug Evaluations.** The American Medical Association (AMA) Department of Drugs prepares this text. The book is written on a level that can be read and understood by medical personnel who have a good background in physiology and pharmacology. American Medical Association Drug Evaluations is divided into sections based upon therapeutic classifications. Each chapter has an introductory statement that discusses considerations involved with that therapeutic category. Further, each chapter contains informative monographs on drugs pertinent to that category. Dosage information is provided under each drug monograph.

e. **Drug Interactions.** Philip D. Hansten wrote this text. It is written for the health-care provider who is concerned about drug interactions and/or the effects upon clinical laboratory tests by specific agents. Section one of the book is divided into chapters based upon drug interactions of particular therapeutic categories. Section two deals with the impact of certain medications upon specific clinical laboratory test results.

f. **Dorland's Illustrated Medical Dictionary.** W. B. Saunders Company publishes this reference. This medical dictionary is a useful reference for all medical personnel. In particular, the dictionary can be used by pharmacy personnel whenever unfamiliar medical terms are encountered.

g. **Handbook of Injectable Drugs.** This book was written by Lawrence A. Trissel. It is especially tailored to meet the needs of pharmacy personnel who are directly involved with the preparation of intravenous admixtures. The text is easily used; however, care should be exercised when using the charts provided in the reference. The drugs listed are limited to injectable products. For each drug, a monograph is provided which includes information on drug concentration, stability, pH, dosage, compatibility, and incompatibility.

h. **The American Hospital Formulary Service.** The American Hospital Formulary Service (AHFS) is a two-volume collection of drug monographs published by the American Society of Health-Systems Pharmacists. The AHFS is designed to be used by all pharmacy personnel. It is divided into sections based upon therapeutic
categories. A general statement pertaining to the therapeutic category is included at the beginning of each individual section. Individual drug monographs that present information on drug chemistry, dosage, and preparations follow this general statement. Information on the drug monographs is kept current by periodic supplements to the AHFS.

i. **The American Drug Index.** Norman Billups writes the American Drug Index (ADI). The book is designed to provide information to all medical personnel in general and to pharmacy personnel in particular. The monographs contained in the ADI are listed in alphabetical order. Both trade and generic names are provided. The monographs in the ADI do not provide information on actions and dosage. Instead, specific information (that is, manufacturer, amount of each ingredient present in the dosage form and the use of the drug) is provided for each product listed.

j. **Pharmaceutical Calculations.** Mitchell J. Stoklosa wrote this reference. It was designed for use as a calculation text. Although it is not a pharmacology text, it is useful to rely on such a reference when questions on dosage calculations arise. Periodic review of calculation concepts is helpful to all pharmacy personnel.

k. **Facts and Comparisons.** Facts and Comparisons, Inc wrote this reference. It is designed to be used by most medical personnel in general and by pharmacy personnel in particular. Facts and Comparisons are organized into twelve main chapters by drug use. Drugs and/or drug products are listed together in such a way as to provide rapid comparisons between drugs or products that are similar in use or content. Individual drug monographs provide comprehensive information on drug actions, contraindications, warnings and precautions, drug interactions, adverse reactions, over-dosage, and administration and dosage. The publisher provides monthly updates of this loose-leaf text. These updates ensure that the most recent information on new products and developments in drug therapy are available to the reader. Moreover, the publisher has available a slide-tape presentation which provides information on the use of the reference.

l. **Handbook of Poisoning: Diagnosis and Treatment.** This text was written by Dr. Robert H. Dreisbach and published by Lange Medical Publications. This reference provides a concise summary of the diagnosis and treatment of many poisons. The book is divided into chapters that discuss such topics as general considerations (that is, prevention and management), agricultural poisons, industrial hazards, household hazards, medicinal poisons, and animal and plant hazards. Information on first-aid measures is found on the front and back covers of the text.

m. **The United States Pharmacopoeia and The National Formulary.** The United States Pharmacopoeia and The National Formulary reference contains standards and tests for quality, purity, strength, packaging, and labeling of drugs in the United States. This reference is designed to be used by researchers and pharmacists who are concerned about the standards that have been established for drugs. The United States Pharmacopoeia and The National Formulary reference has information.
that is useful for personnel who are involved in both inpatient and outpatient pharmacy practice. Annual supplements to the reference ensure that it contains the latest information on the state of the art of pharmacy.

n. **United States Pharmacopoeia Dispensing Information.** The United States Pharmacopoeia Convention, Inc publishes the *United States Pharmacopoeia Dispensing Information* annual publication. This reference is designed to be used by individuals who dispense drugs and by persons who administer drugs after the drugs have been prescribed. The following information about a drug is discussed in the text: category of use, precautions to use, (that is, drug interactions and medical warnings), drug preparation immediately prior to administration, side effects with an indication of their significance, guidelines for patient consultation on safe and effective use of the drug, dosing information, and requirements for packaging and storage. One section, "Advice for the Patient," provides guidelines for patient use of the drug. These guidelines are written in lay terms. Bimonthly updates keep the information in the United States Pharmacopeial Dispensing Information current.

**Section IV. ELECTRONIC DRUG INFORMATION SERVICES**

1-7. **OVERVIEW**

As with journals and texts, electronic forms of drug information are now available to pharmacy personnel. Most of the reference texts discussed previously are available on CD-ROM for single or network use. Some examples are Facts and Comparisons, the PDR, and Clinical Pharmacology. The advantages of this form of information include easy access to information and timely updates (monthly, quarterly, semiannually). Micromedex® is another information system available as a subscription at most military pharmacies. Micromedex® provides drug information monographs, drug identification (Identidex®), poison information (Poisindex®), material safety data sheets, Martindale’s Extra Pharmacopeia, AfterCare Notes®, as well as many other options. The majority of these systems are user friendly and easy to use with minimal orientation.

The most current information about drug use, even prior to approval by the Food and Drug Administration, is available in medical journals. Medical journals are accessed through on-line searches such as Medline® and Grateful Med®. Many U.S. medical teaching institutions and major medical centers offer search capabilities via the Internet or through their respective medical libraries. The use of on-line information services often requires a thorough orientation to perform a good search.

*Continue with Exercises*
INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. A friend has brought several capsules for you to identify; however, at first glance you are unable to name the particular medication. Select, references below, the reference you would use to identify the capsule.
   a. The Physicians' Desk Reference.
   b. Dorland's Illustrated Medical Dictionary.
   c. The United States Pharmacopoeia and the National Formulary.
   d. America Medical Association Drug Evaluations.

2. Select, from the list below, the reference that deals with the theory and practice of the art of pharmacy. It is especially useful as an information source for the extemporaneous compounding of products.
   a. The Pharmacological Basis of Therapeutics.
   b. The United States Pharmacopoeia Dispensing Information.
   c. The American Hospital Formulary Service.
   d. Remington's Pharmaceutical Sciences.

3. Select, from the list below, the journal that focuses on the sterile products/unit-dose area of the hospital pharmacy.
   b. Hospital Pharmacy.
   c. The American Journal of Intravenous Therapy.
   d. American Pharmacy.
4. Select, from the references below, the journal tailored to meet the needs of pharmacy personnel whose practice is in a hospital setting. This journal contains information on drug therapy and new and innovative pharmacy practices.

   a. The American Journal of Intravenous Therapy.
   b. The American Journal of Health-Systems Pharmacists.
   d. American Pharmacy.

5. Select, from the list below, the journal that primarily contains articles related to clinical research in pharmacology.

   b. American Pharmacy
   c. The Pharmacological Basis of Therapeutics.
   d. Hospital Pharmacy.

6. Select, from the list below, the journal that is tailored to meet the needs of pharmacists who work in an outpatient pharmacy environment.

   b. Clinical Pharmacology and Therapeutics.
   c. The Physicians' Desk Reference.
   d. American Pharmacy.
7. You have a question pertaining to the effect upon a particular laboratory test by a specific medication. From the list below, select the reference most likely to provide you the information you need.

   a. America Medical Association Drug Evaluation.
   b. Drug Interactions.
   d. Remington's Pharmaceutical Sciences.

8. During your reading of a journal article, you encounter the word "retroinfection." From the references below, select the reference you would use to find the meaning of that term.

   a. Dorland's Illustrated Medical Dictionary.
   b. America Medical Association Drug Evaluations.
   d. Handbook on Injectable Drugs.

9. A friend of yours is concerned about the safety of his children. It seems that he believes he has many poisonous plants and chemicals in his home. From the list below, select the reference most likely to give him the information he needs to make a decision.

   a. Facts and Comparisons.
   b. The American Hospital Formulary Service.
   c. Handbook of Poisoning: Diagnosis and Treatment.
   d. The American Drug Index.
10. Select, from the list below, the reference that contains a section, which provides pharmacy personnel with specific information that should be communicated to the patient concerning the use of a particular drug.

   a. The American Drug Index.
   b. Handbook of Poisoning: Diagnosis and Treatment.
   c. The Pharmacological Basis of Therapeutics.
   d. The United States Pharmacopeia Dispensing Information.

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 1

1. a The Physicians’ Desk Reference. (para 1-6a)
2. d Remington’s Pharmaceutical Sciences. (para 1-6b)
3. c The American Journal of Intravenous Therapy. (para 1-4c)
4. b The American Journal of Health-Systems Pharmacists. (para 1-4a)
5. a The Journal of Clinical Pharmacology. (para 1-4f)
6. d American Pharmacy. (para 1-4d)
7. b Drug Interactions. (para 1-6e)
8. a Dorland’s Illustrated Medical Dictionary. (para 1-6f)
9. c Handbook of Poisoning: Diagnosis and Treatment. (para 1-6l)
10. d The United States Pharmacopoeia Dispensing Information. (para 1-6n)

End of Lesson 1
LESSON ASSIGNMENT

LESSON 2
Anatomy, Physiology, and Pathology Important to Pharmacology.

TEXT ASSIGNMENT
Paragraphs 2-1 through 2-20.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

2-1. Given a term pertaining to anatomy, physiology or pathology and a group of definitions, select the definition of that term.

2-2. Given the name of a system of the body and a group of functions, select the function of that system.

2-3. Given the name of a structural component of a cell and a group of descriptions, select the most appropriate description of that structure.

2-4. Given the name of a type of tissue and a group of descriptions, select the most appropriate description of that type of tissue.

2-5. Select from a list of functions the function of the skin.

2-6. Given the name or type of a disease of the skin and a group of descriptions, select the best description of that particular disease.

2-7. Given a cause of disease and a group of statements discussing various causes of disease, select the statement that best describes that cause.

SUGGESTION
After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 2
ANATOMY, PHYSIOLOGY, AND PATHOLOGY IMPORTANT TO PHARMACOLOGY

Section I. PRINCIPLES OF ANATOMY AND PHYSIOLOGY

2-1. ANATOMY AND PHYSIOLOGY

a. Anatomy is the study of the structure of the body. Often, you may be more interested in functions of the body. Functions include digestion, respiration, circulation, and reproduction. Physiology is the study of the functions of the body.

b. The body is a chemical and physical machine. As such, it is subject to certain laws. These are sometimes called natural laws. Each part of the body is engineered to do a particular job. These jobs are functions. For each job or body function, there is a particular structure engineered to do it.

c. In order to read and understand basic concepts in pharmacology, you must be familiar with certain topics in anatomy, physiology, and pathology. It is not the intent of this subcourse to discuss these areas in detail. Instead, the content of this lesson should give you the knowledge required to complete this subcourse. If you want, you can read texts and references that discuss these areas in detail.

2-2. ORGANIZATION OF THE HUMAN BODY

The human body is organized into cells, tissues, organs, organ systems, and the total organism.

a. Cells are the smallest living unit of body construction.

b. A tissue is a grouping of like cells working together. Examples are muscle tissue and nervous tissue.

c. An organ is a structure composed of several different tissues performing a particular function. Examples include the lungs and the heart.

d. Organ systems are groups of organs, which together perform an overall function. Examples are the respiratory system and the digestive system.

e. The total organism is the individual human being. You are a total organism.
2-3. SYSTEMS OF THE BODY

A system is a combination of parts or organs, which, in association, perform some particular function. The systems of the body are as follows:

a. **Integumentary.** Covers and protects the body from drying, injury, and infection, and has functions of sensation, temperature regulation, and excretion.

b. **Skeletal.** Provides a framework for the body, supports the organs, and furnishes a place of attachment for muscles.

c. **Muscular.** Provides the force for the motion and propulsion of the body.

d. **Respiratory.** Absorbs oxygen from the air and gives off the carbon dioxide produced by the body tissues.

e. **Cardiovascular.** Functions in the transportation of blood throughout the body.

f. **Lymphatic (System of Vessels and Glands).** Returns protein and fluid to the blood from the various body tissues; also furnishes the body with protective mechanisms against pathogenic organisms.

g. **Gastrointestinal.** Digests and absorbs food substances and excretes waste products.

h. **Genitourinary.** Excretes and transports urine (urinary), and elaborates and transports reproductive cells and sex hormones (reproductive).

i. **Nervous and Special Senses.** Gives the body awareness of its environment, and enable it to react to that environment.

j. **Endocrine.** Manufactures hormones, which are active in the control of much of the body activity and behavior.

Section II. CELLS

2-4. INTRODUCTION

Each of the 100 trillion cells in a human being is a living structure that is capable of surviving indefinitely. In most instances, the cell can reproduce itself provided its surrounding fluids remain intact. To understand the function of the various organs and other structures of the human body, it is essential that you first understand the basic organization of the cell and the functions of its component parts.
2-5. STRUCTURAL COMPONENTS OF A CELL

The cell was once viewed as a bag of fluid, enzymes, and chemicals. Now, we understand that the cell is an extremely complex living entity. With the advent of electron microscopy in the early 1940's, several distinct cellular structures called organelles were clearly recognized. A typical animal cell contains several types of these organelles (Figure 2-1). Each organelle has an important role in the functioning of the cell. It is important for you to become familiar with these organelles.

a. **Cell Membrane.** (Animal cells do not have cell walls; they have cell membranes only. Plant cells have both cell walls and cell membranes.)

(1) Practically all the structures within the cell, as well as the cell itself, are lined with a porous, elastic membrane. The cell membrane is composed primarily of lipids (fats) and proteins that are arranged in layers at right angles to each other (Figure 2-1).

![Diagram of a cell membrane](image)

Figure 2-1. Diagram of a cell membrane.

(2) The lipids of the cell wall are composed of two portions: a long hydrocarbon chain (that is insoluble in water) and a glycerol-phosphate head (that is soluble in water). The long chains are in the center of the protein and the glycerolphosphate group is attached to the end of the protein.

(3) The cell membrane contains many pores. It is through these pores that lipid-insoluble particles, such as water and urea, pass between the interior and the exterior of the cell. Diffusion experiments have shown that particles up to approximately 8-Angstrom units in diameter pass through the pores freely.

(4) The main function of the cell membrane is to regulate the flow of substances into and out of the cell. This regulation of flow is accomplished by the membrane's **selective permeability.** That is, only certain substances may pass through
the pores. This is important, since the cell must obtain the nutrients for its growth from the extracellular fluid (fluid outside the cell) and discard waste products back into the extracellular fluid.

b. **Cytoplasm (Figure 2-2).** Cytoplasm is the fluid or semifluid contained inside the cell membrane, but outside the nucleus. The cytoplasm functions as a medium to contain many substances, such as fats, glucose, proteins, water, and electrolytes. The clear portion of the cytoplasm is called hyaloplasm. Located within the cytoplasm are the organelles that perform highly specialized functions in the cell.

c. **Nucleus (Figure 2-2).** The nucleus is the control center for the cell. It controls the reproduction of the cell as well as the chemical reactions that occur within the cell. The nucleus contains large amounts of deoxyribonucleic acid (DNA). The DNA is responsible for controlling the characteristics of the protein enzymes of the cytoplasm, and thus, it controls cytoplasmic activities. The DNA is also responsible for controlling the hereditary characteristics of individuals.

d. **Mitochondria (Figure 2-2).** The mitochondria may be called the power house" of the cell. The mitochondria are the site of cell respiratory activity. The mitochondria are found in the cytoplasm. They are usually located near energy requiring structures (that is, nodes of nerves, contracting ligaments of muscles, active transport mechanisms in membranes and ribosomes). Their numbers depend on the amount of energy required by the cell to perform its function. Several infoldings of the inner unit membrane form shelves on which practically all of the oxidative enzymes of the cell are said to be absorbed. When nutrients and oxygen meet these enzymes, they combine to form carbon dioxide, water, and energy. The liberated energy is used to synthesize ATP (adenosine triphosphate). This ATP then diffuses throughout the cell and releases its energy whenever it is needed for cellular functions.

e. **Lysosomes (Figure 2-2).** Lysosomes may be called the digestive organs of the cell. Lysosomes are surrounded by a membrane and contain digestive (hydrolytic) enzymes. When this membrane ruptures, it releases the digestive enzymes that will break down particles or molecules located near the ruptured area. For example, they surround pinocyticle vesicles containing food particles and digest them. If a sufficient number of lysosomes rupture, the entire cell may be digested. When the lysosomes function properly, products of digestion can be used by the cell.

f. **Nucleoli (Figure 2-2).** In the nucleus of many cells, there may be one or more structures called nucleoli. The nucleoli do not have a limiting membrane, as do most organelles. These structures are primarily aggregate of loosely bound granules composed mainly of ribonucleic acid (RNA). Hereditary units called genes are thought to synthesize and store in the nucleolus. This stored RNA diffuses into the cytoplasm where it controls cytoplasmic function. Therefore, the main functions of the nucleolus are the synthesis of RNA and the storage of RNA.
Figure 2-2. Diagram of the cell.

g. **Endoplasmic Reticulum (Figure 2-2).** The endoplasmic reticulum is a network of tubules and vesicles (saclike structures) in the cytoplasm. The inside of the tubules and vesicles is filled with endoplasmic matrix, a fluid medium, which is different from the fluid outside the endoplasmic reticulum. In the matrix, there are enzyme systems. The first function of the endoplasmic reticulum is to use these enzymes to synthesize various substances (that is, lipids). The endoplasmic reticulum is connected
to the nuclear membrane and, in some cases, it is connected directly through small openings to the exterior of the cell. A second function of the endoplasmic reticulum is to transport various substances, through the vast network of tubules, from one part of the cell to another area of the cell. A third function of the endoplasmic reticulum is to store various substances within the cell.

h. Ribosomes (Figure 2-2). Ribosomes are small particles that are usually attached to the endoplasmic reticulum. Ribosomes are the site of protein synthesis and are referred to as "protein factories" of the cell. Ribosome is composed mainly of ribonucleic acid (RNA).

2-6. PINOCYTOSIS

Pinocytosis is the engulfing of small particles or fluids by the cell. That is, when these substances meet the cell membrane, they cause the membrane to form a channel. At the end of this channel, small vesicles form. These vesicles contain the substance and some extracellular fluid. The vesicle then breaks away from the rest of the membrane and migrates toward the center of the cell. Figure 2-3 illustrates the process of pinocytosis.

1. Particles contact cell membrane.

2. Vesicle (saclike structure) is formed.

3. Vesicle containing the particles passes into the cell.

Figure 2-3. Pinocytosis.
2-7. PHAGOCYTOSIS

Phagocytosis is the engulfing of solid particles by a cell. For example, bacteria could be surrounded and ingested by a cell. The mechanism of phagocytosis is similar to that of pinocytosis. However, in phagocytosis, the cell acts to surround the particle with the cell membrane and form a vesicle (sac) containing the particle and cytoplasm. Then, the vesicle breaks away from the cell wall and moves toward the center of the cell. Figure 2-4 illustrates phagocytosis.

Figure 2-4. Phagocytosis.

Section III. TISSUE

2-8. DEFINITION OF TISSUE

A tissue is composed of a group of cells, which are the same or similar in nature. For example, liver cells are bound together into a tissue called liver, and bone cells are bound together with a large amount of lime salts to form bony tissue. The various tissues of the body have different characteristics because the cells that make up these tissues are different both in structure and in function.

2-9. TYPES OF TISSUE

There are four primary tissues as follows: epithelial, connective, muscular, and nervous.

a. Epithelial (Figure 2-5). This tissue covers the outer surface of the body and forms the lining of the intestinal and respiratory systems. A special form called endothelium lines the heart and blood vessels. As serous membranes, it lines the cavities of the abdomen, the chest, and the heart, and covers the organs that lie in these cavities. Epithelial tissue forms the glands and parts of the sense organs. According to its location, this tissue has different functions. As the skin, it protects underlying structures; in the small intestine, it absorbs; in the lungs, it is a highly permeable membrane; in glands, it secretes; and in the kidneys and liver, it both secretes and excretes. There are three types of epithelial tissue based on the shape of the cells. These are squamous (flat), cuboidal, and columnar. These cells are further
designated as simple if they are arranged in a single layer, or stratified if arranged in layers.

Figure 2-5. Epithelial tissue.

b. Connective (Figure 2-6). This tissue is widely distributed throughout the body. It binds other tissues together and supports them, forms the framework of the body, and repairs other tissues by replacing dead cells. Principal types of connective tissue are osseous (bony), cartilaginous, fibrous, elastic, and fatty. Areolar tissue, which lies under the skin and serves to fill many of the sharp corners and small spaces of the body, is a mixed type composed of fibrous, elastic, and fatty connective tissue.

Figure 2-6. Connective tissue.
c. **Muscular (Figure 2-7).** This tissue is of three kinds: voluntary (striated), involuntary (smooth), and cardiac.

![Muscle tissue](image)

Figure 2-7. Muscle tissue.

d. **Nervous (Figure 2-8).** This tissue is made up of nerve cells (neurons) and supporting structure of nervous tissue (neuroglia).

![Neuron and neuroglia](image)

Figure 2-8. Neuron and neuroglia.
Section IV. SKIN

2-10. DESCRIPTION OF SKIN

The skin is a tough, elastic structure covering the entire body (Figure 2-9). It is made up of two principal layers, the epidermis or cuticle and the dermis or true skin. The epidermis, which overlies the dermis, is itself composed of a superficial layer and an inner layer. The superficial or horny layer consists of dead cells that are constantly being worn off. These are replaced from the living cells that form the inner layer. The dermis is the thicker part of the skin, and consists of connective tissue containing blood vessels, nerve endings, sweat glands, sebaceous glands, and hair follicles. The dermis is held in place by a layer of areolar connective tissue.

Figure 2-9. Structure of the skin (cross section).

2-11. FUNCTIONS OF THE SKIN

a. Protection. The skin protects underlying structures by acting as a mechanical barrier. When the skin is broken, bacteria may invade the body through the opening.

b. Regulation of Body Temperature. The skin regulates the body temperature by controlling heat loss in two ways:

(1) The blood vessels in the skin change in size; they dilate and bring warm blood to the surface to increase heat loss, and they constrict to decrease heat loss.
(2) The skin produces sweat which, when it evaporates, cools the body surface.

c. **Sensory Perception.** The skin acts as an organ of perception. It contains sensory nerve endings which are specialized to detect heat, cold, pressure (touch), and pain.

d. **Excretion.** The excretion of waste products through the skin is a function of the sweat glands that open by a duct onto the skin surface. The opening is called a pore. These glands are distributed in large numbers over the body and secrete an average of a quart of perspiration each day; although, the amount varies considerably, depending on the temperature and humidity of the atmosphere, and the amount of exercise performed by the individual. Perspiration is continuous, but it may be so slow and the sweat may evaporate so quickly that it is imperceptible. Sweat consists chiefly of water (99 percent), with small quantities of salts and organic materials which are waste products. Skin also secretes a thick substance, sebum. This material is the product of the sebaceous glands, and its purpose is to lubricate the skin and keep it soft and pliable.

e. **Absorption.** Although not one of its normal functions, the skin is capable of absorbing water and other substances. Physicians take advantage of this fact by prescribing local application of certain drugs.

2-12. **APPENDAGES OF THE SKIN**

The appendages of the skin include the glands (sweat and sebaceous), the hair, and the nails. Each hair consists of a shaft (the portion projecting from the surface) and a root (the part implanted in the skin); each hair root is implanted in an involution of the epidermis called the hair follicle. A fingernail or toenail grows from a nail bed. If the bed is destroyed, the nail will no longer grow.

2-13. **DISEASES OF THE SKIN**

a. **General.** Diseases of the skin make up a large portion of the physician's practice, whether in civilian life or in the Army. A specialist in diseases of the skin is called a dermatologist. Descriptive terms used in dermatology are:

1. Bulla--large blister filled with serous fluid.
2. Excoriation--superficial discontinuity or scratch.
3. Induration--hardness.
4. Lesion--any localized abnormality.
5. Macula--small, flat discoloration or freckle.
(6) Papule--small, elevated lesion.

(7) Pruritis--intense itching.

(8) Pustule--vesicle containing pus.

(9) Squamous--scaly.

(10) Vesicle--small blister.

b. Virus Infections. Virus infections of the skin include the follows:

(1) Verruca vulparis. Verruca vulparis is the common wart.

(2) Herpes simplex. This is often called a fever blister, or cold sore.

(3) Herpes zoster. Herpes zoster is a painful infection commonly known as shingles.

c. Bacterial Infections. Bacterial infections of the skin include the following:

(1) Furuncle (also called "boil.") This is an acute, inflammatory lesion produced by the infection of a hair follicle or a skin gland by staphylococci bacteria. The lesion begins as a pustule. As the pustule enlarges, the skin becomes reddened, tense, and shiny. Pain and tenderness develop. The furuncle rapidly matures (comes to a head), and usually ruptures spontaneously, discharging pus. The treatment is heat, and incision and drainage. Under certain circumstances, antibiotics, such as penicillin, are indicated.

(2) Carbuncle. A lesion that resembles the furuncle, since it has the same cause and early course, but carbuncles are larger, and produce fever and leukocytosis (elevated white cell count in the blood). When a carbuncle ruptures, pus is discharged through several openings in the skin. The treatment consists of surgical drainage of the carbuncle and penicillin.

(3) Cellulitis. An acute, deep-spreading inflammation of the skin and subcutaneous tissues. Streptococcic infections tend to spread more than staphylococcic infections, because they produce an enzyme which breaks down the wall the body tries to form around the infection. The skin becomes red, tender, and swollen. The patient has fever. The infection may spread through lymph vessels, producing red streaks on the skin. It may enter the bloodstream and be carried through the body (septicemia or blood poisoning).

d. Fungal Infections. Fungal infections are among the most common of all diseases. In order for the fungi to produce skin infection, certain favorable conditions
are required. Some of these conditions are: lack of cleanliness; excessive moisture, usually due to perspiration; and irritation of the skin, usually because of tight clothing.

(1) Dermatophytosis pedis. Dermatophytosis pedis (also called tinea pedis and athlete's foot) may be recognized by the presence of superficial fissures between and toes, and vesicles on the sides and beneath under the toes. If secondary bacterial infection occurs, pustules appear, and ulceration may result.

(2) Dermatophytosis (tinea) corporis, capitis, and cruris. These fungous infections are commonly called ringworm. Dermatophytosis (or tinea) cruris is also called "jock itch." The diagnosis of ringworm is made by the presence of a few (usually not over two or three) circular, ring-like, red, scaling lesions, clearing at the center, with advancing vesicular margins. Tinea cruris is distinguished by its location on the upper surface of the thighs. Excessive perspiration and friction from clothing are important contributing factors. Therefore, an important part of the treatment consists of exposing the involved parts to the air as much as possible.

e. Arthropod Infestations and Infections. The arthropods are many-celled animals with outer skeletons but without backbones, and include such organisms as crayfish, spiders, mites, ticks, centipedes, and insects (lice, mosquitoes).

(1) Pediculosis. Pediculosis is an infestation of the skin with lice.

(a) Diagnosis of louse infestation. Lice have a habit of living in the clothes and bedding of patients and coming out only at the night to feed. This fact must be taken into account when examining a patient suspected of being infested. The small louse bites may be quite difficult to locate in the absence of the louse, although the patient has usually scratched the skin in the area very vigorously, leaving scratch marks.

(b) Treatment. Pediculosis is treat by application of gamma benzene hexachloride (Lindane ).

(2) Scabies. Scabies is a disease caused by a very small mite that burrows into the skin. The infection often begins between the fingers, and spreads to the body, especially the lower abdomen, buttocks, and genitalia. The mite causes much itching (especially at night), and there is abrasion of the skin from scratching. Secondary infection by bacteria may occur, with the formation of pustules. The abrasions and pustules often obscure the typical lesions of scabies, which are threadlike, twisted lesions with a small raised area at one end. All washable clothing should be thoroughly laundered, and other clothing dry-cleaned.

f. Allergic Conditions. In allergic conditions, the patient is sensitive to certain foreign substances that may contact his skin, or be introduced into his body in the food he eats or the air he breathes. A first contact is necessary to produce the sensitization, following which the patient reacts to contact with the foreign substances in an abnormal manner. Some substances can provoke an allergic reaction in anyone contacting them.
Others appear to produce allergy only in certain individuals who have a constitutional or inherited predisposition to allergy.

(1) **Urticaria.** Urticaria (commonly called hives) is an allergic condition which results in the formation of wheals (rounded or irregular shaped, transitory elevations of the skin). Urticaria is usually caused by eating a substance to which the patient has been sensitized, but may also be caused by a local allergen such as poison ivy; or it might have a psychogenic origin. It is usually associated with much itching and may cover the whole body. Often it is difficult to determine the cause, and the disease may constantly reoccur.

(2) **Contact dermatitis.** Contact dermatitis (dermatitis venenata) is due to sensitization of the skin by direct contact with a sensitizing substance. The development depends on how much of the substance is contacted, and how often. Why sensitivity occurs is not known. At the beginning, the skin is reddened in the contacted area, then raised lesions appear, and then blisters. The lesions may spread over the body. The vesicles may become infected by bacteria, and pustules appear. There is marked itching. The patient may carry the sensitizing substance to other skin areas by his hands. The sensitizing substance may be almost anything. Examples include: poison ivy, medicines, clothes, and soaps. A painstaking and thorough search is necessary to find and remove the allergen. Treatment includes removal of the allergen, mild bland applications, and antihistaminics in some cases.

**h. Other Conditions.**

(1) **Psoriasis.** Psoriasis is a chronic, recurrent disease of the skin, characterized by reddish, rounded lesions that are covered by silvery scales. When a scale is removed, it leaves a small bleeding point. The disease tends to begin on the elbows, knees, or scalp, and to spread over the whole body.

(2) **Acne vulgaris.** Acne vulgaris is a chronic inflammation of the sebaceous glands (oil glands) of the skin, which usually develops during adolescence. Lesions develop rapidly and in crops, located mostly on the face, sometimes on the sternal region, the shoulders, and the back. The lesions may cause considerable scarring on healing. Treatment includes good personal hygiene to help prevent secondary infections, dietary measures, antibiotics, and various skin lotions.

**2-14. SIGNS AND SYMPTOMS OF SKIN DISEASE**

a. **Pruritis (Itching).** The most common, most annoying, and least specific symptom encountered in dermatologic conditions is pruritis. Among the causes of itching may be included infectious agents, allergic conditions, neuroses, parasitic infestations, dryness of the skin, anoxia of the skin, and chronic irritation of the skin. The actual pathological change responsible for this symptom takes place in minute nerve endings in the skin. The exact change is not known, but these endings become
increasingly sensitive to the various causative agents, and itching will appear more easily.

b. **Pain.** Pain is not seen very often in skin disorders, although there may be a burning sensation associated with indurating lesions.

c. **Edema.** Edema is the collection of fluid in the tissues of the dermis. This is usually localized at least to a particular area of the body. When individual lesions take the form of a small area of swelling with associated pruritis, the eruption is called urticaria. The edema may be extensive, involving either the face or part of an extremity. When the edema involves the face, the eyes may be forced shut by the swollen tissues. Edema is seen in numerous systemic disorders, but there are usually enough other symptoms of the underlying disease to prevent confusion with a skin reaction to an allergen.

d. **Scales.** The upper layer of the epidermis may accelerate the production of keratinized (horny) cells, and these will begin to flake off following minimal trauma. These flakes of dry, dead tissue are called scales. Many lesions show scaling as the disease kills additional layers of the epidermis. Occasionally the scales may take characteristic shapes because of plugging pores in the skin.

e. **Weeping.** Weeping is the oozing of fluid from the surface of a lesion. This occurs whenever sufficient layers of epidermis have been destroyed and removed so that the capillary beds of the dermis are near the surface. Weeping is serious because of its tendency to macerate (soften) the lesions and the surrounding skin. As the healthy tissue breaks down, the disease spreads more easily. Weeping is frequently seen in body creases and must be guarded against. The use of powders to dry weeping lesions is the first step in the successful therapy of such conditions.

f. **Scaling and Weeping.** There may be a combination of scaling and weeping. This will result in the formation of a crust over the lesion. Any blood, pus, or other exudate from the lesion may add to this crust. The raw surface of the lesion will be protected by this crust, but the fluid collecting under it will be an excellent growth medium for bacteria, thus adding infection to the existing problems. Crusts may be a cause of itching, and frequently they will be ripped off by the patient, either on purpose or accidentally while scratching.

g. **Fissures.** Fissures are small cracks in the skin. These are very common and occur when there is an excessive drying of the skin. The corners of the mouth are common sites for this condition. Fissure may also be seen in areas of lichenification (places where the tissue has become thickened from continuous irritation). Fissures are open portals of entry for bacteria.

h. **Fever.** Fever is usually seen in infectious diseases, but it may also be present in cases of allergy. This is not a common concern to the dermatologist, because disease limited to the skin will not cause fever.
2-15. TREATMENT

a. **Symptomatic.** Many forms of treatment are available for disorders of the skin. Frequently, treatment is instituted merely to relieve the distressing symptoms and may have no effect on the course of the disease. The antipruritic (anti-itch) medications are of this type. Both lotions and powders are used and are effective in a fair percentage of cases. Systemic antipruritics are not very effective but are of some use in systemic diseases that have itching at some stage. Antihistamines are used primarily in allergic reactions, and they are extremely effective in relieving the itching as well as in suppressing the skin lesions.

b. **Drugs.**

(1) **Antibiotics.** Antibiotics may be used topically when there is an infection in the skin, either primary or secondary. The infection should always be present before the antibiotic is used. The prophylactic (preventive) use of topical antibiotics is dangerous because these drugs have a higher than usual incidence of sensitivity reactions when used in this manner.

(2) **Steroids.** The numerous synthetic steroid preparations have been of great assistance to the dermatologist. Many diseases will be controlled by steroids after all other means of treatment have failed. Steroids usually are given systemically, and they may cause serious consequences; therefore, steroids are normally used only after other means of therapy have failed. The topical use of steroids, however, is effective and safe because negligible quantities are absorbed, even through raw lesions.

(3) **Antipyretics.** Aspirin and acetaminophen are the most effective agents available for reducing temperatures.

Section V. NATURE AND CAUSES OF DISEASE

2-16. DEFINITION OF DISEASE

Disease can be defined as a derangement of the normal functioning of one or more of the body processes. This interference with the normal body functions either prevents them from taking place, or causes them to act in an abnormal manner. For example, a tumor may obstruct the flow of intestinal contents, or bacteria may cause irritation or inflammation. In the following text, consideration will be given to those factors which are responsible for interference with the normal body functions, in other words, the etiology (causes) of disease.
2-17. CAUSES OF DISEASE

There are nine major causes of disease (a through i below). Frequently a disease may be produced by a combination of these causes, or the same disease may be caused by different factors in different patients, or the cause may be unknown (j below).

a. **Prenatal Influences.** By this is meant those factors which may operate before birth to produce disease in the offspring; factors may be manifested at birth (congenital disease) or may not become obvious until later in life.

   (1) Heredity. Among prenatal factors, one influence is heredity. A disease may be genetically transmitted from a parent to offspring. The parents who transmit the disease to their offspring may or may not have the disease themselves. Examples of some hereditary diseases are hemophilia and congenital dislocation of the hip.

   (2) Congenital influence. Diseases affecting the mother while she is pregnant with the baby may adversely affect the offspring. For example, some diseases may be transmitted directly to the baby via the bloodstream, as is often seen in the case of syphilis in the mother. Alternatively, the pregnant woman may have a disease such as German measles, which interferes with the normal development of the child in the uterus (in utero), although, the child does not acquire the disease. Malnutrition in the mother could result in a poorly nourished baby, which could also interfere with the normal development of the child.

   (3) Mechanical. Purely mechanical factors are also felt to be responsible for some abnormalities present at birth. Abnormal positioning of the baby in utero is felt to be occasionally responsible for wryneck; torsion or twisting of the umbilical cord would limit the blood and food supply to the baby, and dire results could occur. Any defect or disease present at the time of birth is called a congenital disease or condition. Injuries or effects sustained during the process of being born may be included here.

b. **Parasites.** Parasites are organisms that live on or within the body of the man or any other living organism, and at the expense of the one parasitized. Parasites may live on the surface of the skin (ectoparasites), or they may enter the body through the skin, the respiratory tract, the gastrointestinal tract, or the genitourinary tract where they may enter the bloodstream and be carried to distant parts of the body. If they live inside the body, but outside the cells, they are called extracellular endoparasites; if they enter the body's cells, they are called intracellular endoparasites. They all cause disease by interfering with the tissue and organ functions; they accomplish this by elaborating toxins, or poisons; by causing inflammation, or irritation; by producing enzymes which destroy tissue; and by causing mechanical blockage of function.

   (1) Viruses. These are the smallest agents known to produce disease; whether they are living organisms or complex chemical compounds is not known. They are known to be intracellular endoparasites that cause such common diseases in man...
as poliomyelitis, common cold, influenza, measles, mumps, chickenpox, smallpox, 
hepatitis, encephalitis, warts, rabies, yellow fever, and lymphogranuloma venereum.

(2) Rickettsiae. These organisms are larger than viruses, but are still very 
small intracellular endoparasites. These organisms are transmitted to man by mites, 
ticks, fleas or lice, and they produce Rocky Mountain spotted fever, typhus (epidemic 
and endemic), scrub typhus (tsutsugamushi fever), Q fever, and Rickettsialpox.

(3) Bacteria. Bacteria are minute, one-celled, organisms that may occur 
alone or in large groups called colonies. Significant bacteria can be divided by their 
shape into three main groups.

(a) Cocci. Cocci are round, one-celled bacteria. The primary 
members of this group are staphylococci, which group themselves in clusters; 
streptococci, which arrange themselves in chains; and diplococci, which arrange 
themselves in pairs. All are pyogenic (produce pus).

(b) Bacilli. Bacilli are rod-shaped; however, they vary from straight to 
irregular-curved and branched shapes. They cause such common diseases as typhoid 
fever, diphtheria, tuberculosis, and leprosy.

(c) Spirochetes. Spirochetes are spiral-shaped and can move or twist. 
Spirilla and Treponema pallidum are examples. The latter causes syphilis.

(4) Fungi. These extracellular endoparasites or ectoparasites are larger and 
higher in the scale of plant life than are the bacteria. They include the yeast and molds, 
and produce infections of the skin such as ringworm, and infections of the mucous 
membranes such as thrush. Some attack internal organs, especially the lungs and 
central nervous system, very often with disastrous results.

(5) Protozoa. These are one-celled animal parasites (either extracellular or 
intracellular) that cause such common diseases as malaria and amoebic dysentery.

(6) Metazoa. These many-celled, larger animals include the helminthes 
(worms) such as the ascaris, the hookworm, the pinworm, the tapeworms, and the 
flukes, as well as the arthropods (mites, lice, and so forth.).

c. Intoxicants. Intoxication is the process of taking any chemical substance that 
causes disease or injury into the body. Many substances are very useful in small 
amounts, and do not cause intoxication; but the same substances may be very toxic in 
larger amounts, and result in severe illness or death.
d. **Trauma.** Trauma may be defined as injury sustained by the body as the result of a physical agent or force. The physical agents that may produce trauma or injury of the body are:

1. **Light.** In excessive amounts, light can cause temporary blindness.
2. **Heat.** Excessive heat can cause burns of the body, heat cramps, heat exhaustion, or heatstroke.
3. **Cold.** Cold is absence or deficiency of heat. Exposure to low temperatures can result in frostbite and other cold injury.
4. **Electricity.** One can sustain burns, electric shock, or both when exposed to this agent.
5. **Ionizing radiation.** Excessive exposure to x-rays or to radioactive elements can produce burns, radiation sickness, malignancies, cataracts of the eye, and genetic changes.
6. **Mechanical forces.** These agents produce contusions, abrasions, lacerations, fractures, sprains, and strains.
7. **Sound.** Exposure to excessive noise can cause temporary or permanent deafness to certain wavelengths.

e. **Circulatory Disturbances.** Any interference with the blood flow to a portion of the body results in a circulatory disturbance.

1. **Ischemia.** A decrease in the normal diameter of an artery supplying a portion of the body results in a decrease in the amount of blood that flows to the part. The area becomes more pale and colder than normal, and is said to be ischemic.
2. **Thrombosis.** Whenever a vessel wall becomes diseased, the blood tends to collect at the diseased or injured site and form a thrombus (clot). The presence of an intravascular blood clot is called thrombosis.
3. **Embolism.** Portions of a thrombus may break loose, and then travel freely in the bloodstream until stopped by a vessel too small for the particle to pass through; or foreign particles, such as air bubbles or fat globules, may be introduced into the bloodstream and travel freely until stopped by a smaller vessel. These foreign particles are known as emboli. The process of obstruction or occlusion of a blood vessel by a transported foreign material is known as embolism.
4. **Gangrene.** When an extremity or portion thereof loses its arterial blood supply as the result of thrombosis, embolism, trauma, or from any other cause, a
massive area of the tissue dies, and is said to have undergone gangrene, or to have become gangrenous.

(5) Infarction. Death of the tissue of an organ or portion thereof as the result of the loss of its blood supply is known as infarction. The necrotic (dead) area itself is called an infarct.

(6) Hemorrhage. This is the loss of blood.

f. Neuropsychiatric Disturbances.

(1) Organic disorders. Injury or disease of the nervous system tissue may result in the loss of the nerve supply to a particular part of the body. Therefore, because of loss of enervation, secondary changes in the tissue occur, such as atrophy. In addition, the normal functions may become paralyzed, and there may be loss of sensation and other changes.

(2) Functional disorders. Disturbances of the mind or psyche may produce neuroses, psychoses, or character and behavior disorders. Such disturbances may or may not be inherited; the environment, childhood experiences, and many other factors have a bearing on the production of psychiatric disturbances.

g. Mechanical Disturbances. Certain static mechanical abnormalities may result in disease within the body. For example, volvulus or twisting of the intestine on itself, torsion of the spermatic cord, strangulation of a hernia, and intussusception, are all often on a purely mechanical basis.

h. Disorders of Metabolism, Growth, or Nutrition. Metabolism has to do with the total chemical cycle of converting substances into forms that are usable to the body. Metabolism occurs in two phases.

(1) Anabolism. In anabolism, foodstuffs are broke down (digested) and reconverted into compounds which can be utilized as energy, or as building blocks for new tissue cells and substances. In anabolism, living tissue is manufactured from nonliving substances. This results in growth or replenishment.

(2) Catabolism. Catabolism is the breaking down of the body’s complex substances by wear, tear, and age into waste products of simpler composition for elimination. Metabolism and growth then are dependent on the body’s receiving enough of the proper foodstuffs in order to supply its needs, in other words, on proper nutrition. Metabolism and growth are further regulated by the vitamins and hormones. The hormones are supplied by the ductless glands of the body (the pituitary, thyroid, parathyroid, pancreas, adrenals, and gonads), and any disorder of these glands will profoundly disturb growth and metabolism. The vitamins are supplied by the diet; if the diet or nutrition is unsatisfactory, disturbances in growth and metabolism can result also. Therefore, metabolism, growth, and nutrition are closely related to one another.
i. **Neoplasms.** Normally, the body grows by multiplication of its cells. At first, in the embryo, these cells are all alike or undifferentiated. However, as they multiply, they come under the influence of certain factors and take on different forms and different functions to make up the different tissues, organs, and systems of the body (that is, they become differentiated). This growth and differentiation is a slow, methodical, controlled process. However, some cells may not differentiate entirely, but for some unknown reasons, retain varying degrees of undifferentiation, break free of their growth control, and form a new growth (neoplasm) or tumor. Tumors cause disease by interfering with the function of normal cells, tissues, and organs. They may cause pressure on an organ so that its normal cells are destroyed or its blood supply is shut off. A tumor may fill the cavity of an organ so that the organ wall cannot contract properly. The tumor may also use up the nutritive materials taken into the body so that there is not enough for the normal tissues. Tumors are of two types: benign and malignant.

1. **Benign.** These are more slowly growing, the cells are more differentiated, the tumor is well separated from the surrounding tissues by its capsule, and can usually be completely removed surgically.

2. **Malignant.** These are more rapidly growing with very little growth control, and the cells are more primitive or undifferentiated. The cells of the tumor infiltrate or grow between the normal tissue cells, and are much more difficult to remove surgically. Because of this, the malignant tumor tends to recur and tends to metastasize or spread via the blood and the lymph vessels. The common term for malignant tumors is cancer. The medical profession speaks of carcinoma when the malignant tumor arises from tissue that covers the surface of the body, lines a hollow structure, or forms glands, and sarcoma when the malignant tumor arises from any other tissue in the body such as fatty, muscular, bony, or fibrous tissue.

j. **Idiopathic (Unknown) Causes.** There are many diseases of known etiology. The affected organ and effective treatment are often known, however, the cause and the mechanism through which the disease disrupts the body’s functions remain unknown.

### Section VI. TREATMENT OF DISEASE AND INJURY

#### 2-18. INTRODUCTION

Patients who have disease or injury must be properly diagnosed and treated. The physician is responsible for these functions; however, the physician may delegate the accomplishment of some of the treatments to other members of the Army Medical Department (that is, physicians' assistants and physical therapists). In general, all types of treatment may be classified as either preventive or corrective.
2-19. PREVENTIVE TREATMENT

Preventive treatment includes all measures used to prevent disease.

a. Preventive procedures include sanitary measures such as cleanliness, proper waste disposal, inspection of food and food handlers, isolation diseased individuals, aseptic surgical technique, and the use insecticides of and rodenticides to control vectors of disease.

b. Another preventive measure is immunization. Active immunity is the result of a direct introduction into the individual's body of an antigenic preparation (frequently bacteria or viruses) so that an individual produces his own antibodies that defend him against the particular antigen introduced. Passive immunity is produced by injecting serum-containing antibodies into an individual. This blood serum may be from animals or humans in which the antibodies were produced by an active immunity process.

c. A third preventive measure consists of preventive psychiatry and mental health work, in which the individual or his environment is manipulated in a manner to prevent excessive mental stress.

2-20. CORRECTIVE/SYMPTOMATIC TREATMENT

People who have some disease or condition want to receive prompt medical treatment. Many people believe that the use of prescribed medications is the only way to ensure that a disease or condition will be cured or improved. The use of drugs does have an important role in the treatment of disease; however, other treatment methods are available. For example, rest, radiotherapy, and physical therapy are very useful in the treatment of certain conditions. In many cases, various treatment methods are used to benefit the patient.

a. Rest prevents overwork of a diseased organ and includes more than freedom from physical work; a patient must have mental rest also.

b. Diet is of extreme importance both in the prevention of disease and in medical care. An adequate intake of proteins, carbohydrates, fats, vitamins, and minerals is necessary in the treatment of all patients. Patients with fever generally require increased amounts of all dietary constituents. Patients with certain diseases require diets in which the various dietary constituents are carefully controlled. One example of a special diet of this type is that for diabetes mellitus, in which the amounts of protein, fat, and carbohydrates must be individually regulated.

c. Nursing care is another essential part of medical care. In addition to doing technical procedures such as administering drugs, nursing service personnel watch for the appearance of changes in the patient's condition. Frequently the personalities of such personnel will be an important factor in promoting the patient's morale, securing his cooperation, and fostering in him a desire to get well.
d. Drugs are substances used in the treatment of disease. They are used to relieve the unpleasant effects of disease and to eradicate the disease. Drugs may be administered externally and internally.

e. Radiotherapy is the use of x-rays, radium, and radioactive isotopes in the treatment of disease.

f. Occupational therapy is treatment that provides a patient with activity to keep his mind and body occupied. It is also used to help the patient regain muscular coordination and control of specific parts of the body.

g. Physical therapy is the treatment of disease by physical means. Various agents used in physical therapy are light, heat, cold, electricity, water, massage, and exercise.

h. Psychotherapy is treatment by various means, which may include the use of drugs, to lessen or rectify abnormal mental conditions. Surgery performed for the same purpose is called psychosurgery.

i. Surgery is the treatment of disease by manual operation or corrective apparatus. It includes the removal of diseased tissue or organs and the repair of injured structures.

*Continue with Exercises*
EXERCISES, LESSON 2

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the definition below, select the definition of the term anatomy.
   a. The study of the functions of the body.
   b. The study of the chemical substances in the body.
   c. The study of the structures of the body.
   d. The study of the systems of the body.

2. From the definitions below, select the definition of the term tissue.
   a. A grouping of like cells working together.
   b. The smallest living unit of body construction.
   c. A group of organs working together.
   d. A group of cells that have nothing in common.

3. From the functions below, select the function of the lymphatic system.
   a. Protects the body from drying.
   b. Returns proteins and fluid from the various body tissues to the blood.
   c. Manufactures hormones.
   d. Provides nutrients to the various limbs of the body.
4. From the descriptions below, select the best description of the cytoplasm.
   a. Organelles that perform highly specialized functions in the cell.
   b. A jelly-like substance that coats the outside of the cell membrane.
   c. The part of the cell which manufactures RNA and DNA.
   d. The fluid or semifluid contained inside the cell membrane, but outside the nucleus.

5. From the descriptions below, select the best description of the mitochondria.
   a. The organelle of the cell responsible for producing DNA.
   b. The site of cell respiratory activity.
   c. The part of the cell which is responsible for producing RNA.
   d. The organelle responsible for monitoring the flow of water into the cell.

6. From the definitions below, select the definition of pinocytosis.
   a. A vesicle which engulfs and destroys the cell.
   b. The organelle responsible for producing extracellular fluid.
   c. The production of fluids by the cell.
   d. The engulfing of small particles or fluids by the cell.

7. From the descriptions below, select the description of connective tissue.
   a. The tissue that binds other tissues together and supports other tissues.
   b. The tissue that covers the outer layer of the body.
   c. The tissue that forms the glands and the sense organs of the body.
   d. The tissue that covers the organs in the abdomen.
8. From the list of function below, select the function of the skin.
   a. Controls the size of the patient.
   b. Produces chemicals for body growth.
   c. Prevents perspiration on hot days.
   d. Detects heat, cold, pressure, and pain.

9. Select, from the group of descriptions below, the best description of pediculosis.
   a. An infestation of the skin with fungus.
   b. An infection of the skin with bacteria.
   c. An infestation of the skin with lice.
   d. An infection of the skin with ringworm.

10. Select, from the group of descriptions below, the best description of scabies.
    a. A disease caused by a very small mite, which burrows into the skin.
    b. A disease caused by small bacteria, which includes the skin.
    c. A disease characterized by itching and fungal growth.
    d. A disease characterized by the growth of bacteria on the skin.

11. Select, from the descriptions below, the best description of a furuncle.
    a. An acute inflammatory lesion produced by the infection of a hair follicle or skin gland by streptococci bacteria.
    b. An acute, inflammatory lesion produced by the infection of a hair follicle or skin gland by staphylococci bacteria.
    c. An acute lesion produced by an infection of a hair follicle by fungal organisms.
    d. An acute, inflammatory lesion produced by the infection of a hair follicle by allergens.
12. Select, from the definitions below, the meaning of the term pruritis.
   a. A chronic, recurrent disease characterized by reddish, rounded lesions.
   b. A chronic inflammation of the sebaceous glands of the skin.
   c. A parasitic infestation of the skin caused by lice.
   d. Itching.

13. Select, from the descriptions below, a description of edema.
   a. A collection of fluid in the tissues, resulting in swelling.
   b. A raised area of the skin characterized by cellulitis.
   c. A collection of protein in injured tissues resulting in bleeding.
   d. A collection of raised swellings on the skin characterized by itching and discoloration.

14. From the definitions below, select the definition of the term disease.
   a. A condition characterized by functioning of certain glands.
   b. A derangement of the normal functioning of one or more body processes.
   c. A dysfunction of the body caused by lack of exercise.
   d. A dysfunction of the systems of the body characterized by lowered blood sugar.

15. Select, from the descriptions below, the description of physical therapy.
   a. The use of drugs to treat disease of mental origin.
   b. The treatment of disease by the administration of antibodies.
   c. The treatment of disease by such methods of heat, light, and cold.
   d. The treatment of disease by the removal of diseased organs or tissues.

Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 2

1. c The study of the structure of the body.  (para 2-1)

2. a A grouping of cells working together.  (para 2-2b)

3. b Returns protein and fluid from the various body tissues to the blood.  
   (para 2-3f)

4. d The fluid or semifluid contained inside the cell membrane, but outside the 
   nucleus.  (para 2-5b)

5. b The site of cell respiratory activity.  (para 2-5d)

6. d The engulfing of small particles or fluids by the cell.  (para 2-6)

7. a The tissue that binds other tissues together and supports other tissues.  
   (para 2-9b)

8. d Detects heats, colds, pressure, and pain.  (para 2-11c)

9. c An infestation of the skin with lice.  (para 2-13e(1))

10. a A disease caused by a very small mite which burrows into the skin. 
    (para 2-13e(2))

11. b An acute, inflammatory lesion produced by the infection of a hair follicle or 
    skin gland by staphylococci bacteria.  (para 2-13c(1))

12. d Itching.  (para 2-14a)

13. a A collection of fluid in the tissues resulting in swelling.  (para 2-14c)

14. b A derangement of the normal functioning of one or more body processes.  
    (para 2-16)

15. c The treatment of disease by such methods of heat, light, and cold.  
    (para 2-20g)

End of Lesson 2
LESSON ASSIGNMENT

LESSON 3
Introduction to Pharmacology.

TEXT ASSIGNMENT
Paragraphs 3-1--3-15.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

3-1. Given a pharmacological term and several definitions, select the definition of that term.

3-2. Given a source of drugs and a list of names of drugs, select the drug that is derived from that source of drugs.

3-3. From a group of statements, select the use(s) of drugs.

3-4. Given a factor that influences drug dosage and a group of statements, select the statement that best describes how that factor influences drug dosage.

3-5. Given a particular route of administration and several statements, select the statement that best describes that route of administration.

3-6. Given a type of adverse reaction to a drug and several statements, select the statement that best describes that type of adverse reaction.

3-7. Given a factor that influences drug action and a group of statements, select the statement that best describes how that factor influences drug action.

3-8. Given one of the following factors that influence drug absorption: water solubility, fat solubility, and transport mechanisms, and several statements, select the statement that best describes how that factor influences drug absorption.
3-9. From a group of statements, select the statement that best contrasts passive transport with active transport.

3-10. Given a group of statements, select the statement that best describes the Receptor Site Theory of the mechanism of drug action.

3-11. Given a group of statements, select the statement that best contrasts competitive antagonists with physiological antagonists.

3-12. From a group of statements, select the statement that best describes the importance of structure activity relationships.

**SUGGESTIONS**

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 3
INTRODUCTION TO PHARMACOLOGY

Section I. TERMS AND DEFINITIONS IMPORTANT IN PHARMACOLOGY

3-1. GENERAL

a. It is important for you to be familiar with some terms and definitions frequently used in the study of drugs. Although the terms and definitions presented here are basic, they will provide you with a sound background for gaining additional knowledge, and understanding as you read the text of this subcourse.

b. The terms and definitions provided in this section do not include all the medical terms used in this subcourse. Whenever possible, the meaning of a fairly difficult and unfamiliar term will be written in parentheses ( ) after that term. In the event you encounter a term you do not understand, you should use a quality medical dictionary (that is, Dorland's Illustrated Medical Dictionary) to learn the meaning of that term.

c. No attempt is made in this subcourse to address the pronunciation of terms and drug names. If you desire assistance in this area, you should seek the services of someone who works with drugs on a frequent basis. "Pharmacists, pharmacy technicians, nurses, physicians, and other medical personnel are well-qualified to help you to learn the pronunciation of drug names."

3-2. TERMS AND DEFINITIONS

a. Drug. A drug may be broadly defined as any substance or group of substances, which affects living tissue. However, the term may be specifically defined as any substance used to prevent, diagnose, or treat disease or to prevent pregnancy.

b. Pharmacology. Pharmacology is the study of the actions and effects of drugs on living systems and their therapeutic uses.

c. Bioavailability. Bioavailability refers to the amount of drug that is available to the target tissue after the drug has been administered. In other words, it is the amount of the drug available to produce the desired effect.

d. Pharmacognosy. Pharmacognosy is the study of the characteristics of natural drugs.
e. **Toxicology.** Toxicology is the science of poisons. Toxicology includes the origin, chemical properties, toxic actions, detection, and proper antidotal therapy of poisons.

f. **Posology.** Posology is the science of dosage. It deals with the amount of drug necessary to produce a desired physiological, therapeutic, or prophylactic effect.

1. **Usual recommended dose.** The usual recommended dose is the amount of drug that will ordinarily produce the effect for which the drug is intended. In addition to the usual recommended dose, the usual dosage range is indicated for many drugs in the United States pharmacopoeia/National Formulary. The usual dose range provides a guide in deciding whether the prescriber should be consulted about the correctness of the prescribed dose.

2. **Minimum dose.** The minimum dose is considered the smallest dose of drug that produces the therapeutic effect.

3. **Maximum dose.** The maximum dose is considered the largest dose of a drug that can be safely administered.

4. **Toxic dose.** The toxic dose of a drug is considered the amount of a drug that will produce noxious (harmful) effects.

5. **Lethal dose.** The lethal dose of a drug is the amount of substance that will cause death. You will often see the term "LD50" in association with lethal dose. LD50 means that 50 percent (or 1/2) of the animals given that amount of drug died. The LD50 of a drug should be used as a guide, rather than an absolute number.

6. **Single dose.** The single dose of a drug is the amount of that substance to be taken at one time.

7. **Daily dose.** The daily dose of a drug is the amount of that substance to be taken in a 24-hour period. The daily dose of a drug is into several individual doses.

8. **Maintenance dose.** The maintenance dose of a drug is the amount of that substance taken to maintain or continue a desired therapeutic effect. Some drugs must be taken on a daily basis in order to maintain the desired therapeutic effect. For example, drugs used to treat high blood pressure often must be taken daily to maintain a lowered blood pressure.

9. **Loading dose.** The first dose given of a drug to achieve maintenance drug levels quickly. Drugs that are given only one or two times a day may take two or three days to reach a maximum effect. To overcome this time, a loading dose is given to achieve the levels associated with the maximum effect more quickly. Loading doses are often used in very sick patients.
Section II. INTRODUCTION TO DRUGS

3-3. SOURCES OF DRUGS

Drugs today are obtained from several sources. Some sources of drugs are discussed below. Some drugs are listed under the sources. The specific drugs mentioned are not the only drugs obtained from that source.

a. Plants. For thousands of years, plants have served as sources of drugs. Ephedrine, a drug used to treat nasal congestion, was used by the Chinese long before western man visited the Orient. Belladonna (or Deadly Nightshade), the source of atropine and scopolamine was used in the Middle Ages. Its name means "beautiful woman" in Italian. A solution obtained by soaking the belladonna plant in water caused the pupils of the eye to dilate and appear black. These were symbols of beauty at the time. Belladonna was a favorite poison. Opium, a product obtained from the poppy plant, is mentioned in early Greek mythology as a sleep producer.

b. Animals. Animals provide us with large supplies of natural products like hormones. Insulin, used in the treatment of diabetes mellitus, used to be obtained from the pancreas of pork, beef, and even fish. Heparin, a potent anticoagulant, is obtained from the intestinal and lung mucosa of beef and hogs.

c. Minerals. Minerals, such as iron and iodine, are essential for normal growth and development. An old remedy for pallor (a very pale complexion) was the water used to cool horseshoes in the blacksmith shop. This water contained small amounts of iron in solution.

d. Microorganisms. You are probably aware of the fact that microbes can cause disease and/or death. Fortunately, some microorganisms can be used to produce antibiotics. These antibiotics can be used to kill or stop the growth of other microbes. Furthermore, chemically treated or killed microorganisms can be used to produce vaccines.

e. Synthetics. Most drugs today are synthetically made. Examples of synthetically produced drugs are aspirin and the sulfa drugs.

3-4. USES FOR DRUGS

Drugs have many uses. In today’s society, the legitimate--and not so legitimate--use of drugs is wide seen. Listed and briefly discussed below are the major uses and some representative examples of drugs:

a. To Maintain Health. Vitamins and minerals are used and abused in the pursuit of good health.
b. **To Reverse a Disease Process.** Antibiotics and chemotherapeutic (anticancer) agents are commonly used in medicine today. Ideally we would like these agents to cure the patient.

c. **To Relieve Symptoms.** Drugs that act to relieve symptoms do not cure the patient. Instead, they help to make the patient more comfortable in order for the patient to work or function. Since only symptoms are being relieved, the body is expected to remedy the problem.

d. **To Prevent Disease.** Vaccines and toxoids are used to prevent disease. In the 1950's, many parents kept their children at home in fear of the dreaded polio disease. Today, the only time most parents think of polio is when they take their children for their periodic (and necessary) vaccinations for this still-present threat. Further, any military veteran can quickly testify to the fact that vaccinations are an essential part of the introduction to military life.

e. **To Prevent Pregnancy.** The old saying that an ounce of prevention is better and cheaper than a pound of cure is most applicable here. The birth control "pill" or oral contraceptives and spermacidal agents in the form of creams, jellies, and suppositories are the drugs currently being used to prevent pregnancy.

**Section III. CONSIDERATIONS OF DRUG THERAPY**

3-5. **FACTORS WHICH INFLUENCE DRUG DOSAGE EFFECTS**

Many factors influence how a dose of a particular drug will affect a patient. Since not all patients are the same size, weight, age, and sex, it would be wise to consider how these factors might influence how much drug a person should receive and the effect(s) that drug might have on the patient. The usual recommended adult dose of medication, as found in standard references, is based on the assumption that the patient is a "normal" adult. Such a "normal" (or average) adult is said to be 5 feet 9 inches (173 centimeters) tall and weigh 154 pounds (70 kilograms). However, many people do not fit into this category. Therefore, the following factors should be considered when patients receive drugs:

a. **Weight.** Obese (overweight) patients may require more medication than thin patients may because the drug has more tissue to which it can go. The dosage of many drugs is calculated on a weight basis. For example, a person might be prescribed a drug that has a dosage of 5 milligrams of drug per pound of patient body weight.

b. **Surface Area.** A person’s height and weight are related to the total surface area of his body. The "normal" (average) adult has a body surface area of approximately 1.73 square meters. A nomogram (see Subcourse MD08O2, Pharmaceutical Calculations) is used to determine the surface area of a patient. The
dosage of certain drugs (for example, the anticancer drugs) is determined by the patient's body surface area.

c. **Age.** As a rule, the very young and the elderly require less than the normal adult dose of most medications. Part of this requirement for less medication is due to the altered metabolism of the drug. Since body enzyme systems greatly influence drug metabolism, considering the differences in these enzyme systems based upon age is important. In the infant, some enzyme systems are not yet fully developed. On the other hand, the enzyme systems of the elderly may not function as well as in the past. Although several formulas are available for calculating a child's dose of medication, the two most accepted methods are those based upon the patient's weight (that is, milligrams per kilogram of body weight) or body surface area (that is, milligrams per square meter of surface area).

d. **Sex.** Physiological differences between the sexes may influence the dose or the requirement for drugs. Since females have proportionately more fat tissue than males, drugs, which have a high affinity (likeness) for fat, may require larger doses in females. Moreover, estrogen and testosterone, two sex hormones, can affect the patient's rate of metabolism which can, in turn, influence the rate at which a drug is metabolized, absorbed, or excreted from the body. The requirement for iron is much higher in the female than in the male, because of the loss of blood in each menstrual cycle.

e. **Genetic Factors.** Various racial and ethnic groups have differences in some metabolic and enzyme systems which can affect the utilization of drugs.

f. **Physical Condition of the Patient.** The physical condition of the patient influences how a particular drug might act. Consequently, the weak or debilitated patient might require smaller doses of some medications. Patients who are in extreme pain may require larger doses of analgesic agents than those patients who are in less pain.

g. **Psychological Condition of the Patient.** The patient's attitude about his disease or treatment can influence the effectiveness of a drug. It has been shown that patients receiving placebo tablets (tablets that contain no active ingredient) sometimes have the same side effects as the patients who were taking tablets of the same appearance that did contain the drug. In some cases, both types of patients (those taking the placebo and those taking the drug) recovered at the same time.

h. **Tolerance.** The therapeutic effects of some drugs are lessened in individuals after the drugs have been used for long periods. Thus, an individual who has used such a drug for a long time needs larger doses of the drug than he did when he first began to take it in order to obtain the same effect. This effect is called tolerance. Persons who use opium, heroin, cocaine, amphetamines, and barbiturates develop a tolerance to these substances. **Cross-tolerance** occurs when the use of one drug
causes a tolerance to another drug. Alcoholics, barbiturate addicts, and narcotic addicts develop a cross-tolerance to sedatives and anesthetics.

i. **Time of Administration.** The time when a drug is administered is important. Some orally administered medications should be taken before meals (that is, on an empty stomach) to increase the amount of drug absorbed into the system. Other oral medications (that is, those that cause irritation to the gastrointestinal tract) should be taken after meals on a full stomach.

j. **Drug Interaction.**

The interaction between two or more drugs may influence the overall effectiveness of each of the drugs.

(1) **Synergism.** Synergism is the joint action of drugs. That is, their combined effects are greater than the sum of their independent effects. Concurrent administration (giving both drugs at the same time) of synergists may require that the dose of each drug be lowered. In the case of synergism, $1 + 1 = 2 1/2$. Synergism may be beneficial or harmful. Beneficial effects may be obtained when combining two potentially toxic drugs to achieve the desired therapeutic effect without causing harm to the patient. Harmful effects may occur when alcohol and some depressants are combined.

(2) **Additive.** In an additive drug interaction, the combined effects are equal to the sum of the independent effects of the drugs. In the case of the additive effect, $1 + 1 = 2$.

(3) **Antagonism.** Antagonism is the canceling effect of one drug upon another. A sedative administered with a stimulant may antagonize or cancel the effects of the stimulant. Of course, the degree of antagonism varies from complete cancellation of the effect to varying degrees of reduced effectiveness.

k. **Routes of Administration.** Drugs may be given to patients using a variety of methods. Some drugs are only effective if they are given in a particular dosage form. Other drugs are administered in forms that enhance or decrease their effect or localize the drug effects.

(1) **Oral.** Most drugs available today can be administered by mouth (orally). Drugs can be orally administered in the form of tablets, capsules, powders, solutions, or suspensions. Drugs administered by the oral route are usually taken for their systemic effect. These medications must pass through the stomach and be absorbed in the intestinal tract. Orally administered medications are usually easy to take and are usually less expensive than other dosage forms.

(2) **Sublingual/buccal.** The sublingual/buccal route of administration is closely related to the oral route; however, in the sublingual/buccal route the dosage
form is not swallowed. The tablet is to be dissolved under the tongue (sublingual) or in the pouch of the cheek (buccal). The drugs administered in this manner are rapidly absorbed and have the advantage of bypassing the gastrointestinal tract. Nitroglycerin, for heart patients, in tablet form is more likely the most frequently administered sublingual drug.

(3) Rectal. Drugs administered by the rectal route may have a local effect (as for hemorrhoids) or a systemic effect (as in the prevention of nausea and vomiting). The rectal route is convenient to use in pediatric patients (children) or in patients who are unconscious or vomiting. The amount of drug absorbed in the rectal route is usually less than if the drug were administered orally. The absorption of drugs administered rectally is unpredictable and can vary among patients.

(4) Vaginal/urethral. Drugs administered using the vaginal/urethral route are used for their local effect. That is, they are usually given to treat an infection or other pathological condition. Drugs administered in this route should not be irritating since systemic absorption may occur.

(5) Inhalation. Drugs administered by inhalation have either may a local or systemic effect. Anesthetics, like nitrous oxide, are inhaled and exert their effect after absorption into the circulatory system. Sprays for nasal congestion have their effect on the tissue in the nose and do not necessarily enter the general circulation.

(6) Topical. The topical route is probably the oldest route of administration. Topical medications are applied directly upon the skin. As long as the skin is intact (not broken or cut), drugs applied in this manner exert a local effect. The base (vehicle) used to carry the ingredients in the local preparation can influence the action of the drug. For example, dimethylsulfoxide (DMSO) will readily penetrate the skin and carry the active ingredient along with it.

(7) Parenteral. The term parenteral literally means to avoid the gut (gastrointestinal tract). Thus, parenterals are injectable drugs that enter the body directly and are not required to be absorbed in the gastrointestinal tract before they show their effect. Parenteral routes of administration usually have a more rapid onset of action (show their effects more quickly) than other routes of administration. Parenteral products must be sterile (free from living microbes). The parenteral route of administration does have its disadvantages: it hurts, it is not a convenient route, and once administered the injected drug cannot be retrieved.

(a) Intravenous (IV). The injection of a drug directly into the patient's veins is the most rapid route of administration. This type of parenteral route results in the most rapid onset of action.

(b) Intraarterial. In this parenteral route, the drug is injected directly into the patient's arteries. This route is not frequently used.
(c) Intrathecal. The intrathecal route involves the administration of a drug directly into the spine (subarachnoid space) as in spinal anesthesia. The intrathecal route is used because the blood-brain barrier often precludes or slows the entrance of drugs into the central nervous system.

(d) Intramuscular (IM). The intramuscular route is used when drugs are injected deeply into muscle tissue. If the drug is in aqueous (water) solution, absorption is rapid. However, if the drug is in an oily liquid or in the form of a suspension, it can prolong the release of the drug.

(e) Intradermal (ID). In this route, the drug is injected into the (top few layers) of the skin. Ideally, the drug is placed within the dermis. The intradermal route is used almost exclusively for diagnostic agents.

(f) Subcutaneous (Sub-Q/SC). This route involves the injection of the drug under the skin into the fatty layer, but not into the muscle. Absorption of the drug is rapid. Insulin is normally administered subcutaneously.

3-6. TYPES OF ADVERSE REACTIONS TO DRUGS

A patient will sometimes have an adverse reaction to a drug. Adverse reactions can have a direct toxic effect on various systems of the body or the adverse reactions can occur in the form of milder side effects.

a. Direct Toxicity.

(1) In general terms, toxicity refers to the poison-like effects certain substances can produce in the body. Fortunately, most drugs do not produce toxic effects in most patients. However, when some drugs are administered to a patient over prolonged periods or when some drugs are given in high dosages, direct toxic effects can result. Direct toxicity may involve one or more of the body's systems. Certain parts of the body (that is, bone marrow) produce red and white blood cells. If a toxic accumulation of a substance affects these parts of the body, blood dyscrasias (the formation of malformed or destroyed white or red blood cells) may occur.

(2) The liver has as one of its main functions the detoxification of chemical substances when they are absorbed. If these substances damage the liver significantly, its ability to detoxify them is greatly affected. Of course, if these substances are not detoxified, the concentration of the substance in the body (that is, blood stream) constantly increases. Thus, hepatotoxicity (the destruction of the cells of the liver) can result in the accumulation of toxic products to the point that other body systems are affected.

(3) The kidneys are responsible for eliminating water-soluble toxic products (that is, waste products from cellular respiration) from the bloodstream. If nephrotoxicity
(damage to the kidneys) results, the accumulation of these toxic products can result in death.

(4) Toxic effects may not be limited to the person who is taking the drug. In the past, it has been demonstrated that some drugs will cross the placental barrier and enter the circulatory system of the fetus. Some drugs can exert serious effects on the developing fetus. For example, the fetus may abort or be born with any number of mental or physical defects. Since few mothers are willing to subject themselves and their unborn children to drug testing, the effects of most drugs on the fetus are unknown. Most of what is known about teratogenicity, fetal malformations, has been learned either from experimental studies with animals or from the unfortunate experiences of some mothers. The fetus is particularly susceptible to the adverse effects of medications during the first three months after conception (the first trimester). Unfortunately, many women do not realize they are pregnant until they are well into their first trimester.

b. Allergic Reactions. A few individuals may be allergic, or hypersensitive, to a drug. This allergy may arise because of a prior contact with a particular substance called an allergen (it may even be the drug itself). This acquiring of an allergy is called sensitization. You should understand that the symptoms of an allergy are not related to the ordinary effects of the drug. Allergic reactions to a drug may range from a mildly irritated skin rash to anaphylaxis (a fatal shock). It has been shown that penicillin, a widely prescribed antibiotic, produces varying types of allergic reactions in from 1 to 10 percent of the patients who are administered the drug.

c. Side Effects. Most drugs do not produce only one single effect. Instead, they may produce several physiological responses at the same time. For example, antihistamines, drugs frequently used for their anti-allergic action tend to produce drowsiness. In this case, drowsiness is a side effect of the antihistamines. With some drugs, the side effects are so worrisome and inconvenient that the patient may stop taking the medication.

d. Drug Dependence. All drugs have the potential of producing dependence, the need to have that drug. There are two major types of dependence: psychological and physiological.

(1) Psychological dependence may occur after a patient has been taking a medication for a long time. With psychological dependence, the patient becomes so convinced that he needs the drug (in order to continue to lead an improved life) that he will go to great lengths to ensure that he receives the medication. Patients habituated to amphetamines may demonstrate this type of dependence. Psychological dependence is very difficult to treat.

(2) With physiological dependence, the patient's body develops a real need for the drug over a long period. Since there is a physiological need for the drug, the body reacts by going through withdrawal symptoms (that is, tremors, nausea, vomiting,
and convulsions) if the drug is suddenly withheld. The patient habituated to narcotics and barbiturates have physiological dependence.

Section IV. FACTORS WHICH INFLUENCE DRUG ACTION

3-7. INTRODUCTION TO PHARMACOKINETICS

Pharmacokinetics deals with the absorption, distribution, metabolism (biotransformation), and excretion of drugs. Any time a drug is administered, these factors will directly affect the amount of drug that will arrive at the site where the drug acts. The amount of drug at the site of action will determine both the intensity of drug action and the length of time the drug will show its effect(s).

3-8. ABSORPTION OF DRUGS

Absorption involves the uptake of the drug by the body. Three factors affect the absorption of a drug: its water solubility, its fat solubility, and the transport mechanisms of the body. It is imperative that you understand that all drugs must be in solution before they can be absorbed.

3-9. FACTORS WHICH AFFECT ABSORPTION

a. Water Solubility. All body fluids are water based. Therefore, a drug must be soluble in water in order to be absorbed. Dissolution of the drug in aqueous (water) solution is dependent on the pH of the solution and the disintegration of the drug.

   (1) Disintegration. Disintegration (Figure 3-1) increases the surface area of a drug. The speed at which a dosage form disintegrates is dependent upon the type of solid dosage form and the manufacturing process used to make that dosage form. The solid dosage form could be a tablet, suppository, capsule, powder, or suspension. Take a tablet for example. The manufacturer may add starch to the tablet in order to make it swell when it is added to water. The tablet may be a sublingual tablet that is made to rapidly dissolve in the mouth. On the other hand, the manufacturer may compress the contents of the tablet under great pressure so that it will slowly dissolve. Further, an enteric coating may be applied to the tablet so that it will dissolve in the intestine. In the case of some capsules, "tiny time capsules" systematically dissolve during a period and prolong the effect of the drug.
(2) pH. The relative acidity or basicity of the fluids into which a drug is placed will affect how rapidly the drug will dissolve. The pH of the stomach can be as low as 1.0 (very acidic), the pH of the small intestine can range from 6.9 to 7.4 (slightly acidic to slightly basic), while the pH of the plasma is approximately 7.4 (slightly basic). Weakly acidic drugs (that is, aspirin) are more soluble in a basic or alkaline solution like the small intestine (pH above 7.4). Weakly basic drugs, such as tetracycline hydrochloride, are more soluble in an acidic solution like the stomach (pH below 7.0).

(3) Ionization. Ionization is the process whereby a substance breaks down into positively and negatively charged particles (Figure 3-2).

(a) For example, when hydrochloric acid ionizes, it forms hydrogen ions (H+) and chloride ions (Cl-).

(b) Equilibrium is established based on the chemical nature of each drug. That is, a certain percentage of the drug ionizes, while the rest remains as the compound. In summary, dosage forms must go into solution. A solid dosage form must disintegrate and dissolve before it can be absorbed. A suspension dosage form has already been partially dissolved; the drug particles must dissolve before absorption can occur. A solution dosage form contains a drug that has already been dissolved; thus, no disintegration or dissolution is required before absorption can occur.

b. Fat Solubility. In the last area, the topic of water solubility was discussed. For instance, a drug is in solution. What other factors must it overcome in order to be absorbed? One is fat solubility. Almost without exception, all body membranes are lipid (fatty) in nature. Membranes separate even the various water compartments of the body. These membranes are selectively permeable. That is, these membranes will only allow certain materials to pass through them. In particular, the membranes favor
the absorption of **unionized** particles (particles which have neither a positive nor a negative charge).

c. **Transport Mechanisms.** The body either in an active or in a passive way can absorb drugs.

1. **Passive transport.** Passive transport (diffusion) follows a concentration gradient. That is, if there is a high concentration of a substance on one side of the barrier and a low concentration of that substance on the other side of the barrier, nature tries to balance the two concentrations so that one is equal to the other. The two concentrations can be equalized in one of two ways. One way is for the liquid containing the substance to move from the side with fewer particles to the side with more particles. This process, called osmosis, will ultimately result in the two sides having the same concentration. The second option is for the drug particles to move from the side of higher concentration to the side of the lower concentration. This process, called diffusion, will also ultimately result in the two sides having the same concentration. Most drugs are absorbed in this manner of diffusion. With diffusion, the drug particles move from the side of higher concentration through the cell membrane into the side of lower concentration.

2. **Active transport.**

   (a) A ride in a roller coaster would give you a background to understand this section on active transport. You have probably observed that a roller coaster car does not have an engine. Common sense would tell you that the car does not need an engine to go down the hills, but up those hills—that is a different story. You have probably observed that a mechanism exists for pulling the car up the hill.

   (b) Active transport works in much the same way. Proteins (in the cells) make up the linings of the cells. Some of these proteins have a particular affinity (attraction) for a selected drug. When the drug molecule meets the cell wall, the protein called a "carrier molecule" attaches itself to the drug, carries it across the cell membrane, and releases the drug on the other side. The drug then enters the circulation and is distributed throughout the body. Active transport can move against a concentration gradient to move a substance to a place of higher concentration. Vitamin **B-12** is an example. Very little of this vitamin can pass through the intestinal wall of the gut by diffusion; however, a carrier molecule, often called "intrinsic factor" transports the vitamin across the gut. Once in circulation, the vitamin is stored in the liver. The concentration of drug in the liver is several hundred times higher than in circulation. Therefore if a drug is unionized, water soluble, and fat-soluble, it may pass through the cells of the gut if taken orally. Once in circulation, the drug must pass through the fatty layer of the individual cell in order to have an effect. So, even injected medications have some of the same problems as oral medications.

3. **Illustration of concepts.** Perhaps some insight can be gained about this whole topic of drug transport mechanisms if a diagram depicting the concepts is shown and discussed. Figure 3-3 is provided for this purpose. In the figure, several concepts are illustrated:
A--Drug A is an undissolved drug. It is not in solution and it cannot be absorbed.

B--B is a molecule of a drug in solution. It is unionized and can be absorbed.

C--C is a molecule of a drug attached to a "carrier molecule" at the cell wall.

D--D is an ion of a drug. It cannot be absorbed since the fatty layer repels it.

E--E is a molecule of a drug. It is in circulation and will be carried away.

F--F is a molecule of the drug that is being released into circulation by a carrier molecule.

Figure 3-3. Illustration of drug transport concepts.

**NOTE:** Passive transport or diffusion has absorbed Molecule B. Once it has been absorbed, the circulating blood will carry it away. Consequently, the concentration of the drug will always remain higher in the gut and diffusion will continue. As the unionized particles are absorbed, the ionized particles will attach to each other to form more unionized drug. This occurs because the drug has equilibrium established.
between the ionized and unionized form; as the unionized form is removed, the balance shifts make up for the loss. Molecules C and F are being moved by active transport. They must also be unionized and fat soluble; however, their transport does not rely on differences in concentration. This transport process also accounts for the absorption of a drug by the individual cells within the body.

3-10. DISTRIBUTION OF DRUGS

a. Once the drug is absorbed, it enters the circulation and is carried throughout the body. The location in the body where the drug goes varies from drug to drug. The drug may be stored in bone or fat, bound to the proteins in the blood plasma, or circulate freely as the unbound drug. The drug will find its way into many organs. Finally, some of the drug will reach the target tissue where it can cause the effect for which it was administered. An equilibrium will be established between the circulating unbound drug and each area of the body.

b. The distribution of a drug in the body happens in a very systematic manner. Figure 3-4 demonstrates the concept of distribution.

![Figure 3-4. Drug distribution within the body.](image)

Assume that 100 micrograms (100 mcg) of a drug have been absorbed and is distributed based on the percentages noted in Figure 3-4. Of the 100 micrograms absorbed, only two micrograms of the drug will arrive at the target tissue to give the desired pharmacological effect. If two micrograms is enough drugs to produce the desired pharmacological effect, the desired effect will be obtained. However, if the amount of drug required to produce the effect is four micrograms, the desired pharmacological effect will not be obtained. The dose of the drug can be increased so that 200 milligrams of the drug can be absorbed, thus providing the amount of drug needed to give the desired pharmacological effect. However, doubling the dose may present problems. Doubling the dose would also double the amount of drug in the other areas of the body. Perhaps this increased dosage may produce some response by another body organ. For example, the patient may become nauseous, vomit, lose his
hair, or go into convulsions. These are side effects of the drug. Thus, it is important to remember that the whole body must be taken into account when a drug is administered. If the problem of the side effects cannot be resolved, the drug may not be released for use.

NOTE: Another areas of concern in the distribution of drugs are those that crosses the placental barrier. Drugs may actively or passively cross the placental barrier and enter the fetal circulation. The enzyme systems of the developing fetus may not be able to adequately metabolize the drug. Toxic effects can result. At this time, it is virtually impossible to predict whether a drug will pass the placental barrier.

3-11. METABOLISM (BIOTRANSFORMATION)

The process of drug absorption and distribution is dynamic. That is, it is continually changing. Even as the drug is being distributed, the individual cells of the body begin to chemically change or alter the drug. This metabolic process of changing the drug is called metabolism or biotransformation. While many cells of the body will be involved in this process, the liver is the organ primarily responsible for this biotransformation. The liver changes drugs to make them more water-soluble so that they may be more easily excreted from the body. During the process of metabolism, a drug may be rendered inactive, converted from an inactive form to an active one, or be made more toxic. The liver may oxidize, reduce, hydrolyze, or conjugate (bind with a protein) the drug. The kidney will also play an active role in conjugating drugs.

3-12. BIOAVAILABILITY

a. The term bioavailability was defined in the first portion of this subcourse. In Figure 3-4, all 100 micrograms of the drug was available to the system, since it was absorbed. The amount of drug originally administered to the patient was not stated. That amount of administered drug could have ranged from 100 micrograms to 1000 milligrams or more. From the reading, you should have noted that absorption is not an easy process, and that any number of things can interfere with the process.

b. The controversy concerning generic drugs deserves consideration at this point. For example, switching a patient from one generic brand of ampicillin to another brand of ampicillin could cause some problems for some patients. Thus, one company's generic brand of a drug might not be able to be absorbed as quickly as another company's generic brand of the same drug. With other drugs and some patients the switch from one company's drug to another company's drug is of little consequence.

c. Drugs that present the most problems in terms of bioavailability are oral solids. That is because oral solids must disintegrate, dissolve, be water soluble, be fat soluble, unionize, and pass through the drastic pH changes from the stomach to the small intestine.
3-13. EXCRETION

a. Excretion is the process of eliminating a drug or its metabolites from the body. The major organ of excretion is the kidney. Secondary routes of excretion are hepatic (liver), through the bile into the feces, lungs, saliva, sweat, and breast milk.

b. The inability of a patient to excrete drugs and other waste can be life threatening. The elimination of drugs through sweat, saliva, and the lungs is of minor interest in this subcourse. Of course, the excretion of drugs in breast milk is of concern to mothers who breast-feed their infants. As a rule, drugs that are weakly basic are more likely to be excreted in breast milk, because the milk is slightly acidic; therefore, the basic drugs are more soluble in breast milk.

c. Patients who have limited liver and kidney function usually require lower doses of medication. This is because more of the drug tends to stay in the body.

3-14. MECHANISMS OF DRUG ACTION

a. Receptor Site Theory. A drug that finally enters a cell may produce an effect. It is able to produce this effect by a variety of complex biochemical processes. Most of the processes can be simplified into one explanation of the mechanism of drug action known as the receptor-site or "lock and key" theory. This theory states that a drug (the key) combines with a receptor-site (the lock) to produce a pharmacological effect. Drugs that will fit into the receptor-site are said to have an "affinity" for that receptor-site. Only drugs that fit into the receptor-site will produce a pharmacological response. Figure 3-5 visually represents the receptor-site theory.

b. Chemical Structure Activity Relationship. As a review, drug molecules have specific chemical structures. The chemical structure of a drug will determine if a drug molecule (the key) will fit into the receptor-site (the lock) and produce a pharmacological effect. For example, whether the hydroxyl (OH-) group is on the left or right side of the molecule or is at a 520 angle with the molecule can determine whether the "key" will fit the "lock." This is referred to as chemical structure activity relationship. From this, we can say that drugs that are similar in composition and chemical structure may have similar effects. The chemical structure of a drug can be altered with no effect upon the pharmacological effect the drug produces. However, the change in the chemical structure of the drug molecule can increase or decrease its side effects. Further, the modification of a drug molecule can influence its pharmacological actions. Therefore, the modification of a drug's molecular structure can result in the formation of a drug that can produce a desired pharmacological effect with a significantly lower dose and with an accompanying decrease in undesired side effects.
c. **Antagonists.** Antagonists are drugs that will or reverse block the action of other drugs. There are two types of antagonists: competitive and physiological.

   (1) **Competitive antagonists.** Competitive antagonists combine with the receptor-site and prevent another drug from combining with the receptor-site. A competitive antagonist does not displace a drug at the receptor-site. Figure 3-6 illustrates the concept of a competitive antagonist.

   (2) **Physiological antagonists.** Physiological antagonists reverse the action of the drug by acting on a different receptor-site to cause a different physiological effect.

### 3-15. DRUG EFFICACY

a. Drug efficacy refers to the effectiveness of a drug. Drug efficacy is measured by the clinical response of the patient. A drug is considered to have a high degree of efficacy, if it achieves desired clinical results.

b. Laboratory tests may be used to determine the amount of drug that has been absorbed. The amount of drug absorbed may be used to predict a patient's response. However, since people respond differently to the same dose of the same drug, merely
knowing the amount of drug absorbed does not always indicate the response of an individual patient.

c. A general rule is that as the dose of a drug is increased, a greater effect is seen in the patient until a maximum desired effect is reached. If more drug is administered after the maximum point is reached, the side effects will normally increase. Figure 3-7 illustrates this principle.

![Figure 3-7. Relationship between dosage and drug effect.](image)

Continue with Exercises
EXERCISES, LESSON 3

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the definitions below, select the definition of the term drug.
   a. A substance that is used to cure all diseases.
   b. A substance used to prevent, diagnose, or treat disease or to prevent pregnancy.
   c. A substance that can only be purchased at a drugstore.
   d. A substance that occurs naturally and cannot cause any toxic reactions.

2. From the definitions below, select the definition of the term toxicology.
   a. The science of chemicals.
   b. The science of drugs.
   c. The science of poisons.
   d. The science of dosage.

3. Select the drug that is derived from an animal source.
   a. Belladonna.
   b. Heparin.
   c. Iron.
   d. Aspirin.
4. Select the statement that best describes a use of drugs.
   a. To produce anxiety or tension.
   b. To relieve the symptoms of a disease or condition.
   c. To cure diabetes.
   d. Both a and b.
   e. Both b and c.

5. Select the statement that best describes how the physical condition of a patient might influence the amount of drug required to obtain a specific effect.
   a. Debilitated patients always require the same amount of drug as a healthy person.
   b. The physical condition of a patient never influences the required dose of a drug.
   c. The weak patient might require smaller doses of a drug to achieve an effect.
   d. Patients in extreme pain usually require smaller doses of analgesic agents rather than patients who are in less pain.

6. Select the statement that best describes drug dependence.
   a. Drug dependence occurs whenever a patient takes a particular drug for a long period.
   b. Drug dependence is said to occur when the patient has either a physiological or psychological need for a drug.
   c. Drug dependence occurs when a patient's body requires a drug, but cannot tolerate its harmful effects.
   d. Drug dependence can only occur with certain types of drugs (like narcotics).
7. Select, from the list below, the definition of the term synergism.

a. Synergism occurs when one drug lives off another drug.

b. Synergism occurs when the combined effect of two drugs is greater than the sum of their independent effects.

c. Synergism occurs when the combined effects of two drugs are equal to the sum of the independent effects of the drugs.

d. Synergism occurs when one drug's effects cancel the effects of another drug.

8. Select the route of administration in which the dosage form is placed in the mouth but not swallowed.

a. Parenteral.

b. Rectal.

c. Sublingual/Buccal.

d. Oral.

9. Select the statement that best describes the sublingual/buccal route of administration.

a. In this route of administration, the drug is swallowed and very quickly absorbed by the patient.

b. In this route of administration, the drugs are absorbed only after being taken into the gastrointestinal tract.

c. In this route of administration, the drug is absorbed without passing through the gastrointestinal tract.

d. In this route of administration, the drug is applied directly to the skin.
10. From the statements below, select the statement that best describes how fat solubility influences drug absorption.

a. Since all body fluids are fat based, a drug must be soluble in fat in order to be absorbed and demonstrate its effect.

b. Since body membranes are lipids in nature, a drug that will pass through lipid material will be absorbed much more quickly than ionized drug particles.

c. The body cannot absorb a fat-soluble drug, because it is unionized.

d. All fat-soluble drugs must be converted into water-soluble substances before they can be absorbed.

11. From the list below, select the definition of the term metabolism.

a. The chemical process of producing a drug.

b. The metabolic process of changing a drug.

c. The process of transforming a living life form.

d. The modification of complex substances to make them powerless.

12. From the list below, select the definition of the term excretion.

a. The process of placing a drug or its metabolites into the body.

b. The process of metabolically changing a drug or its metabolites.

c. The process of eliminating a drug or its metabolites from the body.

d. The process of concentrating a drug and removing it from the patient's gastrointestinal tract.
13. From the descriptions below, select the description that best describes the Receptor-Site Theory of the mechanism of drug action.

   a. A drug (the lock) combines with a receptor-site (the key) to produce a pharmacological effect.

   b. A drug (the key) combines with a receptor-site (the lock) to produce a pharmacological effect.

   c. A drug (the receptor-site) combines with cell components (the lock) to produce a pharmacological effect.

   d. A drug (the lock) combines with a receptor-site in the intestine to produce an essential effect.

14. Select the statement that best contrasts passive transport with active transport.

   a. Active transport occurs when molecules of the drug move from an area of high concentration to an area of low concentration, while passive transport occurs when a "carrier molecule" carries a drug molecule across a cell membrane.

   b. Passive transport occurs in comatose patients whose cells are unable to actively absorb drugs through the normal processes.

   c. Passive transport occurs when molecules of a drug move from an area of high concentration to an area of low concentration, while active transport occurs when a "carrier molecule" carries a drug molecule across a cell membrane.

   d. Passive transport occurs when a "carrier molecule" carries drug molecules from an area of low concentration to an area of high concentration, while passive transport involves the movement of blood plasma from a low concentration to a high concentration.
15. From a group below, select the description that best describes the importance of structure activity relationships.

   a. Drugs that are similar in composition and structure may have similar effects.

   b. Drugs that are not similar are ineffective.

   c. Drugs that are active generally have similar structures.

   d. Drugs that are similar in effect generally have the same trade name.

16. Select the statement that best contrasts competitive antagonist with physiological antagonists.

   a. Competitive antagonists combine with the receptor-site and prevent another drug from combining with the receptor-site, while physiological antagonists reverse the action of a drug by acting on a different receptor-site to cause different physiological reaction.

   b. Competitive antagonists produce pharmacological effects by producing a physiological effect different from the drug, while physiological antagonists physiologically compete for a spot on the receptor-site.

   c. Competitive antagonists combine with the receptor-site and remove the drug from the site, while physiological antagonists physically compete for the receptor-site.

   d. Physiological antagonists physically remove drug molecules from the receptor-site, while competitive antagonists compete for the receptor-site.

   Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 3

1. b A substance used to prevent, diagnose, or treat disease or to prevent pregnancy. (para 3-2a)

2. c The science of poisons. (para 3-2e)

3. b Heparin. (para 3-3b)

4. b To relieve the symptoms of a disease or condition. (para 3-4c)

5. c The weak patient may require smaller doses of a drug to achieve an effect. (para 3-5f)

6. b Drug dependence is said to occur when the patient has either a physiological or psychological need for a drug. (para 3-6)

7. b Synergism occurs when the combined effect of two drugs is greater than the sum of their independent effects. (para 3-5j(1))

8. c Sublingual/Buccal. (para 3-5k(2))

9. c In this route of administration the drug is absorbed without passing through the gastrointestinal tract. (para 3-5k(2))

10. b Since body membranes are lipid in nature, a drug that will pass through lipid material will be absorbed much more quickly than ionized drug particles. (para 3-9b)

11. b The metabolic process of changing a drug. (para 3-11)

12. c The process of eliminating a drug or its metabolites from the body. (para 3-13a)

13. b A drug (the key) combines with a receptor-site (the lock) to produce a pharmacological effect. (para 3-14a)

14. c Passive transport occurs when molecules of a drug move from an area of high concentration to an area of low concentration, while active transport occurs when a “carrier molecule” carries a drug molecule across a cell membrane. (para 3-9c(1) and (2))
15. a Drugs that are similar in composition and structure may have similar effects. (para 3-14b)

16. a Competitive antagonists combine with the receptor-site and prevent another drug from combining with the receptor-site, while physiological antagonists reverse the action of a drug by acting on a different receptor-site to cause a different physiological reaction. (para 3-14c(1) and (2))

End of Lesson 3
LESSON ASSIGNMENT

LESSON 4

Local Anesthetic Agents.

TEXT ASSIGNMENT

Paragraphs 4-1—4-8.

LESSON OBJECTIVES

After completing this lesson, you should be able to:

4-1. Given one of the following terms: local anesthetic, local infiltration, topical block, surface anesthesia, nerve block, peridural, and spinal anesthesia, and a group of statements, select the meaning of that term.

4-2. From a group of statements, select the statement that best describes the mechanism of action for local anesthetics.

4-3. Given a group of statements, select the statement that best describes why vasoconstrictors are used in conjunction with local anesthetics.

4-4. From a group of statements, select the caution and warning associated with the use of a local anesthetic combined with a vasoconstrictor.

4-5. Given a group of statements, select the statement that best describes why hyaluronidase (Wydase®) is used in conjunction with local anesthetics.

4-6. Given a group of statements, select the statement that describes a caution and warning associated with the use of local anesthetics.

4-7. From a list of toxicities, select the toxicity associated with the use of local anesthetics.

4-8. Given the trade name of a local anesthetic agent and a list of generic names, match the trade name of the agent with its generic name.
4-9. Given the trade and/or generic name of a local anesthetic agent and a group of possible uses or cautions and warnings, select the clinical use or caution and warning associated with that agent.

**SUGGESTION**

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 4
LOCAL ANESTHETIC AGENTS

Section I. BACKGROUND INFORMATION

4-1. BACKGROUND INFORMATION

In order to understand what a local anesthetic is and how it is used, you need to study/review the following definitions:

a. **Local Anesthetic.** A local anesthetic is an agent that interrupts pain impulses in a specific region of the body without a loss of patient consciousness. Normally, the process is completely reversible--the agent does not produce any residual effect on the nerve fiber.

b. **Local Infiltration (Local Anesthesia).** Local infiltration occurs when the nerve endings in the skin and subcutaneous tissues are blocked by direct contact with a local anesthetic, which is injected into the tissue. Local infiltration is used primarily for surgical procedures involving a small area of tissue (for example, suturing a cut).

c. **Topical Block.** A topical block is accomplished by applying the anesthetic agent to mucous membrane surfaces and in that way blocking the nerve terminals in the mucosa. This technique is often used during examination procedures involving the respiratory tract. The anesthetic agent is rapidly absorbed into the bloodstream. For topical application (that is, to the skin), the local anesthetic is always used without epinephrine. The topical block easily anesthetizes the surface of the cornea (of the eye) and the oral mucosa.

d. **Surface Anesthesia.** This type of anesthesia is accomplished by the application of a local anesthetic to skin or mucous membranes. Surface anesthesia is used to relieve itching, burning, and surface pain (for example, as seen in minor sunburns).

e. **Nerve Block.** In this type of anesthesia, a local anesthetic is injected around a nerve that leads to the operative site. Usually more concentrated forms of local anesthetic solutions are used for this type of anesthesia.

f. **Peridural Anesthesia.** This type of anesthesia is accomplished by injecting a local anesthetic into the peridural space. The peridural space is one of the coverings of the spinal cord.

g. **Spinal Anesthesia.** In spinal anesthesia, the local anesthetic is injected into the subarachnoid space of the spinal cord.
4-2. MECHANISM OF ACTION OF THE LOCAL ANESTHETICS

a. The nerve fiber is a long cylinder surrounded by a semipermeable (allows only some substances to pass) membrane. This membrane is made up of proteins and lipids (fats). Some of the proteins apparently act as channels, or pores, for the passage of sodium and potassium ions through the membrane.

b. The movement of nerve impulses along a nerve fiber is associated with a change in the permeability of the membrane. The pores widen, and sodium ions (Na+) move to the inside of the fiber. At the same time, potassium ions (K+) diffuse out through other pores (see Figure 4-1). The entire process is called depolarization. Immediately after the nerve impulse has passed, the pores again become smaller. Sodium ions (Na+) are now "pumped" out of the fiber. At the same time, potassium ions are actively transported into the fiber. The nerve membrane is then ready to conduct another impulse.

c. Local anesthetics block depolarization of the nerve membrane. That is, to make the conduction of the nerve impulse impossible.

d. The local anesthetic effect lasts as long as the agent maintains a certain critical concentration in the nerve membrane. There is a potential problem: the local concentration needed to prevent conduction of the nerve impulse is much greater than the tolerable blood level. TO AVOID A SYSTEMIC TOXIC REACTION TO THE LOCAL ANESTHETIC, THE SMALLEST AMOUNT OF THE MOST DILUTE SOLUTION THAT WILL EFFECTIVELY BLOCK THE PAIN SHOULD BE ADMINISTERED.

4-3. THE USE OF VASOCONSTRICTORS IN CONJUNCTION WITH LOCAL ANESTHETICS

a. Indications. Vasoconstrictors (like epinephrine) are sometimes used in conjunction with local anesthetics. Vasoconstrictors are used to prolong the duration of action of local anesthetics. Vasoconstrictors also help to control bleeding. Furthermore, the vasoconstrictor delays the absorption of the local anesthetic by reducing the blood flow to the affected area. This results in a reduction of the toxic effects of the local anesthetic, since the rate of absorption keeps pace with the rate the
local anesthetic is metabolized by the body. Vasoconstrictors are of no value in delaying the absorption of the local anesthetic from mucous membranes (that is, topical blocks).

b. **Cautions and Warnings of the Combination.**

   (1) It should be recognized that the injection of epinephrine-containing solutions in or around fingers, toes, and the penis is not recommended.

   (2) Freshly prepared combinations of vasoconstrictors and local anesthetics are more effective than commercially premixed epinephrine-containing local anesthetic solutions. This is because a very low pH is required to stabilize the epinephrine in these mixtures. In general, the content of one part epinephrine to 200,000 parts of the local anesthetic agent (is optimum) will minimize the side effects inherent with epinephrine. Great care must be taken in calculating this dilution. Small, precisely calibrated syringes should be used in the mixing process. It should be noted that the standard solution of epinephrine supplied is a 1:1000 (1 to 1000) concentration in each glass ampule. This means that 1 milliliter of the 1:1000 epinephrine solution contains 1 milligram of epinephrine. In preparing a 1:200,000 dilution, epinephrine should be added to a local anesthetic solution on a ratio of 0.1 milliliter-20 milliliters of local anesthetic solution. This does not apply to subarachnoid injections, in which a higher concentration of epinephrine is required.

4-4. **ANOTHER AGENT WHICH CAN AFFECT THE ACTIONS OF LOCAL ANESTHETICS**

   Hyaluronidase (Wydase®) is sometimes used in conjunction with local anesthetics. Hyaluronidase is an enzyme that breaks down the material that binds cells together. Thus, when hyaluronidase is combined with local anesthetic, greater infiltration (movement) of the local anesthetic in the tissues is made possible.

4-5. **CAUTIONS AND WARNINGS ASSOCIATED WITH LOCAL ANESTHETICS**

   a. Precautions should be taken against the danger of confusing the various agents with one another or mistaking different concentrations of the same drug.

   b. In order to avoid intravascular (into the veins) injection, aspiration in several planes with the plunger of the syringe should always be done before injecting the anesthetic solution into the tissues.

   c. The instillation of local anesthetic agents into the trachea and bronchi leads to immediate absorption, which soon reach blood levels comparable to those reached by straight intravenous injection.

   d. A previously punctured vial of local anesthetic solution should never be reautoclaved.
e. Discolored local anesthetic solutions should be immediately thrown away.

4-6. TOXICITIES OF LOCAL ANESTHETICS

Essentially all systemic toxic reactions associated with local anesthetics are the result of over-dosage leading to high blood levels of the agent given. Therefore, to avoid a systemic toxic reaction to a local anesthetic, the smallest amount of the most dilute solution that effectively blocks pain should be administered.

a. **Hypersensitivity.** Some patients are hypersensitive (allergic) to some local anesthetics. Although such allergies are very rare, a careful patient history should be taken in an attempt to identify the presence of an allergy. There are two basic types of local anesthetics (the amide type and the ester type). A patient who is allergic to one type may or may not be allergic to the other type.

b. **Central Nervous System Toxicities.** Local anesthetics, if absorbed systematically in excessive amounts, can cause central nervous system (CNS) excitement or, if absorbed in even higher amounts, can cause CNS depression.

   (1) **Excitement.** Tremors, shivering, and convulsions characterize the CNS excitement.

   (2) **Depression.** The CNS depression is characterized by respiratory depression and, if enough drug is absorbed, respiratory arrest.

c. **Cardiovascular Toxicities.** Local anesthetics if absorbed systematically in excessive amounts can cause depression of the cardiovascular system. Hypotension and a certain type of abnormal heartbeat (atrioventricular block) characterize such depression. These may ultimately result in both cardiac and respiratory arrest.

Section II. LOCAL ANESTHETICS AND THEIR CLINICAL USES

4-7. EXAMPLES OF LOCAL ANESTHETICS

The local anesthetics you may encounter in a hospital or fields setting are described below. The discussion does not cover every fact known about the use of a particular drug. Therefore, you are encouraged to read references or to ask knowledgeable personnel your specific questions concerning points not presented in this subcourse.
a. **Lidocaine Hydrochloride (Xylocaine®).**

   (1) **Clinical uses.** Lidocaine is used as a local anesthetic for infiltrations, nerve blocks, spinal anesthesia, topical anesthesia, and for caudal and epidural anesthesia. It has a rapid onset of action and its effects last from 75 to 150 minutes. It has also been used as a cardiac depressant (anti arrhythmic).

**NOTE:** Refer to Table 4-1 for an overview of the clinical uses of various local anesthetics.

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<th></th>
<th>Ophthalmic Topical</th>
<th>Topical</th>
<th>Infiltration</th>
<th>Nerve Block</th>
<th>Spinal</th>
<th>Epidural and Caudal</th>
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<td>7. Lidocaine</td>
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<td>13. Ethyl chloride *</td>
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</table>

*Surface anesthetics for application to the skin.

**Table 4-1. An overview of the clinical uses of various local anesthetics.**
(2) **Forms available.** Lidocaine is available in injection form (various percentage concentrations), jelly form, and in cream form.

b. **Mepivacaine (Carbocaine®).**

(1) **Clinical uses.** Mepivacaine is pharmacologically and chemically related to lidocaine. It is used for infiltration, nerve block, peridural, and regional anesthesia. The duration of action for this drug is from 2 to 2 1/2 hours.

(2) **Forms available.** Mepivacaine is available in injection form.

c. **Prilocaine (Citanes®).**

(1) **Clinical uses.** Prilocaine is pharmacologically similar to both lidocaine and mepivacaine. It is used for infiltration, nerve block, peridural, and regional anesthesia. This drug is less toxic than lidocaine because it is metabolized and excreted faster than lidocaine.

(2) **Forms available.** Prilocaine is available in injection form.

d. **Bipivacaine (Marcaine®).**

(1) **Clinical uses.** Bipivacaine is pharmacologically related to lidocaine. It is used for infiltration, nerve block, and epidural anesthesia.

(2) **Forms available.** Procaine is available in injection form.

e. **Dibucaine (Nupercainal®, Nupercaine®).**

(1) **Clinical uses.** Dibucaine is used for spinal and topical anesthesia. It is the most potent local anesthetic. It is one of the most toxic and longest-acting local anesthetics.

(2) **Forms available.** Dibucaine is available in cream, spray, suppository, ointment, and injection forms.

f. **Procaine (Novocaine®).**

(1) **Clinical uses.** Procaine is used for infiltration, nerve block, and spinal anesthesia. Procaine is not applied topically. Its duration of action is approximately 1 hour. It is a fairly safe local anesthetic to use since it is metabolized quickly.

(2) **Forms available.** Procaine is available in injection form.
g. **Chloroprocaine (Nesacaine®, Nesacaine-C®).**

(1) **Clinical uses.** Chloroprocaine is pharmacologically similar to procaine. Chloroprocaine is used for infiltration, nerve block, caudal, and epidural anesthesia.

(2) **Forms available.** Chloroprocaine is available in injection form.

h. **Tetracaine (Pontocaine®).**

(1) **Clinical uses.** Tetracaine is used for topical, nerve block, infiltration, spinal, and caudal anesthesia. Its onset of action is 15 minutes.

(2) **Forms available.** Pontocaine is available in injection, cream, ointment, and injectable forms.

i. **Proparacaine (Alcaine®, Ophthetic®).**

(1) **Clinical uses.** Proparacaine is used primarily to produce anesthesia when applied to the eye. It has a rapid onset of action (20 seconds) and its duration of action is approximately 15 minutes.

(2) **Forms available.** Proparacaine is supplied in solution form.

j. **Benzocaine (Americaine®).**

(1) **Clinical uses.** Benzocaine is used for topical anesthesia of the mucous membranes and skin. It is used in many over-the-counter spray preparations for the treatment of sunburn and itching.

(2) **Forms available.** Benzocaine is available in solution, ointment, and spray forms.

k. **Cocaine.**

(1) **Clinical uses.** Cocaine is applied to produce local anesthesia with intensive vasoconstriction on mucous membranes. It is applied to procedure anesthesia in the nose, throat, ear, and in bronchoscopy (a procedure in which an instrument is used to inspect the bronchi).

(2) **Forms available.** Cocaine is supplied in the form of a white powder. Cocaine solution must be compounded. It is a Schedule II controlled substance.
4-8. LOCAL ANESTHETICS USED FOR TOPICAL APPLICATION ONLY

a. Dichlorotetrafluorethane (Freon®)

(1) Clinical uses. Dichlorotetrafluorethane is a nonflammable and nonexplosive agent for topical anesthesia of the skin. It is especially useful for localized minor surgical procedures. This agent should not be sprayed on the skin for a period that exceeds 45 seconds.

(2) Forms available. Dichlorotetrafluorethane is available in a spray form.

b. Ethyl Chloride.

(1) Clinical uses. This agent is used for topical anesthesia of the skin.

(2) Forms available. Ethyl chloride is available in a spray form.

Continue with Exercises
EXERCISES, LESSON 4

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which of the following statements best defines the term local infiltration?
   
   a. A type of anesthesia achieved by applying the anesthetic agent to the surface of mucous membranes to block nerve transmissions.
   
   b. A type of anesthesia achieved when the nerve endings in the skin and subcutaneous tissues are blocked by direct contact with a local anesthetic that is injected into the tissue.
   
   c. A type of anesthesia accomplished by injecting a nerve that leads to the operative site.
   
   d. A type of anesthesia accomplished by injecting a local anesthetic into the peridural space.

2. Which of the following statements best describes the mechanism of action of local anesthetics?
   
   a. Local anesthetics destroy the nerve tissue so that electrical impulses cannot be carried.
   
   b. Local anesthetics greatly increase the number of electrical impulses being transmitted so that pain cannot be felt in that particular area.
   
   c. Local anesthetics block depolarization of the nerve membrane so that the conduction of the nerve impulse is impossible.
   
   d. Local anesthetics remove both potassium and sodium ions from the nerve tissue so that polarity in the nerve cannot be accomplished; therefore, the impulses are not allowed to move past a certain point in the tissue.
3. Why is hyaluronidase (Wydase®) used in conjunction with local anesthetics?
   a. Hyaluronidase concentrates the local anesthetic in a particular area in order that its effects might be prolonged.
   b. Hyaluronidase neutralizes the local anesthetic so that undesired adverse effects are greatly reduced.
   c. Hyaluronidase is an enzyme that acts to tenderize the tissue and make the nerves more sensitive to the effects of the local anesthetic.
   d. Hyaluronidase increases the movement of the local anesthetic through the tissue.

4. Select the caution(s) and warning(s) associated with the use of local anesthetics.
   a. When a local anesthetic is to be injected, the plunger should be aspirated in several planes to ensure the drug is not being injected into a vein.
   b. Discolored solutions of local anesthetic should be thrown away.
   c. A previously used vial of local anesthetic solution should never be reautoclaved.
   d. All the above.

5. Select the toxicity(ies) associated with the use of local anesthetics.
   a. Large amounts of systemically absorbed local anesthetics can cause depression of the cardiovascular system.
   b. Local anesthetics, even when given in small amounts, cause tremors, shivering, and convulsions.
   c. Local anesthetics cause respiratory depression.
   d. Local anesthetics tend to produce hypersensitive reactions in most people.
INSTRUCTIONS: In Exercises 6-9, match the trade and generic names of the local anesthetics.

6. Tetracaine ______________________________ a. Americaine®
7. Mepivacaine ______________________________ b. Freon®
8. Dichlorotetrafluorethane ___________________ c. Pontocaine®
9. Benzocaine _______________________________ d. Carbocaine®

10. Select the clinical use of ethyl chloride.
    
    a. Used to produce anesthesia when applied to the eye.
    b. Used for topical anesthesia of the skin.
    c. Used for infiltration and caudal anesthesia.
    d. Used to produce anesthesia in mucous membranes procedures.

11. What is the clinical use of proparacaine?
    
    a. Used to produce topical anesthesia on the skin.
    b. Used to produce both anesthesia and vasoconstriction when applied to certain tissues.
    c. Used in nerve block, spinal, and caudal anesthesia.
    d. Used to produce anesthesia in the eye.

12. What is the clinical use of bupivacaine (Marcaine®)?
    
    a. Used to produce anesthesia when applied to the eye.
    b. Used to produce infiltration, nerve block, and epidural anesthesia.
    c. Used to produce anesthesia when applied to the skin or mucous membranes.
    d. Used to produce anesthesia in a localized area when applied topically (that is, bronchoscopy).
13. Select the caution and warning associated with the use of procaine (Novocaine®).

a. The drug should not be applied topically.

b. The drug should not be used for infiltration anesthesia.

c. The drug should not be used to produce spinal anesthesia.

d. The drug should not be used to produce nerve block anesthesia.

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 4

1. b A type of anesthesia achieved when the nerve endings in the skin and subcutaneous tissues are blocked by direct contact with a local anesthetic that is injected into the tissue. (para 4-1b)

2. c Local anesthetics block depolarization of the nerve membrane so that the conduction of the nerve impulse is impossible. (para 4-2)

3. d Hyaluronidase increases the movement of the local anesthetic through the tissue. (para 4-4)

4. d All of the above. (para 4-5b, d, and e)

5. a Large amounts of systemically absorbed local anesthetics can cause depression of the cardiovascular system. (para 4-6c)

6. c Pontocaine®. (para 4-7h)

7. d Carbocaine®. (para 4-7b)

8. b Freon®. (para 4-8a)

9. a Americaine®. (para 4-7j)

10. b Used for topical anesthesia of the skin. (para 4-8b)

11. d Used to produce anesthesia in the eye. (para 4-7i)

12. b Used to produce infiltration, nerve block, and epidural anesthesia. (para 4-7d)

13. a The drug should not be applied topically. (para 4-7f)

End of Lesson 4
LESSON ASSIGNMENT

LESSON 5

The Central Nervous System.

TEXT ASSIGNMENT

Paragraphs 5-1--5-15.

LESSON OBJECTIVES

After completing this lesson, you should be able to:

5-1. Given a list of types of tissue, select the two types of nervous tissues.

5-2. From a list of functions, select the function(s) for which nervous tissues are specialized.

5-3. Given one of the following terms: neuron, dendrite, or axon, and a group of definitions, select the definition of that term.

5-4. Given the shape, diameter, or function of a type of neuron and a list of types of neurons, select the type of neuron described.

5-5. Given a group of statements, select the statement that best describes the neuromuscular junction.

5-6. Given a group of statements, select the statement that best describes the function of a neurotransmitter.

5-7. From a list of chemical substances, select the substance(s) which is/are neurotransmitter(s).

5-8. Given a list of names, select the names of the three major divisions of the human nervous system.

5-9. Given a list of names, select the names of the two major subdivisions of the central nervous system.

5-10. From a list of functions, select the function(s) of the cerebrospinal fluid.
5-11. Given the name of one of the major subdivisions of the human brain and a list of functions, select the function(s) of that part.

5-12. Given a list of functions, select the function of the meninges surrounding the brain and spinal cord.

**SUGGESTION**

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 5
THE CENTRAL NERVOUS SYSTEM

Section I. BASIC CONCEPTS OF THE NERVOUS SYSTEM

5-1. TYPES OF NERVOUS TISSUES

There are two types of nervous tissues--the neurons (nerve cells) and glia (neuroglia). The neuron is the basic structural unit of the nervous system. The glia are cells of supporting tissue for the nervous system. There are several different types of glia, but their general function is support (physical, nutritive, and so forth.).

5-2. SPECIALIZATION

Nervous tissues are specialized to:

a. Receive stimuli. Cells receiving stimuli are said to be "irritable" (as are all living cells somewhat).

b. Transmit information.

c. "Store" information.
3. DEFINITION OF A NEURON

A neuron (Figure 5-1) is a nerve cell body and all of its branches.

![Neuron Diagram]

Figure 5-1. A neuron.

5-4. TYPES OF NEURON BRANCHES

There are two types of neuron branches--dendrites and axons.

a. **Dendrite.** A **dendrite** is a neuron process that carries impulses toward the cell body. Each neuron may have one or more dendrites. Dendrites receive information and transmit (carry) it to the cell body.

b. **Axon.** An **axon** is a neuron branch that transmits information from the cell body to the next unit. Each neuron has only one axon.
c. Information Transmission. Information is carried as electrical impulses along the length of the neuron.

d. Coverings. Some neuron processes have a covering that is a series of Schwann cells, interrupted by nodes (thin spots). This gives the neuron branch the appearance of links of sausages. The Schwann cells produce a lipid (fatty) material called myelin. This myelin acts as an electrical insulator during the transmission of impulses.

5-5. TYPES OF NEURONS

Neurons may be identified according to shape, diameter of their branches, or function.

a. According to Shape. A pole is the point where a neuron branch meets the cell body. To determine the type according to shape, count the number of poles.

(1) Multipolar neurons. Multipolar neurons have more than two poles (one axon and two or more dendrites).

(2) Bipolar neurons. Bipolar neurons have two poles (one axon and one dendrite).

(3) Unipolar neurons. Unipolar neurons have a single process that branches into a T-shape. One arm is an axon; the other is a dendrite.

b. According to Diameter (Thickness) of Branches. Neurons may be rated according to the thickness of myelin surrounding the axon. In order of decreasing thickness, they are rated A (thickest), B, and C (thinnest). The thickness affects the rate at which impulses are transmitted. The thickest carry the impulses the fastest. The thinnest carry the impulses the slowest.

c. According to Function.

(1) Sensory neurons. In sensory neurons, impulses are transmitted from receptor organs (for pain, vision, hearing, and so forth) to the central nervous system (CNS). Sensory neurons are also known as afferent neurons.

(2) Motor neurons. In motor neurons, impulses are transmitted from the central nervous system to muscles and glands (effector organs). Motor neurons may be called efferent neurons.

(3) Interneurons. Interneurons transmit information from one neuron to another. Interneurons connect sensory neurons with motor neurons.
(4) **Others.** There are other, more specialized types of neurons found in the body (for example, central nervous system).

## 5-6. NEURON "CONNECTIONS"

A neuron may "connect" either with another neuron or with a muscle fiber. A phrase used to describe such "connections" is "continuity without contact." Neurons do not actually touch. There is just enough space to prevent the electrical transmission from crossing from the first neuron to the next. This space is called the **synaptic cleft.** Information is transferred across the synaptic cleft by chemicals called **neurotransmitters.** Neurotransmitters are manufactured and stored on only one side of the cleft. Because of this, information flows in only one direction across the cleft.

### a. The Synapse

A synapse (Figure 5-2) is a “connection” between two neurons.

![Figure 5-2. A synapse.](image)

1. **First neuron.** An axon terminates in tiny branches. At the end of each branch is found a **terminal knob.** **Synaptic vesicles** (bundles of neurotransmitters) are located within each terminal knob. That portion of the terminal knob that faces the synaptic cleft is thickened and is called the **presynaptic membrane.** This is the membrane through that neurotransmitters pass to enter the synaptic cleft.

2. **Synaptic cleft.** The synaptic cleft is the space between the terminal knob of the first neuron and the dendrite or cell body of the second neuron.

3. **Second neuron.** The terminal knob of the first neuron lies near a site on a dendrite or the cell body of the second neuron. The membrane at this site on the second neuron is known as the **postsynaptic membrane.** Within the second neuron is a chemical that inactivates the used neurotransmitter.

### b. The Neuromuscular Junction

A neuromuscular junction (Figure 5-3) is a "connection" between the terminal of a motor neuron and a muscle fiber. The
neuromuscular junction has an organization identical to a synapse. However, the knob is much larger. The postsynaptic membrane is also larger and has foldings to increase its surface area.

Figure 5-3. A neuromuscular junction.

(1) Motor neuron. The axon of a motor neuron ends as it reaches a skeletal muscle fiber. At this point, it has a terminal knob. Within this knob are synaptic vesicles (bundles of neurotransmitters). The presynaptic membrane lines the surface of the terminal knob and lies close to the muscle fiber.

(2) Synaptic cleft. The synaptic cleft is a space between the terminal knob of the motor neuron and the membrane of the muscle fiber.

(3) Muscle fiber. The terminal knob of the motor neuron protrudes into the surface of the muscle fiber. The membrane lining the synaptic space has foldings and is called the postsynaptic membrane. Beneath the postsynaptic membrane is a chemical that inactivates the used neurotransmitter.

5-7. PROCESS OF NEUROTRANSMISSION

a. The dendrites receive the impulse and transfer it to the nucleus. The nucleus will then cause a change in the permeability of the membrane surrounding the axon. Potassium, which is normally present in high concentrations within the axon, will diffuse out. Sodium, which is usually present in high concentrations outside the axon, will rush
into the axon. **This exchange of potassium and sodium is called depolarization.** As these electrolytes change positions, an electrical charge is set up and the impulses will travel down the axon until it reaches the terminal bulbs. When the impulse reaches the terminal bulbs, it will cause a release of neurotransmitters stored there into the synaptic cleft. Once in the synaptic cleft, the neurotransmitters will diffuse across the synapse to the dendrite of the postsynaptic neuron causing it to depolarize (see Figure 5-4).

b. Once the postsynaptic neuron has depolarized, the neurotransmitters must be removed from the synaptic cleft to prevent further depolarization. This is accomplished by two means. The neurotransmitter is either reabsorbed into the terminal bulb or an enzyme destroys it. This process ends the impulse.

c. Before the neuron can depolarize again, the electrolyte sodium and potassium must resume their original positions. The sodium pump theory states that before the neuron can depolarize again the sodium is pumped out and the potassium is pumped back in (repolarized).

5-8. NEUROTRANSMITTERS

A neurotransmitter is a chemical substance that aids in the transmission of an impulse across the synapse. An impulse will cause the release of a neurotransmitter, which is synthesized and stored in terminal bulbs of the axon. The neurotransmitter will diffuse across the synaptic cleft and initiate an impulse in the postsynaptic nerve. The neurotransmitter reacts with a receptor-site on the postsynaptic nerve initiating an impulse. The neurotransmitter must be removed from the synaptic cleft to stop the impulse.

a. **Acetylcholine.** Acetylcholine (Ach) is destroyed by acetylcholinesterase (AchE) in the synaptic cleft.

b. **Norepinephrine.** Norepinephrine (NE) is removed from the synaptic cleft by:

   (1) Reabsorption (reuptake) into the terminal knob.

   (2) Destroyed by catechol-o-methyl transferase (COMT).

   (3) Destroyed by monoamine oxidase (MAO).

   (4) Dilution by diffusion out of the junctional cleft.

5-9. THE ALL OR NONE LAW

This law states that if a stimulus is strong enough to cause a nerve impulse, it will cause the entire fiber to depolarize and not just part of it.
The human nervous system is divided into three major divisions: the central nervous system (CNS), the autonomic nervous system (ANS), and the peripheral nervous system (PNS). The central nervous system is composed of the brain and spinal cord. Both the peripheral nervous system and the autonomic nervous system carry information to and from the central nervous system. The central nervous system is so named because of its anatomical location along the central axis of the body and because it is central in function. If we use a computer analogy to understand that it is central in function, the CNS would be the central processing unit and the other two parts of the nervous system would supply inputs and transmit outputs. Figure 5-4 shows the central nervous system.

a. Major Subdivisions of the Central Nervous System. The major subdivisions of the central nervous system are the brain and spinal cord.

b. Coverings of the Central Nervous System. Bone and fibrous tissues cover the parts of the central nervous system. These coverings help to protect the delicate tissue of the CNS.
c. **Cerebrospinal Fluid.** The cerebrospinal fluid (CSF) is a liquid that is thought to serve as a cushion and circulatory vehicle within the central nervous system.

**5-11. THE HUMAN BRAIN**

The human brain has three major subdivisions: brainstem, cerebellum, and the cerebrum. The central nervous system is first formed as a simple tube-like structure in the embryo. The concentration of nervous tissues at one end of the human embryo to produce the brain and head is referred to as cephalization. When the embryo is about four weeks old, it is possible to identify the early forms of the brainstem, cerebellum, and the cerebrum, as well as the spinal cord. As development continues, the brain is located within the cranium in the cranial cavity. See Figure 5-5 for illustrations of the adult brain.

![Diagram of the human brain](image)

**Figure 5-5.** Human brain: A side view, B bottom view.
a. **The Brainstem.** The term brainstem refers to that part of the brain that would remain after the removal of the cerebrum and the cerebellum. The brainstem is the basal portion (portion of the base) of the brain. The brainstem can be divided as follows:

<table>
<thead>
<tr>
<th>FOREBRAINSTEM</th>
<th>thalamus</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIDBRAINSTEM</td>
<td>corpora quadrigemina</td>
</tr>
<tr>
<td>HINDBRAINSTEM</td>
<td>pons</td>
</tr>
<tr>
<td></td>
<td>medulla</td>
</tr>
</tbody>
</table>

(1) The brainstem is continuous with the spinal cord. Together, the brainstem and the spinal cord are sometimes known as the **neuraxis**.

(2) The brainstem provides major relays and controls for passing information up or down the neuraxis.

(3) The 12 pairs of cranial nerves connect at the sides of the brainstem.

b. **Cerebellum.** The cerebellum is the spherical mass of nervous tissue attached to and covering the hindbrainstem. It has a narrow central part called the vermis and right and left cerebellar hemispheres.

(1) **Peduncles.** The peduncles is a stemlike connecting part. The cerebellum is connected to the brainstem with three pairs of peduncles.

(2) **General shape and construction.** A cross section of the cerebellum reveals that the outer cortex is composed of **gray matter** (cell bodies of neurons), with many folds and sulci (shallow grooves). More centrally located is the **white matter** (myelinated processes of neurons).

(3) **Function.** The cerebellum is the primary coordinator/integrator of motor actions of the body.

c. **Cerebrum.** The cerebrum consists of two very much-enlarged hemispheres connected to each other by a special structure called the corpus callosum. Each cerebral hemisphere is connected to the brainstem by a cerebral peduncle. The surface of each cerebral hemisphere is subdivided into areas known as lobes. Each lobe is named according to the cranial bone under which it lies: frontal, parietal, occipital, and temporal.

(1) The cerebral cortex is the gray outer layer of each hemisphere. Deeper within the cerebral hemispheres the tissue is white. The "gray matter" represents cell bodies of neurons. The "white matter" represents the axons.
(2) The areas of the cortex are associated with groups of related functions.

(a) For example, centers of speech and hearing are located along the lateral sulcus, at the side of each hemisphere.

(b) Vision is centered at the rear in the area known as the occipital lobe.

(c) Sensory and motor functions are located along the central sulcus, which separates the frontal and parental lobes of each hemisphere. The motor areas are located along the front side of the central sulcus, in the frontal lobe. The sensory areas are located along the rear side of the central sulcus in the parietal lobe.

d. Ventricles. Within the brain, there are interconnected hollow spaces filled with cerebrospinal fluid (CSF). These hollow spaces are known as ventricles. The right and left lateral ventricles are found in the cerebral hemispheres. The third ventricle is located in the forebrainstem. The fourth ventricle is in the hindbrainstem. The fourth ventricle is continuous with the narrow central canal of the spinal cord.

5-12. THE HUMAN SPINAL CORD

a. Location and Extent. Referring to Figure 5-6, you can see that the typical vertebra has a large opening called the vertebral (or spinal) foramen. Together, these foramina form the vertebral (spinal) canal for the entire vertebral column. The spinal cord, located within the spinal canal, is continuous with the brainstem. The spinal cord travels the length from the foramen magnum at the base of the skull to the junction of the first and second lumbar vertebrae.

Figure 5-6. The spinal column.
(1) **Enlargements.** The spinal cord has two enlargements. One is the cervical enlargement, associated with nerves for the upper members. The other is the lumbosacral enlargement, associated with nerves for the lower members.

(2) **Spinal nerves.** A nerve is a bundle of neuron branches that carry impulses to and from the CNS. Those nerves arising from the spinal cord are spinal nerves. There are 31 pairs of spinal nerves.

b. **A Cross Section of the Spinal Cord (Figure 5-7).** The spinal cord is a continuous structure that runs through the vertebral canal down to the lumbar region of the column. It is composed of a mass of a central gray matter (cell bodies of neurons) surrounded by peripheral white matter (myelinated branches of neurons). The gray and white matter are thus considered columns of material. However, in cross section, this effect of columns is lost.

![A cross section of the spinal cord.](image)
5-13. COVERINGS OF THE CENTRAL NERVOUS SYSTEM

The coverings of the central nervous center (CNS) are skeletal and fibrous.

a. **Skeletal Coverings.**

   (1) **Brain.** The bones of the cranium form a spherical case around the brain. The cranial cavity is the space enclosed by the bones of the cranium.

   (2) **Spinal cord.** The vertebrae, with the vertebral foramina, form a cylindrical case around the spinal cord. The overall skeletal structure is the vertebral column (spine). The vertebral (spinal) canal is the space enclosed by the foramina of the vertebrae.

b. **Meninges (Fibrous Membranes).** The brain and spinal cord have three different membranes called meninges surrounding them (Figure 5-8). These coverings provide protection.

   (1) **Dura mater.** The dura mater is a tough outer covering for the CNS. Beneath the dura mater is the subdural space, which contains a thin film of fluid.

   (2) **Arachnoid mater.** To the inner side of the dura mater and subdural space is a fine membranous layer called the arachnoid mater. It has fine spider-web type threads that extend inward through the subarachnoid space to the pia mater. The subarachnoid space is filled with cerebrospinal fluid (CSF).

   **ARACHNOID = Spiderlike**

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**Figure 5-8.** The meninges, as seen in side view of the CNS.
Pia mater. The pia mater is a delicate membrane applied directly to the surface of the brain and the spinal cord. It carries a network of blood vessels to supply the nervous tissues of the CNS.

5-14. BLOOD SUPPLY TO THE CNS

a. Blood Supply of the Brain. The paired internal carotid arteries and the paired vertebral arteries supply blood rich in oxygen to the brain. Branches of these arteries join to form a circle under the base of the brain. This is called the cerebral circle (of Willis). From this circle, numerous branches supply specific areas of the brain.

(1) A single branch is often the only supply to that particular part of the brain. Such an artery is called an end artery. If it fails to supply blood to that specific area, the area will die (as in a stroke).

(2) The veins and venous sinuses of the brain drain into the paired internal jugular veins. These veins carry blood back toward the heart.

b. Blood Supply of the Spinal Cord. The blood supply of the spinal cord is by way of combination of three longitudinal arteries running along its length and reinforced by segmental arteries from the sides.

5-15. CEREBROSPINAL FLUID

A clear fluid called cerebrospinal fluid (CSF) is found in the cavities of the central nervous system. Cerebrospinal fluid is found in the ventricles of the brain, the subarachnoid space, and the central canal of the spinal cord. Cerebrospinal fluid and its associated structures make up the circulatory system for the CNS.

a. Choroid Plexuses. Choroid plexuses are special collections of arterial capillaries found in the roofs of the third and fourth ventricles of the brain. The choroid plexuses continuously produce CSF from the plasma of the blood.

b. Path of the Cerebrospinal Fluid Flow. Blood flows through the arterial capillaries of the choroid plexuses. As the choroid plexuses produce CSF, it flows into all four ventricles. Cerebrospinal fluid from the lateral ventricles flows into the third ventricle, through the cerebral aqueduct then into the fourth ventricle. By passing through three small holes in the roof of the fourth ventricle, CSF enters the subarachnoid space. From the subarachnoid space, the CSF is transported through the arachnoid villi (granulations) into the venous sinuses. Thus, the CSF is formed from arterial blood and returned to the venous blood.

Continue with Exercises
EXERCISES, LESSON 5

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which of the following is/are a type of nervous tissue?
   a. Neurons.
   b. Axons.
   c. Dendrites.
   d. Glia.

2. Select the function(s) for which nervous tissues are specialized.
   a. To transmit information.
   b. To "store" information.
   c. To receive stimuli.
   d. All the above.

3. A neuron is defined as _____________________________.
   a. A process that carries impulses toward the cell body.
   b. A branch that transmits information from the cell body to the next unit.
   c. A nerve cell body and all of its branches.
   d. A nerve process that has two or more poles.
4. A dendrite is defined as _________________________.
   a. A neuron process that carries impulses toward the cell body.
   b. A neuron branch that transmits information from the cell body to the next unit.
   c. A neuron that has two poles.
   d. A nerve cell body and all of its branches.

5. From the statement below, select the type of neuron that is being described:
   In this type of neuron, impulses are transmitted from the central nervous system to muscles and glands.
   a. Sensory neurons.
   b. Interneurons.
   c. Afferent neurons.
   d. Motor neurons.

6. Which of the following statements best describe the neuromuscular junctions?
   a. A connection between two neurons.
   b. A connection that relays information from muscle tissue to the brain.
   c. A connection between the terminal knob of a motor neuron and a muscle fiber.
   d. A connection which joins two neurons.

7. Which of the following substances is a neurotransmitter?
   a. Sodium chloride.
   b. Norepinephrine.
   c. Acetylcholinesterase.
   d. Catechol-o-methyl transferase (COMT).
8. Select the names of the three major subdivisions of the human nervous system.

   a. The central nervous system, brain, and spinal cord.
   b. The autonomic nervous system, the peripheral nervous system, and the central nervous system.
   c. The peripheral nervous system, the brain, and the spinal cord.
   d. The autonomic nervous system, the peripheral nervous system, and the autonomic nervous system.

9. What is the function of the meninges surrounding the brain and spinal cord?

   a. They carry nervous impulses into the brain and spinal cord.
   b. They prevent nerve impulses from injuring delicate tissue.
   c. They direct nerve impulses to the proper places in the brain.
   d. They provide protection for the brain and spinal cord.

10. What is the function of the cerebrum of the human brain?

    a. It serves as the primary coordinator/integrator of motor actions in the body.
    b. It serves as the center of speech, hearing, and vision.
    c. It provides major relays and controls for passing information up or down the neuraxis.
    d. It protects the cerebellum.
SOLUTIONS TO EXERCISES, LESSON 5

1. a Neurons. (para 5-1)
   d Glia.

2. d All the above. (para 5-2a, b, and c)

3. c A nerve cell body and all of its branches. (para 5-3)

4. a A neuron process that carries impulses toward the cell body. (para 5-4a)

5. d Motor neurons. (para 5-5c(2))

6. c A connection between the terminal knob of a motor neuron and a muscle fiber. (para 5-6b)

7. b Norepinephrine. (para 5-8b)

8. b The autonomic nervous system, the peripheral nervous system, and the central nervous system. (para 5-10)

9. d They provide protection for the brain and spinal cord. (para 5-13b)

10. b It serves as the center of speech, hearing, and vision. (para 5-11c(2))

End of Lesson 5
LESSON ASSIGNMENT

LESSON 6
Agents Used During Surgery.

TEXT ASSIGNMENT
Paragraphs 6-1--6-10.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

6-1. Given a group of definitions, select the definition of the term general anesthetic.

6-2. Given a list, select the types of general anesthetic.

6-3. Given a type of medication used during surgery and a list of drugs, select the drug that belongs to that category of general anesthetics.

6-4. Given the name of an agent used during surgery and a list of uses, side effects, and/or cautions and warnings, select the use, side effect, or caution and warning associated with that agent.

SUGGESTION
After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
Lesson 6
Agents Used During Surgery

Section 1. General Anesthetic Agents

6-1. Introduction

a. Have you ever undergone surgery? If you have, you can readily appreciate the importance of drugs used during surgery. This group of agents is widely used. The agents within the group differ widely in their uses and indications. This lesson will focus on this group of drugs with the intent of giving you a background in this important area.

b. In days gone by, various substances (that is, whiskey) were used to "put the patient to sleep" during surgery. As surgical procedures became increasingly sophisticated, the need for better anesthetic agents became more apparent. Today, general anesthetic agents comprise an important group of pharmacological agents. Their use promotes patient welfare. This section of the subcourse will discuss this important group of agents.

6-2. Definition

A general anesthetic is an agent that depresses the central nervous system reversibly, producing loss of consciousness, analgesia, and muscle relaxation, with minimal depression of the patient's vital functions. That is, a general anesthetic agent places the patient in a state of anesthesia in which his muscles are relaxed and he feels no pain. Later, after the procedure has been completed, the patient can regain consciousness and recuperate.

6-3. Mechanism of Action of General Anesthetics

It is known that the general anesthetic agents depress the central nervous system. Precisely how this depression occurs is unknown. Several theories attempt to explain this depression. One-theory states the agents affect lipid (fat) structures in the brain in order to produce the central nervous system depression. If you desire a detailed discussion of the various theories, you should consult a pharmacology text.

6-4. Types of General Anesthetic Agents

There are two broad types of general anesthetics: The inhalation agents and the intravenous agents. It is not the purpose of this subcourse to provide a complete listing or a detailed discussion of the agents that are presented. If you desire additional information on these agents, you should consult a pharmacology text.
a. **Inhalation Agents.** Inhalation anesthetic agents are gases or volatile liquids. These substances are often mixed with oxygen and the patient is allowed to breathe the mixture. After a period, a sufficient level of the anesthetic agent is obtained in the blood and anesthesia is produced. In general, anesthesia can be well controlled with these agents because the concentration of the agent in the blood can be increased or decreased easily by either increasing or decreasing the concentration of the agent in the air the patient is breathing. It is relatively uncommon for a patient to have an allergic reaction to one of the inhalation general anesthetic agents. However, the side effects of some of these agents can be quite serious. There is rapid recovery for the patient when this type of agent is used. That is, when the patient is no longer allowed to breathe the agent, the depression of the central nervous system quickly disappears.

1. **Nitrous oxide.** Nitrous oxide is a gas supplied in blue metal cylinders. Nitrous oxide is commonly referred to as laughing gas. Although nitrous oxide is a safe general anesthetic, it is relatively weak in terms of producing anesthesia and muscle relaxation. Consequently, nitrous oxide is often used in conjunction with other agents. Nitrous oxide is often used in dental surgery and in obstetrical practice during delivery.

2. **Halothane (Fluothane®).** Halothane is a volatile liquid inhalation anesthetic. It is one of the most widely used general anesthetics. Since halothane does not produce potent analgesia and muscle relaxation, other agents are sometimes administered with halothane on an as-needed basis. Halothane has popularity because it is nonexplosive, rapid acting, pleasant smelling, and is compatible with other drugs.

3. **Enflurane (Erthrane®).** Enflurane is a volatile liquid inhalation anesthetic with many of the properties of halothane. It produces greater muscle relaxation than halothane, but like halothane, it is a poor analgesic.

b. **Intravenous Agents.** Intravenous general anesthetics are sterile solutions intended to be administered into the patient's circulatory system. Intravenous anesthetic agents do produce loss of consciousness; however, most of these agents lack the ability to produce complete analgesia. In general, the level of anesthesia is more difficult to control with intravenous anesthetics than with inhalation anesthetics.

1. **Thiopental sodium (Pentothal®).** Thiopental sodium is an ultrashort acting barbiturate. That is, this agent acts very quickly to produce anesthesia. Sometimes this agent is used alone for minor surgical procedures. In other cases, the drug is used to initiate anesthesia. Then, other anesthetic agents are used to maintain the anesthesia. Thiopental sodium is a NOTE Q item. That is, it is a controlled substance.

2. **Fentanyl (Sublimaze®) and droperidol (Innovar®).** This agent is an intravenously administered product, which combines the narcotic analgesic effect of fentanyl with the sedative and antiemetic effects of droperidol. This agent produces a semiconscious state in the patient, and it is used in types of surgery in which the surgeon needs the cooperation of the patient. Innovar is usually used in combination
with nitrous oxide because of its slow induction. Innovar may also be used for various diagnostic procedures. This product is a controlled substance (Note R item).

(3) Ketamine (Ketalar®) is a nonbarbiturate anesthetic that can be administered either intravenously or intramuscularly. Ketamine produces a dissociative type anesthesia in which the patient becomes detached mentally from the environment. Ketamine may be used for induction anesthesia or for diagnostic or minor surgical procedures in children.

Section II. OTHER AGENTS USED DURING SURGERY

6-5. INTRODUCTION

No single anesthetic agent is capable of producing the deep levels of analgesia and skeletal muscle relaxation required during all types of surgery. Consequently, other drugs that have certain desired effects are administered along with the general anesthetic being used. Five major categories of these agents will be presented in this subcourse. They are analgesic agents, drying agents, skeletal muscle relaxants, sedative and hypnotic agents, and antianxiety agents.

6-6. ANALGESIC AGENTS

Analgesic agents relieve pain. Although a general anesthetic agent will produce unconsciousness, the patient might still be able to feel some pain. In these cases, a preanesthetic medication might be administered to the patient in order to relieve the pain. A variety of analgesic agents are available to achieve this purpose. Following are some commonly used agents:

a. Meperidine (Demerol®).

b. Morphine.

c. Nubain®.

d. Stadol®.
6-7. DRYING AGENTS

It is sometimes advantageous during an operation to have the patient's mucous membranes (that is, nose, throat) dry. Drying agents are administered for just this reason. You are probably familiar with the use of drying agents in certain over-the-counter cold medications. Following are two commonly used drying medications:

a. Atropine sulfate.

b. Glycopyrrolate (Robinul®).

6-8. NEUROMUSCULAR BLOCKING AGENTS

In some types of surgery (for example, abdominal surgery) it is highly advantageous to have the patient's skeletal muscles (for example, abdominal surgery) in a state of relaxation. Most general anesthetic agents do not produce a sufficient level of skeletal muscle relaxation. Therefore, neuromuscular blocking agents are administered to achieve the desired muscle relaxation effects. Two commonly used neuromuscular blocking agents:

a. Vecuronium (Norcuron®).

b. Succinylcholine (Anectine®).

6-9. SEDATIVE AND HYPNOTIC AGENTS

To ensure a good night's sleep prior to a surgical procedure, patients are sometimes administered either a sedative or a hypnotic agent. Agents commonly used for this purpose are:

a. Pentobarbital (Nembutal®).

b. Secobarbital (Seconal®).

6-10. ANTIANXIETY AGENTS

As one might expect, some patients are highly anxious about upcoming surgical procedures. Such increased anxiety interferes with the functioning of the patient (interferes with rest and decreases appetite). Anti-anxiety agents help to control this anxiety. Diazepam (Valium®) is sometimes used to control anxiety.

Continue with Exercises
EXERCISES, LESSON 6

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the definitions below, select the definition of the term general anesthetic.

   a. An agent that depresses the central nervous system irreversibly to produce a loss of consciousness, analgesia) and muscle relaxation.

   b. An agent that stimulates the central nervous system, thus making it possible for a physician to perform various types of surgeries.

   c. An agent used to produce localized analgesia in a patient.

   d. An agent that depresses the central nervous system reversibly to produce a loss of consciousness, analgesia, and muscle relaxation.

2. From the list below, select the type(s) of general anesthetic.

   a. Local.

   b. Intravenous.

   c. Induction.

   d. Clinical.

3. From the list below, select the agent that is classified as an inhalation anesthetic agent.

   a. Thiopental sodium (Pentothal®).

   b. Enflurane (Ethrane®).

   c. Glycopyrrolate (Robinal®).

   d. Succinylcholine (Anectine®).
4. From the list below, select the agent classified as an intravenous anesthetic agent.
   a. Fentanyl (Sublimaze®) and droperidol (Innovar®).
   b. Glycopyrrolate (Robinal®).
   c. Meperidine hydrochloride (Demerol®).
   d. Succinylcholine (Anectine®).

5. From the list of uses below, select the use of glycopyolate (Robinal®)
   a. Intravenous anesthetic agent.
   b. Skeletal muscle relaxant.
   c. Drying agent.
   d. Inhalation anesthetic agent.

6. From the list of uses below, select the use of succinylcholine (Anectine®).
   a. An antianxiety agent used the night before surgery.
   b. A sedative used the day before surgery.
   c. An analgesic agent used after surgery.
   d. A neuromuscular blocking agent used during surgery.

7. From the list of uses below, select the use of meperidine hydrochloride (Demerol®).
   a. An agent often used as a preanesthetic analgesic.
   b. An analgesic used to produce unconsciousness.
   c. An analgesic agent used for its ability to dry the patient's mouth.
   d. An analgesic agent used to stimulate a patient's breathing during surgery.
8. From the list below, select the use of ketamine (Ketalar®).

   a. An inhalation anesthetic used to induce anesthesia for diagnostic purposes.

   b. An intravenous anesthetic used to perform major surgery in adults over the age of 60.

   c. An intravenous anesthetic used to perform minor surgical procedures in children.

   d. An inhalation anesthetic agent used because of its ability to produce analgesia.

9. From the group below, select the use of the agent fentanyl (Sublimaze®) and droperidol (Innovar®).

   a. An agent that is used because it produces a dissociative type of anesthesia.

   b. An agent used because the patient easily inhales it.

   c. An agent used when the surgeon needs the cooperation of the patient because it produces a semiconscious state in the patient.

   d. An agent used during surgery because it produces a drying effect in the patient's mucous membranes.

10. From the group below, select the use of the agent diazepam (Valium®).

    a. A drying agent used to reduce saliva product in comatose patients.

    b. An analgesic agent administered after surgery.

    c. An antianxiety agent used to reduce a patient's apprehension before surgery.

    d. A nonbarbiturate anesthetic used before surgery.

    Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 6

1. d An agent that depresses the central nervous system reversibly to produce a loss of consciousness, analgesia, and muscle relaxation.  (para 6-2)

2. b Intravenous.  (para 6-4b)

3. b Enflurane (Ethrane®).  (para 6-4a(3))

4. a Fentanyl (Sublimaze®) and droperidol (Innovar®).  (para 6-4b(2))

5. c Drying agent.  (para 6-7)

6. d A neuromuscular blocking agent used during surgery.  (para 6-8)

7. a An agent used as a preanesthetic analgesic.  (para 6-6)

8. c An intravenous agent used to perform minor surgical procedures in children.  (para 6-4b(3))

9. c An agent used when the surgeon needs the cooperation of the patient because it produces a semiconscious state in the patient.  (para 6-4b(2))

10. c Antianxiety agent used to reduce a patient's apprehension before surgery.  (para 6-10)

End of Lesson 6
LESSON ASSIGNMENT

LESSON 7
Sedative and Hypnotic Agents.

TEXT ASSIGNMENT
Paragraphs 7-1–7-9.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

7-1. Given a group of statements, select the best definition of a sedative-hypnotic.

7-2. From a group of statements, select the statement that best describes the mechanism of action of sedative-hypnotics.

7-3. Given a list of possible effects, select the effect(s) produced by sedative-hypnotics.

7-4. Given an effect produced by the sedative-hypnotics and a group of statements, select the statement that best describes that effect.

7-5. From a list of possible clinical uses, select the clinical use(s) of the sedative-hypnotics.

7-6. From a list of adverse reactions, select the adverse effect(s) associated with sedative-hypnotics.

7-7. From a list of cautions and warnings, select the caution(s) and warning(s) associated with the sedative-hypnotics.

7-8. Given a group of statements and two types of barbiturates (for example, ultra short-acting and short-acting), select the statement which best differentiates between the two types.

7-9. Given the trade name of a sedative-hypnotic agent and a list of generic names, match the trade name with its generic name.
7-10. Given the trade or generic name of a sedative-hypnotic agent and a group of possible clinical uses or side effects, select the use(s) or side effect(s) associated with that agent.

**SUGGESTION**

After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 7
SEDATIVE AND HYPNOTIC AGENTS

Section I. BACKGROUND

7-1. INTRODUCTION

Sedative and hypnotic agents form an important class of drugs that are widely used in modern medical practice. The names of many of the agents should be fairly familiar to you since these drugs are so widely used in hospitals and dispensed to patients on an outpatient basis. You probably know that most sedative-hypnotic agents are controlled because of their abuse/misuse potential. The barbiturates have been regarded as the prototypes of this class of drugs because of their extensive use over the past 80 years. Because of their potential for addiction, physical dependence, and side effects, the barbiturates have been replaced by the benzodiazepines (for example, Valium®). The benzodiazepines are currently the most important sedative hypnotics because of their efficacy and safety.

7-2. DEFINITION OF SEDATIVE-HYPNOTIC

A sedative-hypnotic agent is a substance, which, if given in progressively larger doses, produces calm (sedation), sleep (hypnosis), general anesthesia, and ultimately death (because of medullary depression). Sedative-hypnotic agents are commonly used for symptomatic relief of anxiety and for the induction of sleep. Sedatives may be also referred to as anti-anxiety agents.

Section II. CLINICALLY IMPORTANT INFORMATION CONCERNING SEDATIVE-HYPNOTICS

7-3. INTRODUCTION

Sedative-hypnotic agents are an important group of drugs, which are often prescribed to a variety of patients. You should be familiar with the effects and the clinical uses of these drugs.

7-4. THE PHARMACOLOGICAL ACTIONS OF SEDATIVE-HYPNOTIC AGENTS

a. Mechanism of Action. Sedatives and hypnotics selectively depress the reticular activating system (RAS), the mechanism responsible for keeping us awake.
b. Effects Produced by Sedative-Hypnotic Agents.

(1) Sedation. To sedate means to calm; therefore, sedation refers to the act of producing calm in a patient. You can also think of sedation as referring to a decreased responsiveness to a constant level of stimulation. Small doses (small amounts) of a sedative-hypnotic drug administered to a patient will produce sedation.

(2) Disinhibition. Disinhibition refers to actions a person may perform while under the effects of a drug that he would not perform if he were not taking the drug. This effect may be seen as euphoria, (feeling of well being or elation) in some patients and is a potential source of abuse of these agents. Disinhibition is presumed because of depression of a higher cortical (brain) center, which results in a resultant release of lower brain centers from constant inhibitory influence. Larger doses of a sedative-hypnotic agent will produce this effect.

(3) Relief of anxiety. This particular effect probably cannot be separated from the sedative and euphoriant effects produced by the sedative-hypnotic agents.

(4) Sleep. Sedative-hypnotic induced sleep differs in several ways from normal sleep. If a sufficiently large dose of any sedative-hypnotic agent is administered to a patient, sleep will result; however, the dose of a particular agent required to produce sleep will vary with the physiologic and psychologic state of the individual and the environmental situation in which the drug is given.

(5) Anesthesia. State III of general anesthesia (surgical anesthesia--unconsciousness and paralysis of reflexes) can be induced in humans with large doses of sedative-hypnotic agents. Short- and ultra short-acting barbiturates are the only drugs used as anesthetic agents from this class.

(6) Analgesia. Patients who have been deeply anesthetized with barbiturates are totally unresponsive to pain.

(7) Anticonvulsant activity. All the barbiturates commonly used in clinical practice are capable of inhibiting convulsions. Phenobarbital and other long-acting drugs are selectively more effective at lower therapeutic doses in the treatment of epilepsy.

(8) Cardiovascular and respiratory effects. Sedative-hypnotic agents are respiratory depressants that depress the respiratory system. Sedative-hypnotic agents do not, when administered orally, produce significant cardiovascular effects.

(9) Dependence. Both psychic and physical dependence has been reported with both the barbiturate and nonbarbiturate sedative-hypnotic agents. Dependence usually occurs when sedative-hypnotics are given over a long period in large doses. Therefore, continued administration of these agents is usually necessary to prevent a withdrawal state in the patient.
7-5. CLINICAL USES OF SEDATIVE-HYPNOTIC AGENTS

Sedative-hypnotic agents are used to treat a variety of conditions. These include:

a. **Relief of Anxiety.** Sedative-hypnotics are effectively used to temporarily relieve anxiety associated with threatening or fearful situations (for example, anxiety that typically occurs before a surgical procedure).

b. **Treatment of Depression.** Depression is the most common manifestation of anxiety. Treatment of depression with sedative-hypnotic agents may be effective. It should be noted that major (psychotic) depressions might be intensified with sedative-hypnotics.

c. **Induction of Sleep (Hypnosis).** Short-acting sedative-hypnotics are generally used because of less hangover or persistent effects. When used to produce sleep, sedative-hypnotics should not be administered continuously and should only be part of an overall plan of management and counseling.

d. **Anticonvulsant Therapy.** Some sedative-hypnotics (for example, phenobarbital) have been successfully used in the treatment of various types of convulsive disorders.

e. **Skeletal Muscle Relaxation.** Some sedative-hypnotics have been used to produce muscle relaxation in patients. However, the effectiveness of sedative-hypnotics for this use may be related more to their sedative properties than to their ability to produce true muscle relaxation.

f. **Anesthesia.** The ultra short-acting barbiturates (for example, thiopental) are used for surgical procedures of short duration.

7-6. ADVERSE EFFECTS OF SEDATIVE HYPNOTICS

Sedative-hypnotics, although safe when taken as directed, are not without their side effects. You should be familiar with the side effects produced by these agents:

a. **Drowsiness.** As you might anticipate, all of the sedative-hypnotic agents will cause drowsiness if a large enough dose is given to the patient. Furthermore, because of individual reactions to drugs, some patients will be made drowsy even by small doses of these agents. Patients who are prescribed sedative-hypnotics should be told not to drink alcoholic beverages while taking the drug since the alcohol could intensify the drowsiness effect.

b. **Impaired Performance and Judgment.** These agents interfere with a person's ability to think and to perform certain "hands-on" tasks. Sedative-hypnotic agents are equivalent to alcohol in their effects on distorting judgment and minor motor skills.
c. **Hangover Effect.** When a patient arises from a night's sleep after having taken a bedtime dose of a sedative-hypnotic, the patient may complain of feeling dizzy, lethargic, or exhausted. This is referred to as the "hangover effect." This effect is more prevalent with the long-acting sedative-hypnotics.

d. **Chronic Toxicity.**

   (1) **Drug abuse.** The relief of anxiety and the euphoria provided by these drugs has led to the compulsive misuse of every member of this group. Because of their rapid onset of action and intense effect, the short-or intermediate-acting sedativehypnotics are more apt to be misused than are the other types of sedative-hypnotics. These agents do not cause chronic organic toxicity.

   (2) **Withdrawal state.** A patient who has been taking therapeutic doses of a sedative-hypnotic may find that he has a disturbed pattern of sleep with restlessness and nightmares when he suddenly stops taking the drug. Discontinuing larger doses of sedative-hypnotics may produce a hyperexcitable state in the patient characterized by weakness, tremor, anxiety, elevated blood pressure, and elevated pulse rate. The sudden withdrawal of even larger doses may produce convulsions or toxic psychosis with agitation, confusion, and hallucinations.

e. **Acute Toxicity.** The amount of a particular sedative-hypnotic required to produce death in a patient depends upon a variety of factors. An extremely large dose of a sedative-hypnotic will produce a state of prolonged, deep anesthesia. If the stage of severe medullary depression is reached, circulatory shock occurs. In case of acute toxicity, it is necessary for the patient to be immediately taken to the nearest medical treatment facility for emergency treatment.

7-7. **CAUTIONS AND WARNINGS ASSOCIATED WITH THE USE OF SEDATIVEHYPNOTICS**

   a. Ambulatory patients (those patients able to walk) should be warned to avoid activities that require mental alertness, judgment, and physical coordination while taking sedative-hypnotics.

   b. Alcohol should not be consumed with sedative-hypnotic agents. This is because both the alcohol and the sedative-hypnotic would both act to depress the central nervous system.

   c. Caution should be observed when these drugs are given to patients who have impaired liver function, since the sedative-hypnotics are broken down in the liver.

   d. Sedative-hypnotic agents are probably best prescribed and taken only on an irregular basis when needed. Some physicians believe that a short (that is, week long) course of scheduled sedative-hypnotic therapy is the most desirable. The aim is not to
offer the patient the opportunity to become physically or psychologically dependent upon the drugs.

Section III. CLASSIFICATION OF SEDATIVE-HYPNOTIC AGENTS

NOTE: The agents in this section are classified according to their duration of action and whether they are barbiturates or nonbarbiturates.

7-8. BARBITURATE SEDATIVES AND HYPNOTICS

a. Ultra Short-Acting Barbiturates.

(1) Basic information. Ultra short-acting barbiturates usually have a duration of action of 15 to 30 minutes. They are administered intravenously in order to induce anesthesia because of their high degree in lipid (fatty) materials. Ultra short-acting barbiturates are used to counteract the convulsions associated with some chemical substances (for example, tetanus toxin) or by the overdosage of certain drugs.

(2) Examples of ultra short-acting barbiturates.

(a) Methohexital (Brevital®).
(b) Thiopental (Pentothal®).

b. Short-Acting Barbiturates.

(1) Basic information. Short-acting barbiturates usually have a duration of action that lasts from 2 hours to 4 hours. Short-acting barbiturates are effective treatment—when taken by mouth—for the initial and short-term treatment of insomnia. These agents are widely used intramuscularly (IM) for preanesthetic sedation in order to calm the patient and to reduce anxiety often found in patients about to undergo surgery. Pentobarbital and secobarbital (see below) may be used for short-term daytime sedation in patients who suffer from anxiety.

(2) Examples of short-acting barbiturates.

(a) Pentobarbital (Nembutal®).
(b) Secobarbital (Seconal®).

(1) Basic information. Intermediate-acting barbiturates have a duration of action that lasts from 4 hours to 6 hours. These agents are mainly used for the initial and short-term treatment of insomnia.

(2) Example of intermediate-acting barbiturate. Amobarbital (Amytal®).

d. Long-Acting Barbiturates.

(1) Basic information. Long-acting barbiturates have a duration of action that lasts from 6 hours to 8 hours. These agents are used orally to maintain daylong sedation in anxiety-tension states. Furthermore, long-acting barbiturates are useful in the treatment of various convulsive disorders.

(2) Examples of long-acting barbiturates.

(a) Phenobarbital.

(b) Mephobarbital (Mebaral®).

7-9. NONBARBITURATE SEDATIVES AND HYPNOTICS

a. Short-Acting Agents.

(1) Background information. Short-acting nonbarbiturate sedative-hypnotics are generally used orally in the initial and short-term treatment of insomnia.

(2) Examples of short-acting nonbarbiturate sedative-hypnotics.

(a) Chloral hydrate (Noctec®). Drug interactions may occur between chloral hydrate and anticoagulants, furosemide, alcohol, or other drugs that are CNS depressants.

(b) Triazolam (Halcion®). Triazolam is rapidly absorbed through the oral route and is as effective as the barbiturates in inducing sleep. It is excreted in breast milk and should not be administered to nursing mothers.


(1) Background information. Intermediate-acting nonbarbiturate agents are administered orally to effectively control moderate to severe daytime anxiety and tension in patients who have neuroses and mild depressive states.

(2) Examples of intermediate-acting nonbarbiturates.
(a) Diazepam (Valium®). Diazepam may be useful in the treatment of alcohol withdrawal symptoms (for example, delirium tremens, agitation, and so forth.) This agent produces skeletal muscle relaxant effects in humans and has been used with limited success in various neurologic and musculoskeletal disorders. Diazepam may be administered parenterally as a preanesthetic medication to reduce anxiety and to calm the patient. Diazepam is also administered intravenously in the treatment of status epilepticus. It is available in tablet form (2, 5, and 10 milligrams) and in injection form (5 milligrams per milliliter in 2 and 10 milliliter containers). Diazepam is a Note Q controlled substance in the military.

(b) Meprobamate (Equanil®, Miltown®). Meprobamate can produce skeletal muscle relaxant effects in humans; therefore, it has been used with some success in the treatment of various neurologic and musculoskeletal disorders. It appears to be less effective than diazepam in the treatment of anxiety and tension. The most common side effect associated with the agent is drowsiness. It is supplied in tablet and suspension forms. Meprobamate is a Note Q controlled item in the military.

(c) Other examples of nonbarbiturates used in the treatment of anxiety disorders include Lorazepam (Ativan®), Alprazolam (Xanax®), and Buspirone (Buspar®). Lorazepam is used primarily as an antianxiety agent, but is useful for treating insomnia due to stress and anxiety. Lorazepam is also used as a preanesthetic medication to produce sedation and decrease the patient's ability to recall events related to the day of surgery.

(d) Temazepam (Restoril®). Temazepam is administered in a nightly dose of 15 to 30 mg. It is an effective inducer of sleep with a good safety profile. Animal studies indicate a potential for Temazepam to cause teratogenic effects. Therefore, it should not be administered during pregnancy.

(c). Long-Acting Nonbarbiturate Agents.

(1) Background information. These agents depress the central nervous system. Patients taking these drugs should be cautioned against performing hazardous activities while under their effects.

(2) Examples of long-acting nonbarbiturate agents.

(a) Chlordiazepoxide hydrochloride (Librium®). Chlordiazepoxide is orally administered as an antianxiety agent. It is also effective when administered parenterally in the treatment of alcohol withdrawal. Side effects associated with the agent include drowsiness, ataxia, and lethargy.

(b) Oxazepam (Serax®). Oxazepam is generally less effective than either diazepam or chlordiazepoxide in the treatment of tension and anxiety. Drowsiness is the most common side effect associated with this agent.

Continue with Exercises
EXERCISES, LESSON 7

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which statement best describes the mechanism of action of sedative-hypnotics?
   a. They inhibit the flow of potassium and sodium ions across the semipermeable membranes of the nerves.
   b. They inhibit the depolarization of the nerve fibers and thus produce calm or sleep.
   c. They depress the reticular activating system (RAS).
   d. They inhibit the transmission of electrical impulses from the brain by interfering with the passage of certain ions through the nerve fibers.

2. Select the effect(s) produced by the sedative-hypnotics.
   a. Relief of anxiety.
   b. Disinhibition.
   c. Analgesia.
   d. All the above.
3. Which of the following statements best describes the analgesia produced by sedative-hypnotics?

   a. Patients who have been given extremely large doses of barbiturates are unresponsive to pain.

   b. Patients who are administered intravenous doses of sedative-hypnotics are unable to feel any painful stimuli.

   c. Patients who are given sedative-hypnotics seem to be more tolerant of pain than those patients who are not given these drugs.

   d. Patients who are given any amount of sedative-hypnotics are unable to feel pain, but they are also unable to maintain consciousness for long periods.

4. Select the clinical use(s) associated with the sedative-hypnotics.

   a. To induce sleep.

   b. To treat minimal brain dysfunction (MBD).

   c. To treat pain.

   d. All the above.

5. Select the adverse effect(s) associated with the use of sedative-hypnotic agents.

   a. Drowsiness.

   b. Hangover.

   c. Impaired judgment.

   d. All the above.
6. Select the caution(s) and warning(s) associated with the use of sedativehypnotics.

   a. Caution should be observed when giving these drugs to patients who have impaired liver function.

   b. These agents should not be prescribed to those persons who are likely to become dependent upon them.

   c. Sedative-hypnotics should be taken on a continuous and regular basis to ensure desired therapeutic effects.

   d. All the above.

INSTRUCTIONS: Match the generic name of the drug with its corresponding trade name. (Exercise items 7 through 10.)

7. Pentobarbital _______________ a. Librium®

8. Oxazepam _______________ b. Nembutal®

9. Chlordiazepoxide _______________ c. Serax®

10. Triazolam _______________ d. Halcion®

11. Select the clinical use(s) of diazepam (Valium®).

    a. A treatment for minimal brain dysfunction (MBD).

    b. An anorectic for the suppression of appetite.

    c. A preanesthetic medication used to calm the patient.

    d. A drug used for induction of sleep.
12. Select the clinical use(s) of chlordiazepoxide.
   a. Antianxiety agent.
   b. Sleep inducer.
   c. Skeletal muscle constrictor.
   d. All the above.

13. What is the most common side effect associated with oxazepam (Serax®)?
   a. Ataxia.
   b. Lethargy.
   c. Drowsiness.
   d. Blurred vision.

14. What is the duration of action for ultra-short acting barbiturates?
   a. 6 to 8 hours.
   b. 4 to 6 hours.
   c. 2 to 4 hours.
   d. 15 to 30 minutes.

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 7

1. c They depress the reticular activating system (RAS). (para 7-4a)

2. d All the above. (para 7-4b(2), (3), and (4))

3. a Patients who have been given extremely large doses of barbiturates are unresponsive to pain. (para 7-4b(6))

4. a To induce sleep. (para 7-5a)

5. d All the above. (para 7-6)

6. a Caution should be observed when prescribing these drugs to patients who have impaired liver function. (para 7-7c)

7. b Nembutal®. (para 7-8b(2))

8. c Serax®. (para 7-9c(2)(b))

9. a Librium®. (para 7-9c(2)(a))

10. d Halcion®. (para 7-9a(2)(b))

11. c A preanesthetic medication used to calm the patient. (para 7-9b(2)(a))

12. a Antianxiety agent. (para 7-9c(2)(a))

13. c Drowsiness. (para 7-9c(2)(b))

14. d 15 to 30 minutes. (para 7-8a(1))

End of Lesson 7
LESSON ASSIGNMENT

LESSON 8
Anticonvulsant Agents.

TEXT ASSIGNMENT
Paragraphs 8-1–8-5.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

8-1. Given one of the following terms: epilepsy or convulsions, and a group of statements, select the meaning of that term.

8-2. Given a group of statements, select the statement that best differentiates between clonic and tonic convulsions.

8-3. Give the name of a type of epilepsy and a group of descriptions, select the best description of that type of epilepsy.

8-4. From a group of potential causes, select the cause(s) of epilepsy in either a child or an adult.

8-5. Given a group of statements, select the statement that best describes the mechanism of action for anticonvulsants.

8-6. Given the trade name of an anticonvulsant agent and a group of generic names, match the trade name with its generic name.

8-7. Given a trade or generic name of an anticonvulsant agent and a group of statements, select the statement that best describes the clinical use(s) or adverse reaction(s) associated with that agent.

8-8. Given a trade or generic name of an anticonvulsant agent, a description of a situation involving the dispensing of that agent, and a group of statements describing cautions and/or warnings to the patient, select the statement that should be made to the patient receiving that medication.
SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 8
ANTICONVULSANT AGENTS

Section I. REVIEW OF EPILEPSY

8-1. BASIC DEFINITIONS

Before studying about anticonvulsants, you should review/study the definitions that relate to the topic:

a. Epilepsy. Epilepsy is a chronic convulsive disorder of cerebral function. Epilepsy is characterized by recurrent attacks of motor, sensory, psychic, or autonomic nature. The attacks may involve changes in the state of patient consciousness and are usually sudden in onset and brief.

b. Convulsion. A convulsion is a violent involuntary contraction or series of contractions of the voluntary muscles. There are two types of convulsions.

   (1) Clonic convulsions. A clonic convulsion has alternating periods of contraction and relaxation of the voluntary muscles.

   (2) Tonic convulsions. A tonic convulsion is a state of sustained contraction of voluntary muscles.

8-2. TYPES OF EPILEPSY

There are four types of epilepsy. Certain signs and symptoms characterize each type.

a. Grand Mal. Grand Mal is the most common type of epilepsy. In this type of epilepsy, the person often experiences an aura (this can consist of certain sounds, fear discomfort) immediately before a seizure. Then the patient loss consciousness and has tonic-clonic convulsions. The seizures generally last from 2 to 5 minutes.

b. Petit Mal. This type of epilepsy is most frequently found in children. Brief periods of blank spells or loss of speech characterizes petit mal. During the seizures, which usually last from 1 to 30 seconds, the person stops what he is doing and after the seizure resumes what he was doing before the seizure. Many persons are not aware that they have had a seizure.

c. Jacksonian (Focal). This type of epilepsy is rare. It is usually associated with an organic lesion of a certain part of the brain (cerebral cortex). Jacksonian
epilepsy is characterized by focal or local clonic type convulsions of localized muscle groups (for example, thumb, big toe, and so forth). The seizures normally last from 1-2 minutes.

d. **Psychomotor.** Psychomotor epilepsy is rare. Psychomotor epilepsy is characterized by periods of abnormal types of behavior (for example, extensive chewing or swallowing). The localized seizures may advance to generalized convulsions with resultant loss of consciousness.

### 8-3. CAUSES OF EPILEPSY

a. **In Children.** Epilepsy that occurs in infancy usually results from developmental defects, metabolic diseases, or injuries sustained during birth.

b. **In Adults.** Epilepsy that begins in adulthood usually is caused by trauma (an accident), cerebrovascular accident (a "stroke"), tumors, or diseases associated with the brain.

### Section II. ANTICONVULSANT THERAPY

### 8-4. MECHANISM OF ACTION OF ANTICONVULSANTS

The mode and the site of action anticonvulsants are not known for sure. However, it is believed that the anticonvulsants suppress seizures by depressing the cerebral (motor) cortex of the brain, thereby raising the threshold of the central nervous system (CNS) to convulsive stimuli. Therefore, the person is less likely to undergo seizures.

### 8-5. SPECIFIC ANTICONVULSANT DRUGS

a. **Phenobarbital.**

   1. **Clinical uses.** Phenobarbital is orally administered in the treatment of grand mal epilepsy. It is less effective in the treatment of petit mal and psychomotor epilepsy. The injectable form of the drug is used to treat other types of convulsions.

   2. **Adverse effects.** The most common adverse effects associated with phenobarbital are related to sedation and disinhibition (see lesson 7 of this subcourse). These include dizziness, drowsiness, ataxia (lack of muscular coordination), and nystagmus (a rapid involuntary movement of the eyeball). Furthermore, as discussed in lesson 7 of this subcourse, persons taking phenobarbital can experience withdrawal symptoms when they suddenly stop taking the drug. Epileptic patients are unusually susceptible to the hyperexcitable state induced by too rapid reduction of dosage or too rapid withdrawal of phenobarbital.
Cautions and warnings. Patients who take phenobarbital should be warned about drowsiness. Patients who take phenobarbital should not drink alcohol while taking phenobarbital. Dosage of the drug should be reduced by small amounts in order to avoid hastening convulsions. Lastly, phenobarbital may stimulate the activity of a number of enzyme systems and affect the metabolism of various drugs (for example, anticoagulants, phenytoin).

b. **Phenytoin (Dilantin®)**.

(1) Clinical uses. Phenytoin is used alone or in combination with phenobarbital in the treatment of grand mal and psychomotor epilepsy. It is also used in the treatment of other types of convulsions.

(2) Adverse effects. Adverse effects associated with phenytoin include ataxia (lack of muscular coordination, staggering walk), nystagmus (a rapid, involuntary movement of the eyeball), and slurred speech. Drowsiness and fatigue may accompany these adverse effects in some patients by tremors and nervousness and in others.

(3) Caution and warning. Drug interactions can occur between phenytoin and alcohol, barbiturates, folic acid, coumarin-type anticoagulants, disulfirams, the sulfonamides, and sympathomimetic agents. Phenytoin should be used cautiously with patients who are alcoholics or who have blood dyscrasias.

c. **Ethosuximide (Zarontin®)**.

(1) Clinic use. Ethosuxamide is the drug of first choice for the treatment of petit mal epilepsy.

(2) Adverse effects. Drowsiness, ataxia, and gastrointestinal irritation are adverse effects associated with the use of ethosuxamide.

(3) Caution and warning. Ethosuxamide should be used cautiously with patients who have blood dyscrasias or liver or kidney impairment.

d. **Clonazepam (Klonopin®)**.

(1) Clinical uses. Clonazepam is used in the treatment of grand mal epilepsy. It is the alternate drug for the treatment of petit mal in patients who fail to respond to ethosuxamide (Zarontin®) therapy.

(2) Adverse effects. The primary side effect associated with clonazepam is central nervous system depression. Drowsiness is frequently seen in patients who take this medication.
e. **Diazepam (Valium®), lorazepam (Ativan®)**.

(1) **Clinical uses.** Diazepam or lorazepam are drugs of first choice for the treatment of status epilepticus (a particular type of convulsive disorder) when it is given intravenously.

(2) **Adverse effects.** Drowsiness, fatigue, and ataxia are the most common adverse effects seen with diazepam.

**NOTE:** Midazolam (Versed®) may be used as a continuous infusion for the treatment of status epilepticus in patients that fail diazepam or lorazepam.

*Continue with Exercises*
EXERCISES, LESSON 8

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which of the following statements best describes epilepsy?
   a. A mental condition that can be transmitted from one person to another.
   b. A chronic convulsive disorder of brain function.
   c. A chronic mental condition that is always characterized by violent contractions of the involuntary muscles.
   d. A condition that harms the brain in such a way that the person cannot live a normal life.

2. Which of the following statements best describes grand mal epilepsy?
   a. A type of epilepsy characterized by brief periods of blank spells or loss of speech.
   b. A type of epilepsy characterized by focal or local clonic type convulsions of localized muscle groups (for example, thumb, big toe, and so forth).
   c. A type of epilepsy characterized by seizures which generally last from 2 to 5 minutes.
   d. A rare type of epilepsy characterized by periods of abnormal behavior (for example, extensive chewing).

3. Which of the following cause epilepsy in adults?
   a. Tumors.
   b. Trauma.
   c. Cerebrovascular accident.
   d. All the above.
4. The anticonvulsants act by _________________.
   
   a. Depressing the cerebral cortex of the brain, thereby lowering the threshold of the CNS to convulsive stimuli.

   b. Stimulating the cerebral cortex of the brain, thereby raising the threshold of the CNS to convulsive stimuli.

   c. Depressing the cerebral cortex of the brain, thereby raising the threshold of the CNS to convulsive stimuli.

   d. Depressing the cerebral cortex of the brain, thereby deadening the part of the brain that is responsible for the seizures.

**INSTRUCTIONS:** For exercises 5 through 8, match the generic name with its corresponding trade name.

5. Clonazepam _______________ a. Zarontin®
6. Diazepam ________________ b. Klonopin®
7. Phenytoin ________________ c. Valium®
8. Ethosuximide _______________ d. Dilantin®

9. Phenobarbital is orally administered in the treatment of _______________.
   
   a. Grand mal epilepsy.

   b. Petit mal epilepsy.

   c. Jackson epilepsy.

   d. Psychomotor epilepsy.
10. Patients who take phenobarbital should be cautioned not to_________.
   a. Take aspirin with the drug.
   b. Take the drug with meals.
   c. Take the medication immediately after a seizure.
   d. Take the medication with alcohol.

11. Which adverse effect(s) is/are associated with the use of ethosuximide?
   a. Dizziness.
   b. Ataxia.
   c. Nystagmus.
   d. All the above.

12. Which adverse effect(s) is/are associated with the use of phenytoin.
   a. Nystagmus.
   b. Ataxia.
   c. Slurred speech.
   d. All the above.

   Check Your Answers on Next Page
**SOLUTIONS TO EXERCISES, LESSON 8**

1. b  A chronic convulsive disorder of brain function.  
   *(para 8-1a)*

2. c  A type of epilepsy characterized by seizures, which generally last from 2 to 5 minutes.  *(para 8-2a)*

3. d  All the above.  *(para 8-3b)*

4. c  Depressing the cerebral cortex of the brain, thereby raising the threshold of the CNS to convulsive stimuli.  *(para 8-4)*

5. b  Klonopin®.  *(para 8-5d)*

6. c  Valium®.  *(para 8-5e)*

7. d  Dilantin®.  *(para 8-5b)*

8. a  Zarontin®.  *(para 8-5c)*

9. a  Grand mal epilepsy.  *(para 8-5a)*

10. d  Take the medication with alcohol.  *(para 8-5a(3))*

11. b  Ataxia.  *(para 8-5c(2))*

12. d  All the above.  *(para 8-5b(2))*

*End of Lesson 8*
LESSON ASSIGNMENT

LESSON 9
Psychotherapeutic Agents.

TEXT ASSIGNMENT
Paragraphs 9-1–9-20.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

9-1. Given a group of statements and one of the four classes of functional mental disorders, select the best description of that class of mental disorders.

9-2. From a group of statements, select the statement that best differentiates between fear and anxiety.

9-3. Given one of the following terms: fear, anxiety, antianxiety agent, depression, antidepressant, antipsychotic agent, or tranquilizer and a group of definitions, select the correct definition of that term.

9-4. Given one of the following categories of drugs: antianxiety agents, antidepressant agents, and antipsychotic agents and a group of statements that describe uses, advantages, disadvantages, adverse effects, or precautions and warnings select the statement that best describes the use(s) advantage(s), disadvantage(s), adverse effect(s), or caution(s) and warning(s) associated with that category of drug.

9-5. Given a group of statements, select the statement that best describes the advantages of antianxiety agents over drugs that were previously used to calm or sedate patients.

9-6. Given the generic and/or trade name of a psychotherapeutic agent and a group of uses, adverse effects, or cautions and warnings, select the use(s), adverse effects, or cautions and warnings associated with that agent.
SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
9-1. INTRODUCTION

Stress, anxiety, and depression are frequently used words in today’s world. Every living person has problems of one type or another. Some people seem to cope quite well with stress most of the time, while other persons need assistance to make adjustments to life. The wise use of psychotherapeutic agents has become an integral part of assisting others to adjust to certain situations. Of course, psychologists and psychiatrists combine other treatment means with the wise use of drugs in their efforts to help others.

9-2. THE FOUR MAJOR CLASSES OF FUNCTIONAL MENTAL DISORDERS

Later in this lesson, certain drugs and their uses will be discussed. In order for you to understand the use of some of the drugs, you must be aware of the four major classes of functional mental disorders.

NOTE: Reality testing is an ego function that consists of an individual’s ability to recognize and interpret the surrounding world (that is, what’s going on?). The ability to recognize and interpret the surrounding world allows an individual to meet the demands of life and make survival judgments.

a. Neuroses (Neurotic Disorders). Neuroses are a group of conditions characterized by the development of anxiety because of unresolved unconscious conflicts. The neurotic person is anxious, but he does not know the cause of his anxiety. These conditions tend to become chronic. Reality testing is maintained. That is, the neurotic remains in touch with reality.

b. Psychoses (Psychotic Disorders). Psychoses are a group of disorders with more or less severe disturbances of thought, mood, and/or behavior. Psychoses are usually chronic, but short episodes of psychosis do sometimes occur. Reality testing is always lost in one or more important respects. That is, a psychotic is not entirely in touch with his environment.

c. Personality Disorders. Personality disorders are types of mental disorders characterized by lifelong maladaptive patterns of adjustment to life. These types of disorders tend to be chronic. Personality disorders are usually recognized by adolescence. Reality testing is usually preserved.
d. **Transient Situational Disturbances (Adjustment Disorders).** Transient situational disturbances (TSD) are temporary emotional disorders of any severity, which occur as reactions to overwhelming environmental stress. Reality testing may or may not be impaired during the acute phase of these disorders.

### 9-3. TERMINOLOGY ASSOCIATED WITH PSYCHOTHERAPEUTIC AGENTS

Before discussing the various psychotherapeutic agents, some terms and their definitions will be presented. These terms will be used later in the discussion of the psychotherapeutic agents.

a. **Fear.** Fear is a feeling of apprehension caused by a real object in the environment. For example, a person who is unexpectedly confronted with a rattlesnake would probably display fear of the snake. If you closely observed such a surprised person, you would see such signs as increased blood pressure, increased respiratory rate, and increased heart rate. These physiological responses are mediated by the sympathetic nervous system.

b. **Anxiety.** Anxiety is a feeling of apprehension that has no specific object. Most people have experienced the feeling of anxiety that occurs during test-taking time. Anxiety has both positive and negative components. On the positive side, anxiety motivates you to study for the exam rather than to go to the movies. On the negative side, anxiety can interfere with performance on the examination (that is, "black outs" during a pencil and paper test). Interestingly enough, a person who is frightened (that is, with a snake) or is anxious (as with a test) will display the same body signs such as increased blood pressure, increased heart rate, and increased respiratory rate.

c. **Antianxiety Agent.** An antianxiety agent is a drug that is used to calm a patient. Although the drug reduces the subjective feeling of anxiety, it will have no effect on the cause of the anxiety.

d. **Depression.** Depression is a disturbance of mood manifested by decreased self-esteem, decreased vitality, and increased sadness.

e. **Antidepressant.** An antidepressant is a drug that will, after a period, cause an improvement in a depressed patient’s mood.

f. **Antipsychotic Agent.** An antipsychotic agent is a drug that will reduce specific symptoms (that is, hallucinations, delusions) in patients experiencing a psychosis.

g. **Tranquilizer.** The term tranquilizer refers to a wide-variety of drugs that produce a calming change in patient attitude and behavior. At one time, these drugs were categorized into two major categories: the major tranquilizers and the minor tranquilizers. The major tranquilizers are now generally referred to as antipsychotic agents and the minor tranquilizers are referred to as antianxiety agents.
Section II. ANTIANXIETY AGENTS

9-4. INTRODUCTION TO ANTIANXIETY AGENTS

It is not unusual for a person to experience stress and anxiety. Most people can deal with the minor stresses of life without using antianxiety agents. However, when the degree of anxiety increases to the point of causing social and/or economic impairment, the attending physician may decide to prescribe an antianxiety agent. It should be remembered that the antianxiety agent will calm the patient, but the drug cannot remove the cause of anxiety. Often the antianxiety therapy is combined with counseling or therapy to help the patient deal with the stress and anxiety.

9-5. INDICATIONS FOR ANTIANXIETY AGENTS

Antianxiety agents are indicated in patients to control moderate to severe degrees of anxiety. Antianxiety agents are also extremely useful in treating patients when periods of overwhelming stress occur.

9-6. USES OF ANTIANXIETY AGENTS

Antianxiety agents are used in a variety of situations. Listed below are some of those situations.

a. **Control Moderate to Severe Stress and Anxiety in Neurotic and Depressed Patients.** Some neurotic and depressed patients are prescribed antianxiety agents to reduce the amount of subjective anxiety; thus enabling them to more productively participate in counseling or therapy.

b. **Control Stress and Anxiety in Previously Normal Persons in Periods of Overwhelming Stress.** In most cases, normal individuals are able to cope with the stress and anxiety of life. However, when unusual circumstances of extreme stress arise, physicians sometimes prescribe antianxiety agents to assist people during these periods. Antianxiety agents should not be prescribed for dealing with the stresses of everyday life (Food and Drug Administration ruling).

c. **Treat Withdrawal Symptoms in Alcoholism.** These agents are very effective in the treatment of delirium tremens associated with the withdrawal of alcohol from alcoholics.

d. **Treat Psychotic Patients in Periods of Acute Agitation.** Sometimes patients who have certain psychotic conditions undergo periods of acute agitation. Antianxiety agents are used to calm these types of patients during these periods. Thus, the patients become much more manageable. Generally speaking, antipsychotic drugs are more effective when used for this particular purpose.
9. Decrease Preoperative and Postoperative Apprehension. Patients who will undergo or have undergone surgery frequently have periods of apprehension. Antianxiety agents have been used to reduce this type of stress and tension.

9-7. ADVANTAGES OF THE USE OF ANTIANXIETY AGENTS

Anti-anxiety agents have two main advantages over drugs that were previously used to calm or sedate patients:

a. Antianxiety Agents Do Not Cause Excessive Loss of Alertness. Barbiturates were frequently used to calm patients. Unfortunately, the barbiturates sometimes calmed the patients to an undesirable degree. Although the antianxiety agents produce some degree of sedation during the initial days of therapy, this sedation is usually short-lived.

b. Overdosage of Antianxiety Agents Rarely Results in Death to the Patient. As previously stated, the barbiturates were previously used to calm patients. Unfortunately, overdose of barbiturates can frequently result in coma, respiratory depression, and death. Antianxiety agents, on the other hand, are somewhat safe in terms of the amount of drug required to produce coma, respiratory depression, and death. This factor makes the wise use of antianxiety agents in special circumstances useful in the treatment of extremely anxious patients who are entertaining thoughts about suicide.

9-8. DISADVANTAGES OF THE USE OF ANTIANXIETY AGENTS

Although the antianxiety agents do have many advantages over previously used drugs, they are not free from potentially harmful effects. The discussion below focuses on two major disadvantages of the group of drugs classified as antianxiety agents.

a. Drowsiness. Antianxiety agents, especially during the first few days of therapy, produce drowsiness in many patients. Further, many patients who take antianxiety drugs experience loss of judgment and a loss of mental powers. Consequently, patients who are on antianxiety therapy should be cautioned not to operate machinery.

b. Drug Interaction Effects. The antianxiety agents can interact with central nervous system depressants to produce a further degree of depression to the central nervous system. Thus, patients who are on antianxiety therapy should be cautioned against drinking alcohol or taking other central nervous system depressants.

9-9. EXAMPLES OF ANTIANXIETY AGENTS

This area of the subcourse is designed to provide you with a brief overview of some commonly prescribed antianxiety agents. If you desire further information about
the agents discussed below, you should consult a reference (for example, AMA Drug Evaluations) which is well written and easy to understand.

a. **Chlordiazepoxide Hydrochloride (Librium®).**

   (1) **Uses.** Chlordiazepoxide hydrochloride is widely used as an antianxiety agent to help people deal with stress. Further, it is used preoperatively to reduce patient apprehension. As an antianxiety agent, it has less anticonvulsant activity, and it produces less drowsiness than diazepam, another antianxiety drug.

   (2) **Adverse effects.** Chlordiazepoxide is likely to produce such adverse effects as drowsiness and lethargy. These adverse effects are more likely to occur in older patients.

   (3) **Cautions and warnings.** Patients taking chlordiazepoxide should be cautioned not to take a central nervous system depressant like alcohol since the additive effect might produce depression of the central nervous system. Furthermore, patients taking chlordiazepoxide should be cautioned against operating machinery (for example, driving an automobile).

b. **Diazepam (Valium®).**

   (1) **Uses.** Diazepam is widely used for the treatment of anxiety and tension. Further, it is used in the treatment of muscle spasms.

   (2) **Adverse effects.** Diazepam produces such adverse effects as drowsiness, fatigue, and ataxia (lack of coordination). Physical dependence can develop over a period with resultant withdrawal symptoms to include seizures.

   (3) **Cautions and warnings.** An individual taking diazepam should be cautioned against taking central nervous system depressants (that is, alcohol) and operating machinery.

c. **Lorazepam (Ativan®).**

   (1) **Uses.** Lorazepam is primarily used in the treatment of anxiety.

   (2) **Adverse effects.** Lorazepam produces such adverse effects as drowsiness, fatigue, and ataxia (lack of coordination). Physical dependence can develop over a period of time with resultant withdrawal symptoms to include seizures.

   (3) **Cautions and warnings.** An individual taking lorazepam should be cautioned against taking central nervous system depressants (that is, alcohol) and operating machinery.
d. **Alprazolam (Xanax®).**

(1) **Uses.** Alprazolam is primarily used in the treatment of anxiety and has been useful in the management of panic attacks.

(2) **Adverse effects.** Alprazolam produces such adverse effects as drowsiness, fatigue, and ataxia (lack of coordination). Physical dependence can develop over a period with resultant withdrawal symptoms to include seizures.

(3) **Cautions and warnings.** An individual taking alprazolam should be cautioned against taking central nervous system depressants (that is, alcohol) and operating machinery.

e. **Hydroxyzine Hydrochloride (Atarax®) or Hydroxyzine Pamoate (Vistaril®).**

(1) **Uses.** Hydroxyzine has the following three primary uses:

   (a) Antianxiety agent. The drug is used to treat anxiety, tension, and agitation.

   (b) Antiemetic agent. Because hydroxyzine does have some antiemetic (antinausea and vomiting) properties, it is used in its injectable form (hydroxyzine pamoate) to manage postoperative nausea and vomiting.

   (c) Antipruritic agent. Hydroxyzine has been used because of its antipruritic (anti-itch) properties.

**NOTE:** Atarax® is sometimes used as a sedative.

(2) **Adverse effects.** There is an extremely low incidence of adverse reactions with this drug. Some drowsiness may occur during the initial days of therapy; however, this drowsiness is short-lived.

(3) **Cautions and warnings.** An individual taking hydroxyzine should be cautioned against drinking alcohol and taking other central nervous system depressants because of the additive effect that may be produced. Furthermore, persons taking this drug should be cautioned against operating machinery (for example, driving an automobile).

f. **Buspirone (Buspar®).**

(1) **Uses.** Buspirone is used in the management of anxiety or the short term relief of symptoms of anxiety. It is unrelated to the benzodiazepines and therefore lacks the sedative and addictive properties of these agents.
(2) **Adverse effects.** The most common adverse effects include dizziness, nausea, and headache.

(3) **Cautions and warnings.** Although buspirone does not produce significant drowsiness, patients should be cautioned about driving or operating machinery until they are certain that this drug does not affect them adversely.

**NOTE:** Antidepressants, which are discussed in the next section, are becoming the agents of choice for anxiety disorders.

### Section III. ANTIDEPRESSANT AGENTS

#### 9-10. INTRODUCTION TO ANTIDEPRESSANT AGENTS

Depression is a frequently occurring psychiatric disorder. Patients with medical and surgical conditions frequently have signs and symptoms associated with depression. People who are depressed usually have low moods, decreased physical activity and mental alertness, decreased appetite, abnormal sleep patterns, and morbid preoccupations. Depression can be of rapid or slow onset. For example, a soldier who has been denied leave might display several signs of depression. This type of depression could be of rapid onset.

#### 9-11. INDICATIONS FOR ANTIDEPRESSANT AGENTS

a. Most people undergo changes in mood. You can probably remember when you have been "up" (that is, right before a three-day weekend) and when you have been "down" (that is, right after a three-day weekend). Physicians have found antidepressant agents to be useful in the treatment of depression, which is not time limited and causes the patient social and economic difficulties.

b. Depression can be caused by chemical imbalances in the body, by stress, and by situations in the environment. It has been found that psychotherapy, reduction of stress, and improvement in the environment can be successful in treating some types of depression. However, in depression that results from chemical imbalances in the body, these types of treatment have not proven to be very effective.

#### 9-12. EFFECTS OF ANTIDEPRESSANT AGENTS

Antidepressant agents elevate mood, increase physical activity and mental alertness, improve appetite and sleep patterns, and reduce morbid preoccupations. These effects are not seen immediately upon beginning antidepressant therapy. Instead, one to four weeks may pass before the patient shows any signs of improvement in the depression. This period is called the _therapeutic lag period._
9-13. PRECAUTIONS ASSOCIATED WITH THE USE OF ANTIDEPRESSANT AGENTS

Although the antidepressant agents are safe for patient use, there are some precautions associated with their use:

a. Antidepressants should be used cautiously with patients who are hyperactive or agitated.

b. Antidepressants should be used cautiously with the elderly, with patients who have glaucoma, and with patients who have hypertension (high blood pressure).

c. Antidepressants may interact with other types of drugs. For example, references should be consulted to determine if any interaction could occur between a particular antidepressant and a drug a patient is taking to control high blood pressure, since some antidepressants partially block the action of some antihypertensive drugs. In addition, the action of some drugs (that is, the barbiturates) is increased in duration when they are administered to patients who are taking certain antidepressant agents.

9-14. SPECIFIC ANTIDEPRESSANT AGENTS

Immediately following is a discussion of several antidepressant agents. By no means is the listing below complete in terms of the number of agents available to the physician. Further, no attempt has been made to provide an in-depth discussion of each individual agent. If you desire additional information about any of the agents discussed below, you should consult a pharmacology reference (for example, AMA Drug Evaluations).

a. Fluoxetine (Prozac®).

(1) **Uses.** Fluoxetine belongs to a class of antidepressants called Selective Serotonin Reuptake Inhibitors (SSRIs). SSRIs are usually regarded as the treatment of choice for depression due to fewer side effects and a better safety profile than older agents. Fluoxetine is used to treat depression and anxiety disorders. The Serafem® product is approved for premenstrual dysphoric disorder (PMDD).

(2) **Adverse effects.** Fluoxetine may produce the following adverse effects:

(a) Miscellaneous effects (that is, sexual dysfunction).

(b) Central nervous system effects (for example, agitation and insomnia).

(c) Gastrointestinal effects (that is, nausea and diarrhea).
(3) **Cautions and warnings.**

(a) Do not overlap with other antidepressants or monoamine oxidase inhibitors.

(b) The drug may produce drowsiness.

(c) The patient should not consume any alcohol while taking the drug.

**NOTE:** Other SSRIs include sertraline (Zoloft®), paroxetine (Paxil®), citalopram (Celexa®), and fluvoxamine (Luvox®).

b. **Imipramine Hydrochloride (Tofranil®).**

(1) **Uses.** Imipramine is used to treat depression; however, it can paradoxically aggravate the anxiety sometimes associated with depression. Imipramine also produces an anticholinergic effect and is therefore approved by the Food and Drug Administration (FDA) for the treatment of enuresis (bedwetting) in children.

(2) **Adverse effects.** Imipramine may produce the following adverse effects:

(a) Cardiovascular effects (that is, orthostatic hypotension).

(b) Central nervous system effects (for example, confusion and anxiety).

(c) Gastrointestinal effects (that is, nausea and vomiting).

(d) Anticholinergic effects (for example, dry mouth and constipation).

(3) **Cautions and warnings.**

(a) Abruptly taking the drug away from the patient after long-term therapy may produce withdrawal symptoms.

(b) The drug may produce drowsiness.

(c) The patient should not consume any alcohol while taking the drug.

(d) The drug should be used with caution in patients with glaucoma or urinary retention because of its anticholinergic effects.
c. **Desipramine (Norpramin®).**

(1) **Uses.** Desipramine is used to treat depression. It has also been used in facilitating withdrawal from cocaine.

(2) **Adverse effects.** Desipramine is closely related to imipramine but has only minimal cardiovascular, CNS, GI, and anticholinergic effects.

(3) **Cautions and warnings.**

   (a) Abruptly taking the drug away from the patient after long-term therapy may produce withdrawal symptoms.

   (b) The drug may produce drowsiness.

   (c) The patient should not consume any alcohol while taking the drug.

   (d) The drug should be used with caution in patients with glaucoma or urinary retention because of its anticholinergic effects.

d. **Amitriptyline Hydrochloride (Elavil®).**

(1) **Uses.** Amitriptyline is used in the treatment of depression and neuropathic pain syndromes.

(2) **Adverse effects.** Amitriptyline tends to cause confusion in elderly patients. In addition, it has other adverse effects that are similar to those produced by imipramine hydrochloride.

(3) **Cautions and warnings.**

   (a) Abruptly taking the drug away from the patient after long-term therapy may produce withdrawal symptoms.

   (b) The drug may produce drowsiness.

   (c) The patient should not consume any alcohol while taking the drug.

   (d) The drug should be used with caution in patients who have glaucoma or urinary retention due to its anticholinergic effects.

(4) **Precautions.** Amitriptyline can be cardiotoxic to some individuals.
d. **Nortriptyline Hydrochloride (Aventyl®).**

   (1) **Uses.** Nortriptyline is used in the treatment of depression and neuropathic pain disorders.

   (2) **Adverse effects.** The adverse effects produced by nortriptyline are the same as those produced by imipramine hydrochloride (see para 9-14b).

   (3) **Cautions and warnings.** The adverse effects produced by nortriptyline are the same as those produced by imipramine hydrochloride (see para 9-14b).

e. **Trazodone (Desyrel®).**

   (1) **Uses.** Trazodone is used in the treatment of depression. It is unrelated to any of the antidepressants discussed thus far.

   (2) **Adverse effects.** The adverse effects produced by trazodone include skin rash, chest pain, drowsiness, tachycardia, vivid dreams/nightmares, and muscle aches.

   (3) **Cautions and warnings.** Trazodone may produce drowsiness and may cause irregular heartbeat. The patient should observe caution when driving or performing other tasks requiring alertness. Alcohol and other depressant drugs should be avoided while taking trazodone.

f. **Nefazodone Hydrochloride (Serzone®).**

   (1) **Uses.** Nefazodone hydrochloride is an oral antidepressant that is totally unrelated to the other available antidepressants.

   (2) **Adverse effects.** The adverse effects of nefazodone hydrochloride are similar to selective serotonin reuptake inhibitors.

   (3) **Contraindications.**

      (a) The drug is contraindicated in patients who are taking other monoamine oxidase (MAO) inhibitors, and those having hypersensitivity to nefazodone or other phenylpiperazine antidepressants.

      (b) The drug is contraindicated on patients who are taking nonsedating antihistimines (that is, Terfenadine and Astemizole).

   (4) **Cautions and warnings.** Patients taking nefazodone hydrochloride should be cautioned against the following:

      (a) The drug may produce drowsiness.
(b) The patient should not consume any alcohol while taking the drug.

(c) Patients with cardiovascular or cerebrovascular disease that could be exacerbated by hypotension should use with caution.

(d) The potential for a fatal outcome is significantly increased by the concurrent use of alprazolam and triazolam.

Section IV. ANTIPSYCHOTIC AGENTS

9-15. INTRODUCTION TO ANTIPSYCHOTIC AGENTS

The general term psychoses encompass a wide variety of conditions. Each specific condition has particular signs and/or symptoms that assist the psychiatrist in making a diagnosis. Some psychotic conditions require long-term hospitalization, while others can be managed on an outpatient basis. Many psychotic patients show marked disorganization of thought patterns and behavior with either increased or decreased psychomotor activity. Antipsychotic agents help psychotic patients better organize their thoughts and coordinate their motor activities. In some cases, the use of antipsychotic agents can mean the difference between hospitalization and home-care.

9-16. INDICATIONS FOR USE OF ANTIPSYCHOTIC AGENTS

In order for an antipsychotic agent to be wisely used to treat a psychotic patient, the attending psychiatrist must carefully examine the patient and diagnose the specific condition. Proper diagnosis is the key word for beginning drug therapy for the psychotic patient.

9-17. USES OF ANTIPSYCHOTIC AGENTS

a. The antipsychotic agents are used to treat various conditions of psychosis. When used in this manner, they help reduce the patient’s fear, panic, and hostility. With this help, the patient is better able to organize life and more realistically respond to the environment.

b. Some antipsychotic agents are used as adjuncts in anesthesia to control nausea and vomiting.

c. The state of psychotic hyperarousal is the first group of symptoms to respond to antipsychotic medication. Delusions and hallucinations resolve more gradually over a period.
9-18. ADVERSE EFFECTS ASSOCIATED WITH ANTIPSYCHOTIC AGENTS

As with most drugs, the antipsychotic agents produce some adverse effects. Discussed below are some of those reactions:

a. **Extrapyramidal Reactions.** Extrapyramidal reactions are manifested by a parkinson-like syndrome. That is, the patient has tremors, muscular rigidity, postural abnormalities, pill-rolling movements with the fingers, and hypersalivation. Fortunately, these symptoms may be relieved or lessened, or the reactions may be prevented before they occur by the administration of diphenhydramine (Benadryl).

b. **Drowsiness, Dizziness, and Fatigue.** Although a sedative-effect is produced by many of the antipsychotic agents, this effect is short-lived because tolerance develops after one to three days.

c. **Orthostatic Hypotension.** Orthostatic hypotension (low blood pressure) is an adverse reaction produced by some of the antipsychotic agents. Patients experiencing this problem are at risk of fainting and injuring themselves.

d. **Anticholinergic Effects.**

9-19. DOSAGE PRINCIPLE ASSOCIATED WITH THE ANTIPSYCHOTIC AGENTS

You should be familiar with a dosage principle associated with the antipsychotic agents. This principle is: "High dosage-low potency/low dosage-high potency."

a. **High Dosage/Low Potency.** Initially when treating a psychotic patient, a psychiatrist might choose to select a drug that can be given in a high dosage (large amount of drug) because of its low potency. This allows the psychiatrist some freedom in dosage-especially if the patient is uncontrollable--without potential harm to the patient. High dosage/low potency drugs usually have a high incidence of anticholinergic side effects, but low incidence of extrapyramidal side effects.

b. **Low Dosage/High Potency.** After a patient has been on one antipsychotic agent and has been stabilized, the psychiatrist may choose to use another agent that can be given in smaller amounts (low dosage) because of its high potency. Usually, more potent drugs are easier to administer (that is, in tablet form). Low dosage/high potency drugs usually have a low incidence of anticholinergic side effects, but high incidence of extrapyramidal side effects.
9-20. SPECIFIC ANTIPSYCHOTIC AGENTS

a. Chlorpromazine (Thorazine®).

(1) Uses. Chlorpromazine is a phenothiazine drug (a particular class of drugs) used in the treatment of acute and chronic psychoses. It is also used as a preor postoperative agent in the prevention of nausea and vomiting.

(2) Adverse effects. Chlorpromazine produces three major adverse effects:

(a) Extrapyramidal reactions. These reactions are frequently seen in both young and elderly patients who are taking large doses of the drug.

(b) Drowsiness.

(c) Orthostatic hypotension. Orthostatic hypotension is most likely to occur when the patient has been administered the drug intravenously. This can be prevented by having the patient remain reclined for at least one hour after the administration of the drug.

(d) Dryness of the mouth.

(3) Cautions and warnings. Chlorpromazine should not be prescribed to patients who have liver disease or glaucoma. Furthermore, patients taking the drug should be cautioned not to drink alcoholic beverages.

b. Fluphenazine Hydrochloride (Prolixin®, Permitil®).

(1) Use. Fluphenazine hydrochloride is used in the treatment of psychotic disorders.

(2) Adverse effects.

(a) Extrapyramidal reactions.

(b) Drowsiness or lethargy.

(c) Hypertension (increased blood pressure).

(3) Cautions and warnings. Abrupt withdrawal of the drug may result in nausea and vomiting, gastritis, and dizziness.
c. **Thioridazine Hydrochloride (Mellaril®).**

   (1) **Use.** This is a phenothiazine used to treat acute and chronic types of psychosis. Thioridazine is safe in treating psychotic patients who also have liver disease.

   (2) **Adverse effects.** Thioridazine produces the following adverse effects:

      (a) Sedation and lethargy.

      (b) Gastric irritation.

d. **Perphenazine (Trilafon®).**

   (1) **Uses.** Perphenazine is used in the management of psychotic disorders.

   (2) **Adverse effects.** Perphenazine, like chlorpromazine, can produce extrapyramidal reactions, orthostatic hypotension, drowsiness, and dry mouth (drowsiness and orthostatic hypotension are less than that seen with chlorpromazine).

   (3) **Cautions and warnings.** Perphenazine may cause drowsiness. Patients should avoid alcohol and other CNS depressants while taking this drug.

e. **Trifluoperazine Hydrochloride (Stelazine®).**

   (1) **Use.** This phenothiazine is used in the treatment of various types of acute and chronic psychoses. This drug is used primarily in the maintenance treatment of psychotic patients.

   (2) **Adverse effects.** Two adverse effects are produced by this drug:

      (a) Drowsiness may occur with the use of this drug.

      (b) Extrapyramidal reactions may occur with the use of this drug.

   (3) **Cautions and warnings.** The following cautions and warnings are associated with trifluoperazine:

      (a) The use of alcohol with this agent should be avoided because of the possible interaction between the two substances.

      (b) Since the drug can produce sedation, the patient should be cautioned against operating vehicles while under the effects of this drug.
f. Haloperidol (Haldol®).

(1) Use. This drug is used in the treatment of acute and chronic psychosis. In its parenteral (injectable) form (10 milligrams per milliliter of solution), haloperidol is a potent antipsychotic medication which is well suited for emergency room use. Haloperidol can be safely prescribed to patients who have liver disease.

NOTE: Haloperidol is considered the gold standard for antipsychotics.

(2) Adverse effects. Two adverse effects are seen with this drug:

(a) Extrapyramidal reactions.

(b) Depression, anxiety, and/or dizziness.

g. Lithium Carbonate (Eskalith®, Lithane®).

(1) Use. Lithium carbonate is used in the treatment of manic-depressive psychosis. After initial administration, approximately 7 to 10 days are required before the effects of the drug can be observed in the patient.

(2) Adverse effects. The following are some of the adverse effects associated with lithium carbonate:

IMPORTANT NOTE: The level of lithium carbonate in the bloodstream of the patient is very significant. The severity of the toxic symptoms tends to increase as the level of the drug in the patient’s blood increases.

(a) Nausea, vomiting, cramps diarrhea.

(b) Drowsiness and muscular weakness.

(c) Tremors.

(d) Height loss or weight gain.

(3) Cautions and warnings. Cautions and warnings associated with the use of this agent are:

(a) Patients who are administered lithium carbonate should be kept under close medical supervision at all times. This is necessary because the amount of drug required to produce the desired effects is very close to the amount of drug that will produce toxic effects.
(b) Blood levels of lithium carbonate should always be performed at regular intervals to ensure that the appropriate therapeutic levels of the drug are maintained.

(c) Lithium carbonate should not be administered to patients who are taking diuretics (that is, some antihypertensive medications), because diuretics tend to cause an accumulation of the drug, and toxic levels of the drug could rapidly occur.

(d) The efficacy (clinical effectiveness) of lithium carbonate in the treatment of the depressive phase of manic depressive illness remains controversial. The drug is the most effective treatment for true bipolar illness, particularly in the control of manic episodes. The drug is not effective in established depressed episodes. It may prevent reoccurrence of both manic and depressive episodes.

(e) Drowsiness. Patients taking the drug should be cautioned against operating heavy machinery (for example, driving an automobile).

h. Risperidone (Risperdal®).

(1) Use. This drug belongs to the class of antipsychotics called “atypical”. They are used for treatment resistance in older agents and reduce the likelihood of extrapyramidal side effects. They may be used as first line agents.

(2) Adverse effects. Adverse effects seen with this drug are:

(a) Extrapyramidal reactions.

(b) Orthostatic hypotension.

NOTE: Other atypical antipsychotics include Olazapine (Zyprexa®), Clozapine (Clozaril®), and Quetiapine (Seroquel®).
EXERCISES, LESSON 9

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of these exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Select the best description of personality disorders.
   a. Types of conditions characterized by the development of anxiety because of unresolved unconscious conflicts.
   b. Temporary emotional disorders that occur as reactions to overwhelming environmental stress.
   c. Types of mental disorders characterized by lifelong maladaptive patterns of adjustment to life.
   d. A group of disorders with more or less severe disturbances of thought, mood, and/or behavior.

2. From the statements below, select the statement that best differentiates between fear and anxiety.
   a. Fear is a feeling of apprehension caused by a real object in the environment, while anxiety is a feeling of apprehension that has no specific object in the environment.
   b. Fear and anxiety produce entirely different physiological reactions.
   c. Fear cannot be controlled, while anxiety can be controlled without the use of drugs.
   d. Fear is a feeling of apprehension that has no specific object in the environment, while anxiety is a feeling of apprehension caused by a real object in the environment.
3. Select the correct definition of the term antianxiety agent.
   
   a. A drug used to improve the depressed mood of a patient.
   
   b. A drug used to calm a patient.
   
   c. A drug which will reduce certain symptoms such as hallucinations and delusions.
   
   d. A drug which will remove a patient’s fear.

4. Select the statement that best describes the use(s) of antidepressant agents.
   
   a. The treatment of depression that results because of chemical imbalances in the body.
   
   b. The treatment of depression that is not a result of chemical imbalances in the body.
   
   c. The treatment of patients who are experiencing periods of overwhelming stress.
   
   d. The treatment of acute and chronic psychoses.

5. Select the statement that best describes the adverse effects associated with antipsychotic agents.
   
   a. Antipsychotic agents are noted for the lack of adverse effects they produce.
   
   b. Antipsychotic agents can cause severe stimulation in many patients.
   
   c. Antipsychotic agents produce orthostatic hypertension.
   
   d. Antipsychotic agents can produce reactions that consist of tremors, muscular rigidity, and hypersalivation.
6. Select the statement that best describes the disadvantage(s) of antianxiety agents.
   a. Antianxiety agents can produce drowsiness in patients and can interact with central nervous system (CNS) depressants to produce a greater degree of CNS depression.
   b. Antianxiety agents produce an excessive loss of alertness.
   c. Because of their side effects, overdosage of antianxiety agents frequently results in death.
   d. Antianxiety agents produce tremors, muscular rigidity, and hypersalivation in many patients.

7. From the statements below, select the statement which best describes the advantage(s) of antianxiety agents over drugs which were previously used to calm or sedate patients.
   a. Antianxiety agents do not cause excessive loss of alertness.
   b. Antianxiety agents can be safely taken while driving or operating machinery.
   c. Overdosage of antianxiety agents rarely results in death to the patient.
   d. Both a and c.
   e. Both b and c.

8. Select the use of hydroxyzine hydrochloride (Atarax®).
   a. Antidiarrheal agent.
   b. Antianxiety agent.
   c. Antipsychotic agent.
   d. Antipyretic agent.
9. Select the statement that best describes an adverse reaction associated with haloperidol (Haldol®).

   a. This drug may cause extrapyramidal reactions.
   
   b. This drug may produce hypotension.
   
   c. This drug may produce overstimulation.
   
   d. This drug may produce withdrawal.

10. Select the statement which best describes the use(s) associated with chlorpromazine (Thorazine®):

   a. The drug is used to treat acute and chronic types of psychosis.
   
   b. The drug is used as an antiemetic to prevent pre- or postoperative nausea and vomiting.
   
   c. The drug is used as an antianxiety agent.
   
   d. a and b.
   
   e. b and c.

   Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 9

1. c Types of mental disorders characterized by lifelong maladaptive patterns of adjustment to life. (para 9-2c)

2. a Fear is a feeling of apprehension caused by a real object in the environment, while anxiety is a feeling of apprehension which has no specific object in the environment. (para 9-3a, b)

3. b A drug used to calm a patient. (para 9-3c)

4. b The treatment of depression that is not a result of chemical imbalances in the body. (para 9-11b)

5. d Antipsychotic agents can produce reactions that consist of tremors, muscular rigidity, and hypersalivation. (para 9-18a)

6. a Anxiety agents can produce drowsiness in patients and can interact with central nervous system (CNS) depressants to produce a greater degree of CNS depression. (para 9-8a, b)

7. e Both b and c. (para 9-7a, b)

8. b Antianxiety agent. (para 9-9e)

9. a This drug may cause extrapyramidal reactions. (para 9-20f)

10. d Both a and b. (para 9-20a)

End of Lesson 9
LESSON ASSIGNMENT

LESSON 10  Central Nervous System Stimulants.

TEXT ASSIGNMENT  Paragraphs 10-1--10-9.

LESSON OBJECTIVES  After completing this lesson, you should be able to:

10-1.  Given several categories, select the category(ies) of central nervous system (CNS) stimulants.

10-2.  Given a group of possible effects, select the pharmacological effect associated with xanthine derivatives.

10-3.  Given the trade name of a CNS stimulant and a group of generic names, match the trade name with its generic name.

10-4.  Given the trade or generic name of a CNS stimulant and a group of possible clinical uses, side effects, or cautions and warnings, select the clinical use, side effect, or caution and warning associated with that agent.

SUGGESTION  After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 10
CENTRAL NERVOUS SYSTEM STIMULANTS

Section I. BACKGROUND

10-1. INTRODUCTION TO THE CENTRAL NERVOUS SYSTEM

a. Many people are familiar with the class of drugs known as CNS stimulants. Unfortunately, most people are aware of these agents because of the abuse/misuse associated with these drugs. The central nervous system stimulants do have a variety of medically approved uses. This subcourse lesson will focus on those uses.

b. This lesson will introduce you to the topic of CNS stimulants, how they act, their approved uses, and drugs representative of the drug class. Much has been written on CNS stimulants. If you wish to learn more about these agents, you should obtain an appropriate reference (see the lesson on reference selection, lesson 1 of this subcourse).

10-2. OTHER DRUGS WHICH ACT UPON THE CENTRAL NERVOUS SYSTEM

This lesson will focus on drugs that stimulate the central nervous system. There are, as you know, many classes of drugs that have other effects on the central nervous system. These drug classes include sedative and hypnotic agents (lesson 7), antianxiety agents (lesson 9), and anti-psychotic agents (lesson 9), centrally acting skeletal muscle relaxants (SC MD0805), and anticonvulsants (lesson 8). You should be familiar with the types of responses produced by these agents because, as you know, patients take a variety of medications. Some combinations of medications may not be desirable.

10-3. CLASSIFICATION OF CENTRAL NERVOUS SYSTEM (STIMULANTS)

a. Central nervous system stimulants excite the nerve cells of the central nervous system. These agents are classified according to their main site of action and their primary pharmacological effects. Following are the three categories of agents:

(1) Cerebral of psychomotor agents.

(2) Analeptics (brain stem stimulants).

(3) Convulsants (spinal cord stimulants).
b. As you might anticipate, when increasingly larger doses of a drug are administered to the patient, the effects produced by the drug cause stimulation of more than one area.

c. Some central nervous system stimulants produce high levels of stimulation at other sites in the body (for example, the heart). In some cases, the usefulness of several CNS agents is limited because of the stimulation they produce in body organs.

Section II. CEREBRAL OR PSYCHOMOTOR AGENTS

10-4. INTRODUCTION

A variety of agents are classified as cerebral or psychomotor central nervous system agents. These drugs have one characteristic in common: they primarily stimulate the cerebral cortex of the brain.

10-5. CLASSES OF CEREBRAL OR PSYCHOMOTOR CENTRAL NERVOUS SYSTEM STIMULANTS

a. The Xanthine Derivatives. The xanthine derivatives have several pharmacological effects. One, they directly relax the smooth muscle of the bronchi and pulmonary blood vessels. By such dilation of the bronchi, more oxygen can be drawn into the lungs. Two, they stimulate the central nervous system and produce diuresis (they increase the production of urine) by direct action on the kidney. There are several examples of xanthine derivatives:

   (1) Caffeine. Caffeine is found in coffee, tea, and in kola nuts (used to make some soft drinks). Caffeine is a stimulant that has been long used as a morning "picker-upper" for workers and students. Caffeine is found in some headache remedies products promoted to prevent drowsiness, and in some products designed to suppress appetite (in these preparations caffeine acts to stimulate the person). Although caffeine does have some desirable qualities (that is, small doses of the drug can promote better performance on tasks like typing and thinking), it is possible for a person to develop a psychological dependence on the drug. Withdrawal of the drug results in some persons' having mild withdrawal symptoms (for example, headaches).

   (2) Aminophylline (Theophylline ethylenediamine). This drug is used in the treatment of bronchial asthma. It is given intravenously to provide rapid relief of pulmonary edema and dyspnea seen in the acute congestive heart failure patient because it increases cardiac output, slightly increases venous pressure, and relaxes the bronchial muscle. Side effects associated with the oral administration of this agent include nausea, vomiting, and nervousness. The patient should be informed to take this medication with food. The medication is supplied in 100 and 200-milligram tablets, 250
and 500-milligram suppositories, and in injectable form (25 milligrams per milliliter in a 10-milliliter ampule).

(3) Theophylline (Theo-dur®, Elixophyllin®). This xanthine derivative is used for the symptomatic relief of asthma because of its bronchial dilation effect. Theolair is but only one of many anhydrous theophylline products in use today. The side effects usually associated with the use of the drug are nausea, vomiting, and nervousness. The patient should be told to take theophylline with food. The drug is usually administered in a dosage of 3 to 5 milligrams per kilogram of body weight. It is supplied in various dosage forms (elixir, tablets, capsules, and sprinkles).

b. The Amphetamines. Many health care professionals are concerned about the abuse/misuse of the amphetamines. These Schedule II medications certainly have been abused in the past. Today, physicians and pharmacists cooperate to ensure these drugs are wisely used for medically acceptable purposes. Amphetamines act pharmacologically to produce two primary effects. One, they increase an individual's state of alertness. Two, they elevate a person's mood. Now, several agents will be discussed. The particular use(s) for each agent will be presented.

(1) Methylphenidate (Ritalin®). Methylphenidate (Ritalin®) is used to treat attention deficit hyperactivity disorder (ADHD), formerly known as minimal brain dysfunction, and narcolepsy. Observed abnormalities in ADHD include impulsiveness, short attention span, purposeless hyperactivity, emotional overreactivity, coordination and learning deficits, distractibility, and deficits in the perception of space, form, movement, and time. Since the first clinical sign seen with ADHD is purposeless hyperactivity, the terms hyperkinetic and hyperkinesia are sometimes used in place of attention deficit hyperactivity disorder (ADHD). Narcolepsy can be defined as an inability to stay awake. The most common side effect associated with this agent is nervousness. Methylphenidate is a Schedule II drug (Note R). The usual dosage of methylphenidate is 20 to 30 milligrams daily in divided doses. It is supplied in the form of 5 milligram, 10 milligram, and 20-milligram tablets.

(2) Dextroamphetamine sulfate (Dexedrine®). Dextroamphetamine was once prescribed as an anorectic (an appetite depressant) for many years. Recently, it has been found that dextroamphetamine’s inhibitory effect on the appetite lasts only for four or five weeks. This finding, coupled with its increased abuse, has drastically reduced the quantity of the prescriptions for this drug. This agent is not used in the military for the inhibition of appetite. It is used only for the treatment of attention deficit hyperactivity disorder (ADHD) and narcolepsy. Most military and civilian physicians believe that exercise and the restriction of food (caloric) intake is the method of choice for weight reduction. The most common side effects associated with dextroamphetamine are nervousness and headaches. This drug has a very high abuse potential. It is controlled as a Schedule II (Note R) item. Dextroamphetamine is supplied in 5-milligram tablets, 10- and 15-milligram capsules.
(3) Methamphetamine hydrochloride (Desoxyn®). This drug is similar to dextroamphetamine in terms of its ability to suppress the appetite. However, its abuse potential is such that it is rarely used any longer for this purpose.

c. Other Agents. Many other drugs produce pharmacological effects similar to those produced by the amphetamines. These are most often used for their ability to suppress the patient's appetite. Sometimes you will find these medications combined with other drugs (for example, a sedative or an antianxiety agent) in order to counteract the stimulation they produce.

(1) Pemoline (Cylert®). This drug is used in the treatment of ADHD. It is usually prescribed in a graduated dose - beginning with a 37.5-milligram daily dose. It is then gradually increased at 1-week intervals of 18.75 milligrams until a desired clinical response is observed. The most common side effect seen with this agent is insomnia. Pemoline appears to have a lower abuse potential than methylphenidate; pemoline is classified as a Note Q drug. The drug is supplied in the form of 18.75, 37.5, and 75 milligram tablets.

(2) Diethylpropion hydrochloride (Tenuate®). Diethylpropion hydrochloride is used as an appetite suppressant. It is less effective in this use than the amphetamines. It produces such side effects as dryness of the mouth, nausea, and headaches. It is available in both 25-milligram tablets and 75-milligram (timed-release) tablets. Diethylpropion is a Note Q drug.

(3) Phendimetrazine tartrate (Prelu-2®). This drug is used as an appetite suppressant. Long-term use of the drug, especially in large doses, may produce psychic dependence. It produces such side effects as nervousness, excitement, euphoria, and dryness of the mouth. It is supplied in 35-milligram tablets and capsules and 105-milligram (timed-release) capsules. Phendimetrazine is a Note Q drug.

Section III. ANALEPTIC AGENTS (BRAIN STEM STIMULANTS)

10-6. INTRODUCTION

a. Analptic agents are drugs that produce two primary effects. One, they stimulate the nerve cells of the body's respiratory center when it has been depressed by some condition (for example, illness or drugs). Two, they stimulate nerve cell centers responsible for keeping a person conscious.

b. Analptic agents are not commonly used today because of the stimulation they produce in doses sufficient to produce their analeptic effect. These agents can produce such undesirable effects as convulsions, respiratory problems, or vomiting.
10-7. EXAMPLE OF AN ANALEPTIC AGENT

Doxapram (Dopram®) is an analeptic agent used for postanesthetic arousal and drug-induced central nervous system depression. It has the ability to arouse the patient after surgery without reducing the analgesia produced by opiates (for example, morphine). Thus, it is used to hasten recovery time. The faster the patient becomes aware of his or her surroundings, the faster nursing personnel are relieved of intensive care responsibilities. Doxapram is also used to stimulate respiration and hasten arousal in patients who have mild to moderate respiratory and central nervous system depression because of overdose. The most common side effects associated with this drug are headaches, nausea, and vomiting. The usual dose of the drug is 0.5 to 2.0 milligrams per kilogram of body weight. It is supplied as an injectable containing 20 milligrams per milliliter of solution.

Section IV. CONVULSANTS (SPINAL CORD STIMULANTS)

10-8. INTRODUCTION

Some chemical substances can so stimulate the motor areas of the central nervous system that a person's muscles begin to powerfully convulse (begin uncontrollable violent contractions). Some natural and manmade chemicals are capable of producing such reactions. For example, tetanospasmin, a chemical produced by the bacteria Clostridium tetani, is such a natural agent. Strychnine, a poison, once was used as a respiratory stimulant; however, its medicinal use has been stopped because of its toxicity.

10-9. THERAPEUTIC USE OF CONVULSANTS

Drugs in this classification have little clinical usefulness. Some drugs in this class have been used in the treatment of some types of psychotic agents.

Continue with Exercises
INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise. After you have completed all of the exercises, turn to "Solutions to Exercises" at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Select the category(ies) of central nervous system stimulants.
   a. Cerebral agents.
   b. Convulsants.
   c. Analeptics.
   d. All the above.

2. Select the pharmacological effect(s) associated with xanthine derivatives.
   a. Bronchoconstriction.
   b. Smooth muscle relaxation.
   c. Enuresis.
   d. All the above.

Match the generic names below with their corresponding trade names.

3. Diethylpropion hydrochloride_______________ a. Dopram®
4. Methyl phenidate__________________________ b. Aminophylline®
5. Theophylline ethylenediamine _______________ c. Ritalin®
6. Theophylline______________________________ d. Desoxyn®
7. Methamphetamine hydrochloride____________ e. Elixophylline®
8. Doxapram_______________________________ f. Cylert®
9. Pemoline________________________________ g. Tenuate®
10. What is the clinical use of diethylpropion hydrochloride?
   a. Used in the treatment of attention deficit hyperactivity disorder (ADHD).
   b. Used to suppress a patient's appetite.
   c. Used to treat a patient's anxiety.
   d. Used to stimulate a patient's respiratory system.

11. Long-term use of phendimetrazine tartrate (Prelu-2®) may produce _________________.
   a. Nausea or vomiting.
   b. Decreased metabolic rate.
   c. Psychic dependence.
   d. Insomnia.

12. What is the clinical use of dextroamphetamine sulfate (Dexedrine®)?
   a. To suppress a patient's appetite.
   b. To increase a patient's ability to concentrate.
   c. To treat narcolepsy.
   d. To stimulate respiration.

13. When taking Aminophylline orally, the patient should be cautioned _________________.
   a. Not to take the medication with alcohol.
   b. Take the medication with food.
   c. Discontinue the medication immediately if any slight nervousness is detected.
   d. Not to drive while taking the medication.

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 10

1. d All the above. (para 10-3a)

2. b Smooth muscle relaxation. (para 10-5a)

3. g Tenuate®. (para 10-5c(2))

4. c Ritalin®. (para 10-5b(1))

5. b Aminophylline. (para 10-5a(2))

6. e Elixophylline®. (para 10-5a(3))

7. d Desoxyn®. (para 10-5b(3))

8. a Dopram®. (para 10-7)

9. f Cylert®. (para 10-5c(1))

10. b Used to suppress a patient's appetite. (para 10-5c(2))

11. c Psychic dependence. (para 10-5c(3))

12. c To treat narcolepsy. (para 10-5b(2))

13. b Take the medication with food. (para 10-5a(2))

End of Lesson 10
LESSON ASSIGNMENT

LESSON 11
Narcotic Agents.

LESSON ASSIGNMENT
Paragraphs 11-1--11-7

LESSON OBJECTIVES
After completing this lesson, you should be able to:

11-1. Given a group of definitions, select the definition of analgesia.

11-2. Given a group of pharmacological effects, select those that are produced by narcotic agents.

11-3. Given a group of definitions, select the meaning of the following terms: dysphoria, euphoria, tolerance, and miosis.

11-4. Given a general pharmacological effect produced by the narcotics and a group of statements, select the term that best describes that effect.

11-5. Given several statements, select the statement that best contrasts psychological and physiological dependence.

11-6. Given a group of side effects, select those side effects associated with the narcotic agents.

11-7. Given the trade and/or generic name of a specific narcotic agent, and a list of uses, side effects, or cautions and warnings, select the use, side effect, or caution and warning associated with that agent.

11-8. Given a group of cautions, select the caution associated with the use of narcotic agents.

11-9. Given the name naloxone (Narcan®) and a group of uses/indications, select the use/indication associated with the drug.
SUGGESTION

After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 11
NARCOTIC AGENTS

Section I. BACKGROUND

11-1. GENERAL COMMENTS

Most people have legally used narcotic agents. Conditions characterized by a degree of discomfort (that is, pain, diarrhea, or cough), often are treated with medications that have narcotics as the active ingredient. It is very important for all medical personnel to be familiar with narcotic agents.

11-2. HISTORY OF NARCOTIC AGENTS

a. There is evidence that the opium poppy was used in Sumeria as early as 4000 B.C., and it is mentioned in the medical records of ancient Greece and Rome. During the Dark Ages, it passed to the Arabs, who took it to China about 900 A.D. It was either smoked or taken orally.

b. Opium was first used injectably around 1800; the U.S. Civil War saw the first widespread use in this manner. Because of a lack of knowledge and caution, a condition called “Soldier’s Disease” was described—addiction. This coupled with the large influx of Chinese laborers who smoked, and the ready availability of opium caused a great deal of concern. There were no packaging or distribution laws; indeed, a children’s formulation was marketed called “Mrs. Winslow’s Soothing Syrup.” This concern was an important factor in motivation for the Pure Food and Drug Act of 1906.

c. In 1805, a German Pharmacist’s assistant isolated a pure alkaloid (a basic substance found usually in plant parts) from opium that he called morphine. It was subsequently found that opium contains two general categories of alkaloids; narcotics (phenanthrene) such as morphine and codeine, and nonnarcotics (benzylisoquinoline)

11-3. PHARMACOLOGICAL EFFECTS OF THE NARCOTICS

Narcotics produce pharmacological effects when administered to a patient. Some of these effects are desirable, while others are undesirable. Always remember that the legitimate use of these agents is implied in our discussion.

a. Analgesic Effect. Analgesia means relief of pain without the loss of consciousness. Analgesia is the most common use of narcotics. Although the exact mechanism of action by which narcotics act is unknown, it is thought that analgesia is obtained by the action of these agents on the cerebral cortex. The relief of pain is enhanced because narcotics raise a patient’s pain threshold and thus produce a
calming and soothing effect. Narcotic agents have particular application in the relief of continuous, dull pain. Consequently, these drugs are widely used in patients who are terminally ill.

b. **Antitussive Effect.** An antitussive agent acts to control or prevent cough. Some narcotics will depress the cough center of the brain and produce this antitussive effect. In general, the antitussive dose of a narcotic is lower than the analgesic dose of that same drug. Before progressing, it should be noted that a narcotic is not indicated for all types of coughs. Indeed, sometimes it is useful for a patient to cough in order to remove substances from the lungs.

c. **Mood Alteration Effect.** Some narcotics will produce a mood alteration in patients. The types of mood changes can be classified in two categories.

   (1) **Dysphoria.** Dysphoria is a mood alteration characterized by feelings of anxiety, fidgetiness, or being ill at ease.

   (2) **Euphoria.** Euphoria is characterized by an exaggerated feeling of well-being.

d. **Gastrointestinal Effect.** Narcotics produce some significant effects upon the gastrointestinal system (that is, stomach and intestines). Some narcotics are used specifically for their effect upon this system of the body.

   (1) **Decrease gastrointestinal motility.** Narcotics decrease the peristaltic (wavelike) movements of the gastrointestinal tract. Consequently, they may cause constipation. This effect of narcotics is the basis of their being used to treat diarrhea. When used to treat diarrhea, the agents are referred to as antidiarrheals.

   (2) **Stimulate the chemoreceptor trigger zone.** The chemoreceptor trigger zone (CTZ) is located at the base of the brain. When stimulated, the CTZ produces nausea and vomiting. Like many other categories of drugs, narcotics can stimulate the chemoreceptor trigger zone and cause nausea and vomiting.

e. **Respiratory System Effect.** Narcotics cause respiratory system depression because they reduce the sensitivity of the medullary centers to carbon dioxide in the blood. This depression of the respiratory system usually occurs at higher narcotic doses.

11-4. **SIDE EFFECTS OF NARCOTICS**

Side effects are frequently seen with the use of narcotics. Some of these side effects are characteristics of the narcotic agents.
a. **Dependence.** Dependence is a side effect of narcotics, which has caused much concern among many health-care professionals. There are two types of dependence.

(1) **Psychological.** Psychological dependence is produced when the drug causes an emotional or mental desire to repeat the use of the drug. Consequently, the individual taking the drug has a craving for the pleasurable mental effects produced by the drug (that is, euphoria, and so forth).

(2) **Physiological (physical).** Physical dependence is produced by prolonged use of a drug whose pharmacological action causes the body to adapt to its presence. When the drug is withdrawn after the person has become physically dependent, the body of the individual reacts in a hyperexcited way. You have probably read about or seen heroin (narcotic) addicts who are undergoing withdrawal. These episodes of withdrawal are characterized by stimulation of the central nervous system.

b. **Tolerance.** Tolerance is the body’s ability to adapt to the presence of a foreign chemical substance (drug). This results in the requirement for progressively larger doses of the drug in order to obtain the same effect in the patient. It should be noted that tolerance is frequently seen in patients who abuse narcotics. Tolerance is not of great concern in narcotic therapy of short duration. However, for those chronically ill patients who are on long-term narcotic therapy, increased doses of the narcotic agents might be indicated to maintain the desired level of analgesia.

c. **Drowsiness.** Drowsiness is another side effect of narcotics. For this reason, individuals who are receiving narcotics should seriously examine their activities (that is, driving) for safety purposes.

d. **Miosis.** Miosis (constricted pupils) is an effect commonly known as “pinpoint” pupils. Miosis is commonly seen in patients who are taking narcotic agents.

Section II. NARCOTIC AGENTS AND NARCOTIC ANTAGONISTS

11-5. SPECIFIC NARCOTIC AGENTS

a. **Morphine.** Morphine is the basis of the narcotic effect of opium and is the standard by which other analgesics are judged. It is used in moderate to severe pain, is the analgesic of choice for myocardial infarction, and is used to treat acute pulmonary edema. Morphine is most frequently given IM or SC, 10-15 mg every 4 hours, or IV, where 4-10 mg are diluted and given slowly over 4-5 minutes. It is used less frequently by the oral route (1/15--1/6 the effectiveness of parenteral administration) in a dose of 8-20 mg every 4 hours. The most common side effects associated with morphine are drowsiness, nausea, and vomiting. Morphine is supplied as an injection containing 8, 10, and 15 milligrams per milliliter; in tablets of 10, 15, and 30 milligrams; and as an oral
solution containing 10-milligrams per 5-milliliters. Morphine in all forms is a Note R substance.

b. **Codeine.** Codeine is the second naturally occurring narcotic. Its use is very widespread; in some states it can be sold without prescription in combination products if its concentration is weak enough (ETH & codeine, Robitussin AC®). For our purposes, however, when codeine is dispensed as a single agent, it is Note R, when in combination, it is Note Q. Codeine is used as an antitussive, 5-15 mg every 4-6 hours, and as an analgesic in mild to moderate pain, 30-60mg every 4-6 hours. Its most common side effects include drowsiness, nausea/vomiting, and constipation; patients must be cautioned about the drowsiness and the additive effect seen with concurrent use of alcohol. Codeine is available as an injection of 15, 30, and 60 mg/ml, and in 15 and 30 mg tablets. A powder form for compounding is also available.

c. **Hydromorphone (Dilaudid®).** Hydromorphone (Dilaudid®) is a drug that was obtained by chemical modification of morphine, used as an analgesic in moderate to severe pain. It is frequently used in pain associated with cancer. Its usual dose is 2 mg every 4 to 6 hours. Its major side effects are nausea and vomiting, dizziness, and constipation. Although the manufacturer states that drowsiness occurs infrequently, patients should be made aware of this possibility; also alcohol may intensify its effects. Dilaudid® is a Note R drug and is supplied in tablet or injectable form, both in 1, 2, 3, and 4 mg strengths.

d. **Meperidine (Demerol®).** Meperidine was the first synthetically produced narcotic. It is one of the first widely used agents for moderate to severe pain. Usual doses of this agent (50-150 mg every 3-4 hours) produce some drowsiness, nausea, and vomiting. Patients who are prescribed meperidine should be cautioned that drowsiness might occur. Further, they should be advised that alcohol might intensify this drowsiness. Meperidine is a Note R drug, which is available as an injection (25, 50, 75, and 100 mg/ml), a tablet (50 or 100 mg tablets), and in a syrup (50 mg/5ml).

e. **Fentanyl (Sublimaze®, Duragesic®, Oralet®, Actiq®).** Fentanyl is a synthetic agent with actions similar to morphine, but on a weight basis, Sublimaze® is 80-100 times more potent. It is used as an analgesic component in general anesthesia or conscious sedation and given intramuscularly (IM) or intravenously (IV). The dosage is dependent upon its intended role during anesthesia, and ranges from 0.025 to 0.1 mg. Respiratory depression is the side effect of concern for this agent. Fentanyl is unique in that it is available as an injection (Sublimaze®), in a topical patch formulation (Duragesic®), a lozenge (Fentanyl Oralet®) and a lozenge on a stick (“lollipop”) (Actiq®) formulation. The latter three formulations are prescribed primarily for severe pain conditions. Fentanyl is handled as a Note R product.

f. **Methadone (Dolophine®).** Methadone (Dolophine®) is a synthetic agent that has been used as an analgesic for moderate to severe pain, and to treat withdrawal symptoms of narcotics in a dose-tapering fashion. The usual dose for analgesia is 2.5-10 mg every 4 hours, and common side effects include drowsiness and
nausea/vomiting. The effects of methadone may be intensified by alcohol, and the patient also should be cautioned about drowsiness. The injection, 10 mg/ml, and the tablets, 5 and 10 mg, are all Note R.

g. **Percodan®**. Percodan® is a popular semisynthetic narcotic intended for the relief of moderate pain that contains two salts of oxycodone, combined with aspirin. It is, of course, a fixed combination and is given in a usual dose of one tablet every 6 hours. In addition to the side effects of drowsiness and nausea/vomiting, pruritis is also a fairly frequent complaint. Patient cautionary statements regarding drowsiness and alcohol apply to this agent. It is a Note R product even though it is a combination. Percodan® is available in tablet form, and a half-strength product called Percodan-Demi® is also produced.

**NOTE:** Combination products of acetaminophen with oxycodone are Tylox® and Percocet®.

h. **Combination Products.** Codeine is combined with aspirin or acetaminophen (Tylenol®) to produce products that are used to treat mild to moderate pain. Common side effects of these combination products include nausea, vomiting, and drowsiness. Patients who are taking these products should be cautioned about the drowsiness. Further, patients should be warned against taking these with alcohol. These combination products are handled as Note Q items.

(1) **Empirin® with codeine.** Empirin® with codeine is a combination of aspirin and codeine. The usual dosage of these products is from one to two tablets every four hours. The various products are numbered based upon the amount of codeine contained in each product as noted below:

(a) Empirin® with Codeine #2 - 15 mg of codeine per tablet.

(b) Empirin® with Codeine #3 - 30 mg of codeine per tablet (most widely used of these products).

(c) Empirin® with Codeine #4 - 60 mg of codeine per tablet.

(2) **Tylenol® with codeine.** Tylenol® with codeine is a combination acetaminophen with codeine. The usual dosage of these products is from one to two tablets every four hours. As with Empirin® with codeine, the products are numbered based upon the amount of codeine contained in each tablet as noted below:

(a) Tylenol® with Codeine #1 - 7.5 mg of codeine per tablet.

(b) Tylenol® with Codeine #2 - 15 mg of codeine per tablet.

(c) Tylenol® with Codeine #3 - 30 mg of codeine per tablet (most widely used of these products).
(d) Tylenol® with Codeine #4 - 60 mg of codeine per tablet.

11-6. CAUTIONS OF NARCOTIC USE

a. Narcotics should not be used in patients experiencing any form of respiratory depression (that is, asthma).

b. Narcotics cause an increase in intracranial pressure (pressure within the skull). Therefore, they should not be used in the presence of head injuries.

c. Narcotics should be used cautiously in combination with other drugs that depress the central nervous system.

11-7. NARCOTIC ANTAGONISM

a. **Explanation.** As previously mentioned, narcotics depress the respiratory system. Sometimes it is necessary to reverse this respiratory depression (that is, overdose of narcotics) in order to save a patient’s life.

b. **Naloxone (Narcan®).** Naloxone (Narcan®) is the only true narcotic antagonist in that it does not possess agonist or morphine-like properties and, most importantly, it has no respiratory depressant action in therapeutic doses. Because it does not depress respiration, naloxone is the drug of choice in the treatment of respiratory depression of unknown causes, but which is suspected of being produced by a narcotic. Narcan® is given in a usual dose of 0.4 mg IM, SC, or IV, and may produce some nausea and vomiting. It is not a controlled substance, and is available as an injection, 0.4 mg/ml or 0.2 mg/ml for pediatric use.

c. **Indications/Uses.** Naloxone (Narcan®) is indicated/used to reverse respiratory depression caused by natural and synthetic narcotics, pentazocine (Talwin®), and propoxyphene (Darvon®). It is not effective against the respiratory depression caused by the barbiturates or benzodiazepines. Naloxone is a competitive antagonist.

*Continue with Exercises*
EXERCISES, LESSON 11

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the exercise, by completing the incomplete statement, or by writing the answer in the space provided at the end of the exercise.

After you have completed all of the exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. From the group of definitions below, select the meaning of the term analgesia.
   a. The decrease in a patient’s pain threshold.
   b. The relief of pain with loss of consciousness.
   c. The relief of pain without the loss of consciousness.
   d. The loss of consciousness with no effect on pain level.

2. From the group of pharmacological effects below, select the response that contains those produced by narcotic agents.
   (1) Relief of pain.  (6) Depress respiratory rate.
   (2) Antitussive.  (7) Increase blood pressure.
   (3) Antipyretic.  (8) Increase respiratory rate.
   (4) Decrease gastrointestinal motility.  (9) Decrease clotting time.
   (5) Produce diarrhea.  (10) Produce loss of consciousness.
   a. (1), (2), (3), (6) and (10).
   b. (1), (2), (4) and (6).
   c. (1), (2) and (5).
   d. (1), (2), (4), (5), (6), (7) and (10).
3. From the group of definitions below, select the meaning of the term euphoria.
   
   a. A mood alteration characterized by feelings of anxiety.
   
   b. A mood alteration characterized by feelings of being ill at ease.
   
   c. A mood alteration effect characterized by analgesia.
   
   d. A mood alteration characterized by exaggerated feelings of well-being.

4. Narcotic agents produce an effect on a patient’s respiratory system. From the list of descriptions below, select the best description of the specific effect produced by the narcotic agents.
   
   a. Narcotic agents stimulate a patient’s respiratory system.
   
   b. Narcotic agents depress a patient’s respiratory system.
   
   c. Narcotic agents decrease the levels of carbon dioxide in the blood.
   
   d. Narcotic agents depress the respiratory rate only in small doses.

5. Narcotic agents produce an effect on a patient’s gastrointestinal system. From the list of descriptions below, select the best description of that specific effect.
   
   a. Narcotic agents stimulate the patient’s CTZ to produce nausea and vomiting.
   
   b. Narcotic agents stimulate the patient’s CTZ to produce diarrhea.
   
   c. Narcotic agents stimulate the patient’s CTZ to produce constipation.
   
   d. Narcotic agents stimulate the patient’s CTZ to produce peristalsis.
6. From the group of side effects below, select the response that contains the side effects associated with the narcotic agents.

(1) Independence.  
(2) Mitosis.  
(3) Tolerance.  
(4) Miosis.  
(5) Dependence.  
(6) Drowsiness.

a. (1), (2), (3), (6).  
b. (1), (3), (5), (6).  
c. (3), (4), (5), (6).  
d. (1), (2), (5), (6).

7. From the definitions below, select the best definition of the term tolerance.

a. The ability of the body to adapt to the presence of foreign substances that result in the requirement for progressively larger doses of the drug to obtain the same effect.

b. The ability of the body to adapt to the presence of foreign substances that result in the requirement for progressively smaller doses of the drug to obtain the same effect.

c. The ability of the body to adapt to the presence of foreign substances that result in the requirement for changing the route of administration of the drug.

d. The ability of the body to adapt to the presence of foreign substances that result in the requirement for changing the dosage form of the drug.

8. From the list of uses below, select the use of codeine.

a. Antitussive.  
b. Antiemetic.  
c. Antipyretic.  
d. Sedative.
9. From the list of uses below, select the use of hydromorphone (Dilaudid\textsuperscript{®}).
   a. Analgesic for moderate to severe pain.
   b. Analgesic for mild to moderate pain.
   c. Antidiarrheal in severe diarrhea.
   d. Emetic in poisoning.

10. From the list of cautions and warnings, select the caution and warning associated with the use of meperidine hydrochloride (Demerol\textsuperscript{®}).
   a. The patient should be cautioned against taking aspirin with meperidine.
   b. The patient should be warned that alcohol can intensify the drowsiness caused by meperidine.
   c. The patient should be warned against not taking the drug on a regular basis.
   d. The patient should be cautioned against exercise when taking the drug.

11. From the list of uses below, select the use associated with Methadone (Dolophine\textsuperscript{®}).
   a. An agent used to treat withdrawal symptoms associated with narcotic antagonists.
   b. An agent used in the treatment of mild to moderate pain.
   c. An agent used in the treatment of alcohol withdrawal symptoms.
   d. An agent used in the treatment of the withdrawal symptoms associated with narcotic agents.
12. From the group of cautions below, select the caution associated with the use of narcotic agents.
   a. Narcotics should not be administered to patients over the age of 65.
   b. Narcotics should not be administered intravenously.
   c. Narcotics should be used cautiously with drugs that depress the central nervous system.
   d. Narcotics should not be used by cardiac patients.

13. Select the use of Naloxone (Narcan®) from the list of uses below.
   a. Narcotic.
   b. Narcotic analgesic.
   c. Narcotic suppressant.
   d. Narcotic antagonist

Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 11

1. c The relief of pain without the loss of consciousness.  (para 11-3a)

2. b (1), (2), (4), and (6).  (para 11-3a, b, d(1), and e)

3. d A mood alteration characterized by exaggerated feelings of well being.  (para 11-3c(2))

4. b Narcotic agents depress a patient's respiratory system.  
   (para 11-3e)

5. a Narcotic agents stimulate the patient's CTZ to produce nausea and vomiting.  (para 11-3d(2))

6. c (3), (4), (5), and (6).  (para 11-4a, b, c, and d)

7. a The ability of the body to adapt to the presence of foreign substances which results in the requirement for progressively larger doses of the drug to obtain the same effect.  (para 11-4b)

8. a Antitussive.  (para 11-5b)

9. a Analgesic for moderate to severe pain.  (para 11-5c)

10. b The patient should be warned that alcohol can intensify the drowsiness caused by meperidine.  (para 11-5d)

11. d An agent used in the treatment of the withdrawal symptoms associated with narcotic agents.  (para 11-5f)

12. c Narcotics should be used cautiously with drugs which depress the central nervous system.  (para 11-6c)

13. d Narcotic antagonist.  (para 11-7b)

End of Lesson 11
This Drug Pronunciation Guide was developed to help you to learn how the trade and generic names of commonly prescribed medications are frequently pronounced. Not all the drugs in the guide are discussed in this subcourse. Remember, it is not enough to know the uses, indications, cautions and warnings, and contraindications for a drug—you must also know how to pronounce that drug's name.

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LESSON ASSIGNMENT

LESSON 1
Dermatological Agents.

TEXT ASSIGNMENT
Paragraphs 1-1--1-5.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

1-1. Given a group of definitions and one of the following terms: dermatological agent, antiseborrheic agent, astringent, keratolytic agent, or keratoplastic agent, select the definition of that term.

1-2. Given a group of statements, select the statement that best describes a general consideration pertaining to dermatological agents.

1-3. Given a group of statements and the name of a particular category of dermatological agents, select the statement which best describes a general consideration or indication of that particular category.

1-4. Given the trade or generic name of a dermatological agent and a list of trade and/or generic names, select the agent’s corresponding name.

1-5. Given the generic and/or trade name of a dermatological agent and a group of statements, select the statement which best describes the indication, use, or side effect associated with that agent.

SUGGESTION
After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
1-1. DEFINITION OF DERMATOLOGICAL AGENTS

Dermatological agents are drugs that exert either a chemical or physical action on the skin to aid in the correction of a disorder of the skin.

1-2. GENERAL CONSIDERATIONS INVOLVING DERMATOLOGICAL AGENTS

a. The vehicles (creams, lotions, ointments, and so forth.) in which therapeutic ingredients are incorporated and diluted have been found to have pharmacological properties of their own. This subcourse will not mention these pharmacological properties of the vehicles. Instead, it will focus strictly on the pharmacological actions and effects of the therapeutic ingredients.

b. There is a great variation in the manner in which vehicles hold, release, or assist in the absorption of their therapeutic ingredients. Therefore, it is important that the vehicle selected to contain a therapeutic ingredient be suitable for use on the portion of skin on which it will be applied.

c. The distribution of the therapeutic ingredient(s) throughout a vehicle is an important factor in the determination of a dermatological's effectiveness. You must be aware of this fact because you might one day be required to compound or manufacture some of the dermatological products discussed in this subcourse.

Section II. THERAPEUTIC CATEGORIES OF DERMATOLOGICAL AGENTS

1-3. ANTISEBORRHEICS

a. Definition. Antiseborrheics are used in the management of seborrheic dermatitis. Seborrheic dermatitis is characterized by a yellowish and greasy scaling of the scalp and/or mid-parts of the face (around eyebrows and nose) and ears.

b. General Considerations. The ideal antiseborrheic agent should be nontoxic, relieve pruritus (itching), modify excessive dryness, and demonstrate wide antifungal and antibacterial spectra.
c. **Specific Antiseborrheic Agents.**

(1) **Chloroxine (Capitrol®).** This agent is used in the treatment of dandruff and seborrheic dermatitis of the scalp. The patient should be instructed not to use this medication if blistered, raw, or oozing areas are present on the scalp and to keep the medication away from the eyes. This medication may slightly discolor light-colored hair.

(2) **Selenium sulfide (Selsun®).** This shampoo product is used to treat dandruff and seborrheic dermatitis of the scalp. The patient should be instructed not to use this medication if blistered, raw, or oozing areas are present on the scalp and to keep the medication away from the eyes. This medication should be thoroughly rinsed from the hair of persons with light-colored hair because it can cause discoloration.

(3) **Sebulex® or Sebra® Shampoo.** This product is made of salicylic acid (2%) and sulfur (2%). It is used as a shampoo to treat seborrheic dermatitis, dandruff, and psoriasis of the scalp. Present in these concentrations, salicylic acid and sulfur are used for their keratoplastic (mild keratolytic) actions. The patient using this product should be informed of two things. One, this product may discolor light-colored hair. Two, the patient should not use this product on the same area to which has been applied any topical mercury-containing product (such as ammoniated mercury ointment) because doing so might stain that area and produce a foul odor (interaction between sulfur and mercury).

(4) **Sebutone® or Sebra T® Shampoo.** This product is made of salicylic acid (2%), coal tar (0.5%), and sulfur (2%). In these concentrations, the salicylic acid and sulfur are used for their keratoplastic (mild keratolytic) actions, and coal tar is used for its antipruritic (controls itching), antibacterial, and keratoplastic actions. The patient using this product should be informed of two things. One, this product may discolor light-colored hair. Two, the patient should not use this product on the same area to which has been applied any topical mercury-containing product (such as ammoniated mercury ointment) because doing so might stain that area and produce a foul odor.

1-4. **ASTRINGENTS**

a. **Definition.** An astringent is an agent that dries mucous secretions, shrinks skin, and causes blanching (whitening).

b. **Indications for the use of Astringents.** Astringents are used to reduce inflammation of mucous membranes, to promote healing, and to toughen skin.

c. **Specific Astringent Agents.**

(1) **Aluminum acetate tablets (Domeboro®, Burow’s solution).** When these tablets are added to water, aluminum acetate solution is prepared. This product is used as an astringent for inflammatory skin conditions such as insect bites, poison ivy, and athlete’s foot. The patient receiving these tablets should be warned that they are for
external use only. The patient should be told to see his physician if the inflammatory condition does not improve and to avoid getting the prepared solution in contact with his eyes. Usually one or two of the tablets are dissolved in a pint of water. The patient is then to soak the affected area two or three times daily in the freshly prepared solution for 15 minutes.

(2) **Calamine lotion (calamine and zinc oxide lotion).** This product is used as an astringent and as a protectant (used to cover and protect epithelial surfaces). Both these actions aid in reducing inflammation associated with insect bites, poison ivy, and sunburn. The patient receiving this product should be told that the preparation is for external use only and that he should shake the product well before using it.

(3) **Phenolated and mentholated calamine lotion.** Phenol and menthol have been added to the product above because they produce an antipruritic effect.

**1-5. KERATOLYTICS**

a. **Definition.** A keratolytic is an agent that induces sloughing of cornified epithelium (horny or hard layer of the skin).

b. **General Considerations.** Keratolytic drugs act to damage the cornified layer of skin that is then sloughed off to whatever depth the agent has acted. A keratoplastic (mild keratolytic) effect is seen when the drug does not produce a rapid destruction and sloughing, thereby softening the keratin and loosening the cornified epithelium.

c. **Indications for the Use of Keratolytic Agents.** Keratolytic agents are used to remove warts and corns. They are also used in the treatment of severe acne.

d. **Indications for the Use of Keratoplastic Agents.** Keratoplastic agents are used in the treatment of acne, eczema, psoriasis, and seborrheic dermatitis.

e. **Specific Keratolytic Agents.**

**NOTE:** You will see chemicals (1) through (4) present in several manufactured products. You might be called upon to compound or manufacture products containing one or more of these substances. If you handle these chemicals, remember that they are irritating to the skin. You should wash your hands immediately after working with them.

(1) **Coal tar (chemical name).** This agent is used as a keratoplastic in the treatment of eczema, psoriasis, and seborrheic dermatitis.

(2) **Salicylic acid (chemical name).** It is used as a keratolytic when present in concentrations of from 5% to 20%. It is used as a kerato- plastic when present in concentrations of from 1% to 2%.
(3) Sulfur (chemical name). Sulfur is used as a keratoplastic in the treatment of acne and seborrheic dermatitis.

(4) Tretinoin (topical) (Retin A®). This agent is used in the treatment of severe acne. The application of this agent to the skin will produce a horny layer of skin that is more easily removed. It is important that the patient use this preparation as directed by the physician and package directions. This medicine should not be applied to windburned or sunburned skin. It should not be applied to open wounds. Furthermore, the medication should not be applied inside the nose, around the eyes, or around the mouth. While the patient is using the medication, he should avoid exposing the area being treated to too much wind or sun (or sun lamp). When the patient begins using this product, he may find that he is more sensitive to cold temperatures and to wind than before; therefore, protection should be worn until the person sees how he reacts. This product is available in cream, liquid, and gel.

(5) Salicylic acid 2% and sulfur 2% (Fostex®). This preparation is available in cream or soap. It is used to treat acne.

(6) Salicylic acid 2% and Sulfur 2% shampoo (Sebulex® or Sebra®). This shampoo is used to treat dandruff.

(7) Salicylic acid 2%, coal tar 0.5%, and sulfur 2% shampoo (Sebutone® or Sebra T®). This product is used to treat dandruff.

Continue with Exercises
EXERCISES, LESSON 1

INSTRUCTIONS: Answer the following exercises by marking the lettered response which best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson, and, check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Select the definition of the term antiseborrheic agent.
   a. An agent that dries mucous secretions, shrinks skin, and causes blanching.
   b. An agent used to manage a skin condition characterized by a yellowish and greasy scaling of the scalp and/or mid-parts of the face and ears.
   c. An agent used in the treatment of severe acne and in the removal of warts or corns.

2. Which of the following statements best describes a general consideration associated with the use of keratolytic agents?
   a. These agents are not to be used on mucous membranes.
   b. These agents sometimes produce a yellowish and greasy scaling around the mid-parts of the face when they are applied as a treatment for acne.
   c. These agents usually make a person excessively sensitive to the effects of cold and wind.
   d. These agents are used to damage the cornified layer of skin so that it will be sloughed off.

3. Select the correct use of Burow’s solution.
   a. An astringent for inflammatory skin conditions.
   b. An agent used in the treatment of seborrheic dermatitis.
   c. An agent used in the treatment of eczema.
   d. An astringent used in the treatment of warts and corns.
4. Match the generic name in Column A with its corresponding trade name in Column B.

<table>
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<tr>
<td>A. Salicylic acid 2% and sulfur 2% soap</td>
<td>______ Fostex®</td>
</tr>
<tr>
<td>B. Selenium sulfide</td>
<td>______ Retin A®</td>
</tr>
<tr>
<td>C. Tretinoin</td>
<td>______ Selsun®</td>
</tr>
<tr>
<td>D. Aluminum acetate tablets</td>
<td>______ Capitrol®</td>
</tr>
<tr>
<td>E. Coal tar</td>
<td>______ Burow’s solution</td>
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5. Select the information you should give a patient who has been prescribed selenium sulfide shampoo for the first time.

a. “You should wear some sort of protection because you might be more sensitive to cold temperatures and to wind.”

b. “You should not use this medication if you have applied any medicine containing mercury on your scalp.”

c. “You should not use this medication if your scalp is raw or blistered.”

d. “You should stop using this medication if your scalp condition has not improved within five days.”
6. Select the information you should give to a person who has been prescribed aluminum acetate tablets for the first time.

   a. “These tablets are not to be taken by mouth. Instead, make a solution as prescribed on the container label and use the prepared solution as a soak.”

   b. “Do not be alarmed if your hair turns slightly orange for a few days after you use this product.”

   c. “Do not expose the portion of your body you are soaking in the prepared solution to sunlight or wind.”

   d. “Do not use the solution you prepare from these tablets on any part of your body to which has been applied any medication containing mercury.”

7. Select the correct use of coal tar.

   a. A keratoplastic agent used in the treatment of eczema, psoriasis, and seborrheic dermatitis.

   b. A keratolytic agent used in the treatment of severe acne.

   c. An astringent used in the treatment of acne and seborrheic dermatitis.

   d. A product used as a protectant and astringent in the treatment of inflammation associated with insect bites and sunburn.

Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 1

1. **b** An agent used to manage a skin condition characterized by a yellowish and greasy scaling of the scalp and/or mid-parts of the face and ears. (para 1-3a)

2. **d** These agents are used to damage the cornified layer of skin so that it will be sloughed off. (para 1-5b)

3. **a** An astringent for inflammatory skin conditions. (para 1-4c(1))

4. **A** Fostex® (para 1-5e(5))
   **C** Retin A® (para 1-5e(4))
   **B** Selsun® (para 1-3c(2))
   **E** Capitrol® (para 1-3c(1))
   **D** Burow's Solution (para 1-4c(1))

5. **c** “You should not use this medication if your scalp is raw or blistered.” (para 1-3c(2))

6. **a** “These tablets are not to be taken by mouth. Instead, make a solution as prescribed on the container label and use the prepared solution as a soak.” (para 1-4c(1))

7. **a** A keratoplastic agent used in the treatment of eczema, psoriasis, and seborrheic dermatitis. (para 1-5e(1))

*End of Lesson 1*
LESSON ASSIGNMENT

LESSON 2

The Human Muscular System.

TEXT ASSIGNMENT

Paragraphs 2-1--2-4.

LESSON OBJECTIVES

After completing this lesson, you should be able to:

2-1. Given one of the following terms: motor unit, tonus, or all or none law and a group of definitions, select the definition of that term.

2-2. Given a list of properties, select the properties of muscle tissue.

2-3. Given one of the properties of muscle tissue and a group of statements, select the statements that best describe that property.

2-4. From a list, select the types of muscle tissue found in the human body.

2-5. Given the name of a type of muscle tissue found in the body and a group of statements, select the statement that best describes that type of muscle tissue.

2-6. Given the name of a type of muscle tissue found in the body and a group of statements, select the statement that best describes the physiology of that type of tissue.

2-7. Given a statement relating to muscle physiology and a list of the types of muscle tissue, select the type of muscle tissue to which the statement applies.

SUGGESTION

After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 2
THE HUMAN MUSCULAR SYSTEM

2-1. BACKGROUND

Muscular tissue is useful to the body because it contracts and thereby produces movement. The contraction of striated muscle attached to bone results in movement of the skeleton. Cardiac muscle contracts rhythmically and acts as a pump to move blood through the cardiovascular system. The contraction of smooth or visceral muscle results in the movement of materials inside the body, such as the propulsion of food through the digestive tract.

2-2. TERMS ASSOCIATED WITH THE HUMAN MUSCULAR SYSTEM

a. **Motor Unit.** A motor unit is a single motor neuron and the number of striated muscle fibers activated by it (innervation). The importance of the motor unit is that its fibers work in unison.

b. **Tonus.** Tonus is defined as a slight continuous contraction of muscle tissue that aids in the maintenance of posture and in the return of blood to the heart.

c. **All or None Law.** Under the influence of nervous stimulation, a single muscle fiber will always contract to its maximum capacity.

2-3. PROPERTIES OF MUSCLE TISSUE

Muscles have certain key properties:

a. **Irritability.** Irritability refers to the ability of a muscle to respond to a stimulus.

b. **Contractability.** Contractability refers to the muscle’s ability to shorten in length.

c. **Extensibility.** Extensibility refers to a muscle’s ability to extend in length.

d. **Elasticity.** Elasticity refers to a muscle’s ability to stretch and return to its normal position.
2-4. TYPES OF MUSCLE TISSUE

a. **Skeletal Muscle.** Each skeletal muscle is an individual organ of the human body. Each is composed of several types of tissues, mainly striated muscle fibers, and fibrous connective tissue (FCT). Each is attached to and moves bones. Bones are parts of the skeleton serving as levers. The large portion of a muscle is known as its belly or fleshy belly. The muscle is attached to bones by tendons or aponeuroses. Tendons and aponeuroses are similar to each other. However, tendons are cord-like, and aponeuroses are broad and flat. The fleshy portion may be directly connected to the bone. If it is attached to the bone, it is called a “fleshy attachment.”

(1) **Anatomy.** The muscle cells of skeletal muscles are elongated and are called fibers. The fibers of the skeletal muscles are striated (a striped appearance) to give strength. Movement of the skeleton, such as lifting a leg, is voluntary, as are all of the movements characterized by the skeletal system.

(2) **Physiology.** The neuromuscular junction consists of a nerve fiber and a skeletal muscle fiber. The nerve fiber is branched at the end to form a structure called the end plate. This end plate invaginates into the muscle fiber, but it always stays outside the membrane of the muscle. The sole feet are located at the tips of the numerous branches of the end plate. The space between the fiber membrane and the sole foot are referred to as the synaptic cleft. A gelatinous substance fills the synaptic cleft. Mitochondria that supposedly synthesize the substance acetylcholine are located in the sole foot. Numerous small vesicles (bags) serve as storage locations for acetylcholine. The enzyme cholinesterase, which is used to destroy acetylcholine, is also found in the area of the synaptic cleft.

(a) **Secretion of acetylcholine.** The vesicles release acetylcholine when a nerve impulse reaches the neuromuscular junction. Shortly after the acetylcholine is released (around two milliseconds), it diffuses and no longer has any effect upon the muscle. During the short time, the acetylcholine produces its effects upon the muscle; the muscle becomes very permeable to sodium ions (Nat). Because of the influx of sodium ions into the muscle, the electrical potential of the membrane increases. Hence, the muscle fiber is stimulated. Figure 2-1 illustrates the contraction of skeletal muscle.

(b) **Destruction of acetylcholine.** Shortly after the acetylcholine is released, cholinesterase begins to destroy it. Such a rapid destruction of the acetylcholine prevents it from re-stimulating the muscle until another nerve impulse reaches the neuromuscular junction. Figure 2-2 illustrates the relaxation of the muscle tissue.
Figure 2-1. Contracted skeletal muscle.

Figure 2-2. Relaxed skeletal muscle.
Disorders.

(a) Muscle cramps. Muscle cramps are persistent involuntary contractions of the skeletal muscles. Muscle cramps can be caused by over-exercise, lack of blood flow, or severe cold.

(b) Myasthenia gravis. Myasthenia gravis is a major disorder of the skeletal muscle system. Muscle weakness and excessive fatigue characterize it. In myasthenia gravis, the muscular system is marked by progressive paralysis of the muscles, which is caused by an abnormal condition at the neuromuscular junction due to a lack of acetylcholine or an excess of cholinesterase. If there is either too little acetylcholine or an excess of cholinesterase, a contraction will not occur.

b. Cardiac Muscle. The muscles of the heart are called cardiac muscles.

(1) Anatomy. Cardiac muscle is made up of branched, striated fibers and responds to stimuli as if it were a single muscle fiber. Cardiac tissue is responsible for the propulsion of blood through the circulatory system. The contraction and relaxation of the heart move the blood.

(2) Physiology. In order for an individual to live (without the assistance of life-support equipment), his heart must never stop beating. Cardiac muscle must maintain a steady rhythm and not become fatigued. Cardiac muscle does not become fatigued because it can use both glucose and lactic acid, its waste product. The contraction of the cardiac muscle is involuntary and does not directly respond to any nervous stimulation. This property is referred to as inherent rhythmicity. The heart rate may be modified by the autonomic nervous system. Sympathetic or adrenergic stimulation will increase heart rate and parasympathetic or cholinergic stimulation will decrease heart rate. To ensure rhythmical contractibility, cardiac muscle must be supplied with appropriate ions in proper concentrations. These ions are supplied in the blood. Too little sodium leads to weak and rapid heart contractions. Too much potassium makes the cardiac muscle cells lose their excitability and complete heart blockage can occur. Excessive levels of calcium in the blood can lead to increased contractibility of the cardiac muscle. Extremely high levels of the calcium ion in the heart tissue can cause the heart to remain in a state of contraction.

(3) Disorders. An irregular heart beat pattern is called an arrhythmia. There are different types of cardiac arrhythmias (that is, flutter or fibrillation). Arrhythmias can sometimes be treated with drugs. More specific information on arrhythmias and the drugs used to treat them will be given to you in another subcourse (MD0806, Pharmacology III).
c. **Smooth Muscle.** All muscles that are not found in the heart or are not attached to the skeletal system are called **smooth muscles.**

(1) **Anatomy.** The fibers of smooth muscles are elongated and nonstriated. The size of the fiber varies with the location of the muscle. For example, the smallest smooth muscles are found in the blood vessels and the largest are found in the digestive tract. Smooth muscle is responsible for such important functions as peristalsis, blood pressure, and air volume. Peristalsis is the rhythmic wave-like motion of the alimentary canal and other tubular organs caused by waves of contraction passing along the smooth muscle in the tube. Smooth muscle is involved in blood pressure by altering the diameter of blood vessels. It is involved in the control of air volume by altering the diameter of the bronchial tubes. Smooth muscle contracts involuntarily—it is an unconscious act.

(2) **Physiology.** The same chemical substances are found in smooth muscle as are found in skeletal muscle. Contraction of smooth muscle tissue occurs by the activation by ions—just the same as with skeletal muscles: Contraction occurs during depolarization of the muscle membrane, and it stops after repolarization. Smooth muscle tissue does not contract as rapidly as skeletal muscle tissue. Furthermore, the relaxation of the smooth muscle following contraction is likewise slower than in skeletal muscle. Smooth muscle is capable of maintaining tonic contractions over a long period of time. Smooth muscle can undergo changes in length without significant change in tension. This is called stress-relaxation.

**Continue with Exercises**
EXERCISES, LESSON 2

INSTRUCTIONS: Answer the following exercises by marking the lettered response which best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson, and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. The term tonus is best defined as:
   
a. The process by which all muscle fibers always contract to their maximum capacity.

   b. The ability of a muscle to stretch and return to its normal position.

   c. A slight continuous contraction of muscle tissue which aids in the maintenance of posture and in the return of blood to the heart.

   d. The ability of a muscle fiber to contract and expand in order to meet the requirements of extension.

2. Which of the following is a property of muscle tissue? (More than one response may be correct.)

   a. Irritability.

   b. Malleability.

   c. Extensibility.

3. Elasticity, one of the properties of muscle tissue, is best defined as:

   a. The ability of a muscle to stretch and return to its normal position.

   b. The ability of a muscle to shorten in length.

   c. The ability of a muscle to respond to a stimulus.

   d. The ability of a muscle to extend in length.
4. Which of the following is a type of muscle tissue found in the human body? (More than one response may be correct.)

a. Skeletal muscle tissue.

b. Adipose muscle tissue.

c. Cardiac muscle tissue.

d. Smooth muscle tissue.

5. Select the statement that best describes skeletal muscle.

a. Muscle tissue that is made up of branched, striated fibers and responds to stimuli as if it were a single muscle fiber.

b. Muscle fibers that are striated and elongated.

c. Muscle fibers that are elongated and non-striated.

d. Muscle tissue which is branched and striated and is found in the alimentary canal.

6. Which of the following statements best describes the physiology involved with cardiac muscle tissue?

a. The contraction is involuntary and does not respond directly to any nervous stimulation.

b. In this tissue, relaxation occurs during depolarization of the muscle membrane and stops after repolarization.

c. In this tissue, the chemical acetylcholine is released by the vesicles in the neuromuscular junction with a resultant influx of potassium ions into the muscle.

d. The secretion of acetylcholinesterase near the neuromuscular junction produces the contraction of this type of tissue.

Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 2

1. c A slight continuous contraction of muscle tissue which aids in the maintenance of posture and in the return of blood to the heart. (para 2-2b)

2. a Irritability (para 2-3a)
   c Extensibility (para 2-3c)

3. a The ability of a muscle to stretch and return to its normal position. (para 2-3d)

4. a Skeletal muscle tissue. (para 2-4a)
   c Cardiac muscle tissue. (para 2-4b)
   d Smooth muscle tissue. (para 2-4c)

5. b Muscle fibers which are striated and elongated. (para 2-4a(1))

6. a The contraction is involuntary and does not respond directly to any nervous stimulation. (para 2-4b(2))

End of Lesson 2
LESSON ASSIGNMENT

LESSON 3  Skeletal Muscle Relaxants.

TEXT ASSIGNMENT  Paragraphs 3-1--3-7.

LESSON OBJECTIVES  After completing this lesson, you should be able to:

3-1. Given a group of definitions, select the definition of the term muscle relaxant.

3-2. Given a group of statements, select the statement that best describes the mechanism of action of neuromuscular blocking agents.

3-3. Given a group of statements, select the statement that best describes the process of normal nerve transmission.

3-4. Given a list of uses, select the use of neuromuscular blocking agents.

3-5. Given one of the two classifications of neuromuscular blocking agents and a group of statements, select the statement that best describes that classification’s mechanism of action.

3-6. Given a group of statements, select the statement that best describes the mechanism of action of centrally-acting skeletal muscle relaxants.

3-7. Given the trade or generic name of a skeletal muscle relaxant and a list of trade or generic names select the appropriate name of that particular drug.

3-8. Given the trade or generic name of a skeletal muscle relaxant and a group of uses or side effects, select the use or side effect of that agent.

SUGGESTION  After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 3

SKELETAL MUSCLE RELAXANTS

Section I. GENERAL

3-1. BACKGROUND

Some Indian tribes in South America have used muscle relaxants for centuries. They have used curare, a potent muscle relaxant, to kill game and to protect themselves because of curare’s ultimate pharmacological effect-death. Today, anesthesiologists use this agent to relax skeletal muscles in some surgical procedures. This lesson will focus on skeletal muscle relaxants and their use in modern medicine.

3-2. DEFINITION OF A MUSCLE RELAXANT

A skeletal muscle relaxant may be defined as an agent that reduces skeletal muscle tone. Even when muscles are at rest, there is a certain amount of tension or tautness that is present. This remaining degree of contraction of skeletal muscle is called skeletal muscle tone. It is believed that skeletal muscle tone results entirely from nerve impulses originating from the spinal cord. If these nerve impulses are blocked in some manner, the result is decreased skeletal muscle tone: skeletal muscle relaxation. The degree of skeletal muscle relaxation ranges from partial to complete depending upon the effectiveness of the skeletal muscle relaxant being used and its site of activity.

Section II. THE NEUROMUSCULAR BLOCKING AGENTS

3-3. MECHANISM OF ACTION

a. The neuromuscular blocking agents act by blocking the action of acetylcholine (Ach) at the neuromuscular junction or at the muscle receptor site.

b. What occurs at the neuromuscular junction during normal nerve transmission? The nerve impulse enters the terminal knob, and the neurotransmitter acetylcholine (Ach) is released and attaches to appropriate receptor sites on the muscle receptor site, much like a lock and key (Figure 3-1). When Ach attaches, there is a great influx of sodium into the muscle receptor site, and potassium flows out. This causes the receptor site to depolarize; therefore, muscle contraction results.

c. The Ach does not remain in the receptor sites forever. When it releases, it is destroyed by acetylcholinesterase (Ache). The resultant release causes an influx of potassium back into the muscle receptor site, and sodium is pumped out. The nerve that stimulates the muscle receptor site repolarizes and returns to normal. Because of repolarization, the skeletal muscle relaxes.
3-4. USE OF THE NEUROMUSCULAR BLOCKING AGENTS

The neuromuscular blocking agents are used with general anesthetics to provide sustained muscle relaxation. This sustained muscle relaxation reduces the tone of the skeletal muscles (that is makes them flaccid or flabby) during surgical procedures. Because of this skeletal muscle relaxation, the surgeon can easily cut through the muscle.

3-5. CLASSIFICATION OF THE NEUROMUSCULAR BLOCKING AGENTS

The neuromuscular blocking agents are classified as either non-depolarizing agents or depolarizing agents.

a. The non-depolarizing agents compete with the neurotransmitter, acetylcholine, for the muscle receptor site. Therefore, they prevent depolarization. This produces flaccid paralysis of the skeletal muscles for a period of about one hour—depending upon the concentration of the agent administered. The non-depolarizing blocking agents are often referred to as competitive neuromuscular blocking agents. Examples of non-depolarizing blocking agents are curare, vecuronium (Norcuron®), pancuronium (Pavulon®), and cisatricurium (Nimbex®).
(1) **Curare.** Curare is used to produce a complete skeletal muscle relaxation or flaccid paralysis of skeletal muscle during general anesthesia and other procedures. It is a potentially dangerous drug for obvious reasons: Too much of a drug administered too quickly can result in paralysis of the muscles that control respiration. The primary side effects associated with curare are bradycardia and hypotension. The individual responsible for administering the curare during anesthesia must monitor the vital signs of the patient to ensure that the patient does not experience toxic effects from the curare. That person will also have to ensure that the patient is able to breathe (sometimes mechanical assistance is required) when curare is administered since curare relaxes all the skeletal muscles of the body, and the patient sometimes finds difficulty in breathing. Curare is supplied in an injectable form.

(2) **Pancuronium (Pavulon®).** Pancuronium is five times more potent than curare and it produces complete skeletal muscle relaxation. It poses the same risk factors for the patient, as does curare. The primary side effects seen with pancuronium are cardiac arrhythmias of various types.

b. The depolarizing blocking agents act like an excess of acetylcholine to depolarize the muscle receptor site and prevent its repolarization. Thus, there is an initial depolarization at the neuromuscular junction producing muscle contraction; but since the muscle receptor site cannot depolarize, complete skeletal muscle relaxation follows. In general, the relaxation effects produced by the depolarizing agents are of shorter duration than the relaxation produced by the non-depolarizing agents.

(1) **Succinylcholine (Anectine®).** Succinylcholine is a depolarizing agent used to produce complete muscle relaxation for various surgical procedures. The primary side effects associated with succinylcholine are cardiac arrhythmias and postoperative apnea (temporary stoppage of breathing).

(2) **Decamethonium bromide (Syncurine®).** Decamethonium bromide is used as a muscle relaxant for relatively short surgical procedures. Side effects associated with this agent include muscle soreness, respiratory depression, and prolonged apnea.

**Section III. CENTRALLY ACTING SKELETAL MUSCLE RELAXANTS**

**3-6. BACKGROUND**

Centrally acting skeletal muscle relaxants are so called because they act on the central nervous system to decrease muscle tone. They decrease muscle tone by depressing the internuncial neurons at the spinal cord (Figures 3-2 and 3-3). When given in normal therapeutic doses, these agents are not potent enough to produce flaccid paralysis. However, large oral or injectable doses of these drugs may produce hypotension, flaccid paralysis, and respiratory depression. Many of these drugs are similar in chemical structure to antianxiety agents. These agents are used to relieve skeletal muscle spasms. Whether relief of pain achieved by patients taking these drugs is due to their muscle relaxant effect or to their sedative effect is unknown.
3-7. EXAMPLES OF CENTRALLY ACTING SKELETAL MUSCLE RELAXANTS

a. **Diazepam (Valium®)**. Diazepam is an antianxiety agent that is also used as a skeletal muscle relaxant in a dosage of from 2 to 10 milligrams three or four times daily. The main side effect of diazepam is central nervous system depression. The patient taking diazepam should be warned that the drug might cause drowsiness. Furthermore, the patient should be warned not to drink alcoholic beverages while taking diazepam. Diazepam is a controlled substance (Note Q).
b. **Cyclobenzaprine (Flexeril®)**. This skeletal muscle relaxant is usually given in a dosage of between 20 to 40 milligrams in 2 to 4 divided doses on a daily basis. Central nervous system depression is the primary side effect of this drug. The patient taking cyclobenzaprine should be warned that he might experience drowsiness because of the drug. He should also be warned not to drink alcoholic beverages while taking the drug. This agent is supplied in tablet form.

c. **Orphenadrine Citrate (Norflex®)**. This skeletal muscle relaxant is given in a dosage of 100 milligrams twice daily. The drug causes central nervous system depression. The patient should be warned that he might become drowsy while taking the drug. Furthermore, the patient should be warned not to drink alcoholic beverages while taking Norflex®. Norflex® is available in tablet form.

d. **Chlorzoxazone (Paraflex®, Parafon Forte DSC®)**. This skeletal muscle relaxant is used as an adjunct to rest, physical therapy, and other measures to relieve the discomfort associated with acute, painful musculoskeletal conditions. It does not directly relax tense muscles. Chlorzoxazone has some antianxiety properties and causes some CNS depression. The patient taking this medication should be warned of the potential drowsiness and should not drink alcohol while taking this medication. The usual adult dosage is 250-mg three or four times a day. Initial dosage for painful musculoskeletal conditions is 500-mg three or four times daily and increased to 750 mg three or four times daily if needed. Chlorzoxazone is supplied as 250-mg tablets (Paraflex®) and 500-mg tablets (Parafon Forte DSC®).

e. **Methocarbamol (Robaxin®)**. Methocarbamol is a skeletal muscle relaxant which is usually administered in a dosage of 1 gram four times daily for muscle spasms. Since it can produce central nervous system depression, the patient should be warned of the drowsiness that could accompany its use. When administered intravenously, methocarbamol is used to treat acute muscle spasms associated with trauma and inflammation. Methocarbamol is also used in producing skeletal muscle relaxation for orthopedic procedures when it is administered intravenously.

f. **Dantrolene (Dantrium®)**. Dantrolene is a skeletal muscle relaxant that reduces skeletal muscle tone through a direct effect on muscle contraction. It is believed that dantrolene affects the uptake of calcium by muscle tissue. This drug is used to relieve the muscle spasticity associated with such diseases as multiple sclerosis or cerebral palsy. It is given in oral form initially in a dose of 25 milligrams once or twice daily; the dosage of the drug is then increased in increments until the desired therapeutic effect is attained. Although it does not produce its effects on the central nervous system like the other oral skeletal muscle relaxants, it may cause drowsiness. You should warn the patient about this potential drowsiness. Dantrolene may also cause nausea and vomiting. Dantrolene is used in the treatment of malignant hyperthermia.

*Continue with Exercises*
EXERCISES, LESSON 3

INSTRUCTIONS: Answer the following exercises by marking the lettered response which best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson, and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Select the best definition of the term muscle relaxant.
   a. An agent that prevents the transmission of any nerve impulses.
   b. An agent that causes a patient to become less anxious.
   c. An agent that reduces skeletal muscle tone.
   d. An agent that causes muscles to be relaxed because it increases the amount of acetylcholine present at the neuromuscular junction.

2. Which of the following statements best describes the mechanism of action of neuromuscular blocking agents?
   a. They decrease muscle tone by depressing the internuncial neurons at the spinal cord.
   b. They block the action of acetylcholine at the neuromuscular junction or at the muscle receptor site.
   c. They act on the terminal knob to cause a release of acetylcholine at the neuromuscular junction to produce the depolarization of the receptor site.
   d. They cause a great influx of sodium into the muscle receptor site and a great influx of potassium out of the receptor site in order to make the muscle become relaxed.

3. Centrally acting skeletal muscle relaxants act by:
   a. Decreasing the muscle tone by depressing the internuncial neurons at the spinal cord.
   b. Blocking the action of acetylcholine at the neuromuscular junction or the muscle receptor site.
   c. Causing the sodium and potassium at the receptor site to flow into and out of the area.
   d. Destroying the acetylcholine at the neuromuscular junction.
4. Match the generic names in Column I with the appropriate trade name in Column II.

<table>
<thead>
<tr>
<th>Column I</th>
<th>Column II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclobenzaprine</td>
<td>A. Flexeril®</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>B. Parafon Forte DSC®</td>
</tr>
<tr>
<td>Orphenadrine citrate</td>
<td>C. Anectine®</td>
</tr>
<tr>
<td>Succinylcholine</td>
<td>D. Pavulon®</td>
</tr>
<tr>
<td>Chlorzoxazone</td>
<td>E. Norfiex®</td>
</tr>
<tr>
<td></td>
<td>F. Syncurine®</td>
</tr>
<tr>
<td></td>
<td>G. Dantrium®</td>
</tr>
</tbody>
</table>

5. Select the use of decamethonium bromide.
   a. Used to produce complete muscle relaxation during general anesthesia.
   b. Used to calm or relax a patient prior to surgery.
   c. Used to relieve muscle spasms.
   d. Used as a muscle relaxant for relatively short procedures.

6. The patient taking Parafon Forte DSC® should be warned:
   a. Not to drink alcoholic beverages while taking the drug.
   b. That the drug may produce muscle spasms if taken in excess.
   c. That the drug may produce hypertension and bradycardia.
   d. That the drug may produce cardiac arrhythmias.
7. The person who administers curare during general anesthesia must carefully observe the patient because curare might produce:
   
   a. Cardiac arrhythmias.
   b. Too deep a level of analgesia in a patient.
   c. Respiratory depression.
   d. Tachycardia.

8. The patient taking orphenadrine citrate should be warned that:
   
   a. He may become drowsy while taking the drug.
   b. The drug may produce skeletal muscle relaxation.
   c. He may experience cardiac arrhythmias.
   d. The drug may produce tachycardia.

9. Methocarbamol (Robaxin®) when administered intravenously is used to treat:
   
   a. Multiple sclerosis and cerebral palsy.
   b. Hypercalcemia.
   c. Trauma.
   d. Acute muscle spasms associated with trauma and inflammation.

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 3

1. c  An agent that reduces skeletal muscle tone.  (para 3-2)

2. b  They block the action of acetylcholine at the neuromuscular junction or at the muscle receptor site.  (para 3-3a)

3. a  Decreasing the muscle tone by depressing the internuncial neurons at the spinal cord.  (para 3-6)

4. A  Cyclobenzaprine  (para 3-7b)
   D  Pancuronium  (para 3-5a(2))
   E  Orphenadrine citrate  (para 3-7c)
   C  Succinylcholine  (para 3-5b(1))
   B  Chlorzoxazone  (para 3-7d)

5. d  Used as a muscle relaxant for relatively short procedures.  (para 3-5b(2))

6. a  Not to drink alcoholic beverages while taking the drug.  (para 3-7d)

7. c  Respiratory depression.  (para 3-5a(1))

8. a  He may become drowsy while taking the drug.  (para 3-7c)

9. d  Acute muscle spasms associated with trauma and inflammation.  (para 3-7e)

End of Lesson 3
LESSON ASSIGNMENT

LESSON 4
Analgesic, Anti-inflammatory, and Anti-gout Agents.

TEXT ASSIGNMENT
Paragraphs 4-1--4-8.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

4-1. Given one of the following terms: analgesic, anti-pyretic, anti-inflammatory agent, rheumatism, arthritis, or gout, and a list of definitions select the definition of the given term.

4-2. Given the trade or generic name of an analgesic, anti-inflammatory, or anti-gout agent and a list of trade and/or generic names, select the appropriate name for that agent.

4-3. Given the trade and/or generic name of an analgesic, anti-inflammatory, or anti-gout agent and a group of statements pertaining to indications, use, side effects, or cautions and warnings, select the statement that best applies to that drug.

4-4. Given a group of statements, select the statement that best describes the cause of gout.

SUGGESTION
After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
Lesson 4

Analgesic, Anti-Inflammatory, and Antigout Agents

Section I. Background

4-1. Introduction to Analgesic, Anti-Inflammatory, and Anti-Gout Agents

Since the beginning of time, every civilization has sought a perfect medicinal agent that would relieve pain. As far back as the third century, B.C., physicians were administering the juice of the opium poppy to patients for the relief of pain. Opium derivatives are still widely used in the treatment of severe pain. Fortunately, agents with less abuse potential have been discovered for the relief of pain. This lesson will focus on analgesics, anti-inflammatory, and anti-gout agents.

4-2. Definitions

a. Analgesic. An analgesic is an agent that relieves pain.

b. Antipyretic. An antipyretic is an agent that lowers elevated body temperature.

c. Anti-Inflammatory Agent. An anti-inflammatory agent is a drug that decreases inflammation.

d. Rheumatism. Rheumatism is a condition characterized by inflammation of connective tissue.

e. Arthritis. Arthritis is a form of rheumatism in which the inflammation is confined to body joints.

f. Gout. Gout is a form of arthritis that is caused by an excess of uric acid in the blood that periodically precipitates in the peripheral joints as monosodium urate.

Section II. Analgesic Agents

4-3. Background

Analgesic agents relieve pain. Some agents (like morphine or meperidine) are used to relieve severe pain, while others (like acetaminophen) are administered to relieve less severe pain. The material in this section of the lesson will consider agents used to relieve less severe pain.
4-4. SPECIFIC ANALGESIC AGENTS

a. Acetaminophen (Tylenol®). Acetaminophen is used as an analgesic and as an antipyretic. It is not an anti-inflammatory agent: Acetaminophen will not relieve the swelling or redness found in arthritis or rheumatism. Side effects associated with this agent are itching or skin rash (most likely caused by hypersensitivity reactions), hemolytic anemia (persons with G-6-PD deficiency are especially susceptible), and kidney damage. This drug may cause liver damage with chronic use. Acetaminophen is available in capsule, elixir, suspension, syrup, tablet, chewable tablet, and suppository forms.

b. Aspirin (A.S.A.). Aspirin is used as an analgesic, anti-pyretic, and anti-inflammatory agent. Aspirin produces gastric irritation. Taking aspirin with a full glass of water or milk (8 fluid ounces) can help minimize stomach irritation. Tinnitus (ringing of the ears) is a symptom of aspirin overdose. Aspirin interacts with a variety of medications. One, the effects of oral hypoglycemic or insulin is increased when aspirin is administered concurrently with them. Two, since aspirin has some anti-coagulant effects, concurrent administration of aspirin, and some anti-coagulants can result in increased risk of patient bleeding. Patients should be cautioned against taking any oral aspirin preparation that has a strong vinegar-like odor. Aspirin is available in a variety of dosage forms (tablets, enteric coated tablets--dissolve in the intestines, and suppositories).

c. Aspirin, Magnesium Hydroxide, and Aluminum Hydroxide Tablets (Cama®). This aspirin-containing product is an analgesic, anti-inflammatory, and antipyretic agent. The magnesium hydroxide and aluminum hydroxide is in the formulation to reduce the stomach irritation associated with the aspirin. Patients taking this medication should be told not to take this medication with tetracyclines because the tetracycline’s therapeutic effect might be decreased: This medication and tetracyclines should not be taken within one hour of each other. This product should be taken with at least 8 fluid ounces of water. Patients should be cautioned against taking this product if it has a strong vinegar-like odor.

d. Propoxyphene Hydrochloride (Darvon®). Propoxyphene is a centrally acting opioid analgesic. The drug may produce side effects such as dizziness, drowsiness, or blurred vision. Patients taking propoxyphene should be cautioned against taking alcohol or other central nervous system depressants while they are taking propoxyphene. Propoxyphene is a Note Q controlled substance.

e. Propoxyphene Napsylate (Darvon N®). Propoxyphene napsylate is used as an analgesic. It may produce such side effects as drowsiness and dizziness. Patients should be warned against taking alcohol or other central nervous system depressants when they are taking this drug. Darvon N® is a Note Q controlled substance.

f. Pentazocine (Talwin®). Pentazocine is a centrally acting opioid analgesic. Side effects associated with this agent are gastrointestinal upset, sedation, blurred
vision, hallucinations, mental confusion, and shortness of breath. This medication should be used with caution in-patients who have a history of drug abuse or dependence. The oral dosage form (Talwin NX®) is combined with naloxone, a narcotic antagonist, to discourage the abuse of this substance. When the tablet is dissolved and then injected, the naloxone negates the euphoric effects of the pentazocine. Patients taking pentazocine should not take alcohol or any other central nervous system depressant at the same time, since this agent is a central nervous system depressant.

g. Butalbital with Aspirin and Caffeine (Fiorinal®). This product contains butalbital (a short-to-intermediate-acting barbiturate--50 mg), aspirin (325 mg), and caffeine (40 mg). The product is used as an analgesic. Side effects associated with this agent are gastrointestinal upset and sedation. This product may cause drug dependence. Patients taking this drug should not take any alcohol or any other central nervous system depressant. Fiorinal® is a Note Q controlled substance. (NOTE: Fiorinal® with Codeine is another formulation of this product. It is used to raise the threshold of pain.)

Section III. ANTI-INFLAMMATORY AGENTS

4-5. BACKGROUND

In certain conditions (that is, arthritis) or injuries, affected tissues become inflamed. The net effect of such inflammation is to surround the affected area and “wall it off” so that the movement of toxic products or bacteria from the affected part is delayed. Blood flow to the area is increased and certain changes happen in the capillaries to increase the fluid level of the tissues. Hence, the area becomes swollen. Redness of the area follows. Although this is a protective mechanism for the body, it is desirable at times to use drugs to decrease this effect.

4-6. SPECIFIC ANTI-INFLAMMATORY AGENTS

a. Indomethacin (Indocin®). Indomethacin is used in the treatment of various medical problems, including certain types of arthritis. Indomethacin is used to relieve swelling, inflammation, joint pain, stiffness, and fever. Patients hypersensitive to aspirin may also be hypersensitive to indomethacin. Side effects associated with the agent are gastrointestinal upset, headache, dizziness, and ringing or buzzing in the ears. Patients should be instructed to take this medication with food or milk or right after meals in order to lessen the possibility of gastrointestinal upset. Furthermore, in order to lessen gastrointestinal upset, patients should be instructed not to regularly drink alcoholic beverages or take aspirin unless their physician has told them otherwise. Since the drug does have the side effect of dizziness, the patient should be told not to drive or operate hazardous machinery until he or she has been taking the drug and has determined its effects on alertness.
b. **Ibuprofen (Motrin®)**. Ibuprofen is used to treat the symptoms of arthritis. Ibuprofen relieves swelling, joint pain, stiffness, and inflammation. Some patients may have to take the drug for one to two weeks before they begin to feel its full effects. Side effects associated with the use of this agent include skin rashes, itching of skin, ringing or buzzing in the ears, dizziness, or a bloated feeling. Since the drug can cause some stomach irritation, the patient should not take alcohol or aspirin regularly while taking this drug unless the patient's physician has directed otherwise. Furthermore, since the drug does cause dizziness in some patients, the patient should be instructed not to drive or operate hazardous machinery until he or she has been taking the drug and has determined it affects on alertness.

c. **Fenoprofen (Nalfon®)**. Fenoprofen is used to treat the symptoms of arthritis. Fenoprofen relieves swelling, joint pain, stiffness, and inflammation. Side effects associated with the use of this drug include ringing or buzzing in the ears, skin rash, black tarry stools, constipation, and drowsiness. Since the drug can cause some stomach irritation, the patient should not take alcohol or aspirin regularly while taking this drug unless the patient's physician directs otherwise. Furthermore, since the drug does cause drowsiness in some patients, the patient should be instructed not to drive or operate hazardous machinery until he or she has been taking the drug and has determined its effects on alertness.

d. **Tolmetin (Tolectin®)**. Tolmetin is used to treat the symptoms of arthritis. The information for this drug is the same as for fenoprofen (Nalfon®)--see 4-6d above.

e. **Naproxen (Naprosyn®)**. Naproxen is used to treat the symptoms of arthritis. Naproxen relieves swelling, joint pain, stiffness, and inflammation. Side effects associated with this agent include black tarry stools, blurred vision, skin rash, ringing or buzzing in the ears, and dizziness. Since this drug can cause some stomach irritation, the patient should not take alcohol or aspirin regularly while taking this drug unless the patient's physician directs otherwise. The drug may be taken with food, antacids, or milk to reduce stomach irritation.

f. **Sulindac (Clinoril®)**. This drug is used to treat arthritis. This drug should be given with food twice daily; otherwise, the information for this drug is the same as is listed under naproxen (Naprosyn®).

g. **Piroxicam (Feldene®)**. This drug is a unique agent because it has a 45-hour half-life. This long half-life permits once daily dosing. Piroxicam is used in the treatment of rheumatoid arthritis, ankylosing spondylitis, and osteoarthritis. The average daily dose is 20 mg. Gastrointestinal side effects are encountered in approximately 20 percent of patients.

h. **Celecoxib (Celebrex®)**. This drug is unique because it may cause less risk of gastrointestinal side effects than other anti-inflammatory agents. Celecoxib is used in the treatment of rheumatoid and osteo arthritis.
4-7. BACKGROUND

a. Gout is a metabolic disease characterized by attacks of acute pain, tenderness, and swelling of such joints as the instep, ankle, great toe, and elbow. Gout is caused by the deposition of sodium urate microcrystals. This condition is seen primarily in males. It is thought that heredity plays a major factor in gout, because gout occurs more often in relatives of those who have gout than in the population in general.

b. Gout is caused by defective purine metabolism. Humans lack the enzyme uricase, an enzyme that converts uric acid to allantoin. Uric acid is a major end product of the metabolism of purine (indirectly of amino acid metabolism). The level of uric acid in the plasma and urine is normally high (saturated). Sometimes a moderate increase in uric acid production can lead to the deposition of sodium urate microcrystals as described above.

c. The treatment of gout is usually designed to (1) relieve pain and (2) increase the elimination of uric acid from the body. Drugs administered to increase the elimination of uric acid from the body are referred to as uricosuric agents.

4-8. DRUGS USED TO TREAT GOUT

a. Colchicine. While the exact mechanism of action of colchicine is unknown, the administration of the drug causes a decrease in the amount of urate crystals deposited in the various parts of the body—the result is a decrease in the inflammatory process. This drug is the oldest and most effective agent used in the treatment of acute attacks of gout. The usual dose of an acute gout attack is 1.2 milligrams immediately, then 0.6 milligram every 30 minutes to one hour until nausea and vomiting or diarrhea starts or pain is relieved. Each patient must initially titrate his own dosage. If seven tablets caused adverse effects the first administration, the patient should reduce the dosage to six tablets on the next acute attack. The usual side effect associated with the administration of colchicine is gastrointestinal irritation. Occasionally antidiarreheals are prescribed to offset this adverse effect. The patient should be informed to allow an interval of at least three days between treatments—otherwise, toxic effects may occur from accumulation.

b. Sulfinpyrazone (Anturane®). Sulfinpyrazone potentiates the urinary excretion of uric acid. This anti-gout agent has the primary side effect of gastrointestinal upset. The patient taking this medication should be told to take this medication with food or milk. This medication should not be taken with salicylates.

c. Allopurinol (Zyloprim®). Allopurinol acts by decreasing the production of uric acid. This drug is not effective in the treatment of acute gout attacks, because it has no anti-inflammatory action. In fact, allopurinol may actually intensify the inflammation seen during an acute gout attack. Although the drug cannot be used to
treat acute gout attacks, the patient should be instructed to continue taking allopurinol if he has such an attack. Allopurinol may produce such side effects as skin rash and gastrointestinal upset. If the drug causes too much gastrointestinal upset, the patient can take it after meals. The patient taking allopurinol should be instructed to drink at least 10 to 12 full glasses (8 fluid ounces per glass) of fluids each day--unless informed otherwise by his physician. This is done to prevent the formation of kidney stones while taking the drug.

d. **Probenecid (Benemid®)**. Probenecid increases the urinary excretion of uric acid. This anti-gout agent has the following side effects associated with its use: bloody urine, lower back pain, and painful urination. The patient should be instructed not to drink too much alcohol while taking this drug since doing so could lessen the therapeutic effect of probenecid. Furthermore, the patient should be told not to take aspirin with this agent because salicylates antagonize the uricosuric action of probenecid.

*Continue with Exercises*
INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson, and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Rheumatism is best described as:
   a. A form of arthritis that is caused by an excess of uric acid in the blood.
   b. A painful inflammation of body joints.
   c. A condition characterized by inflammation of connective tissue.
   d. A painful form of arthritis that causes gradual destruction of body joints.

2. Arthritis is best described as:
   a. A form of rheumatism in which the inflammation is limited to body joints.
   b. A destructive condition that attacks body joints by the accumulation of uric acid.
   c. A chronic condition characterized by the inability of the body’s joints to become lubricated.
   d. An acute inflammation of the body joints and related connective tissue caused by infection or excess amounts of certain chemical substances in the body.

3. A patient complains that some aspirin she has at home is beginning to smell like vinegar. What should you tell her?
   a. Take the medication as usual -- nothing is wrong with it.
   b. Take the aspirin with at least 8 fluid ounces of water or milk.
   c. Never take more than two of those aspirin tablets at one time since the vinegar-like smell indicates the aspirin has increased in potency.
   d. Discard the aspirin and obtain a fresh supply.
4. A patient has been prescribed propoxyphene napsylate (Darvon N®). What should the patient be told?
   a. Take the medication with at least eight fluid ounces of water or milk.
   b. This medication should be taken at least one hour after taking tetracyclines.
   c. This medication should not be taken with alcohol or other CNS depressants.
   d. This medication should not be taken if it has a strong vinegar-like odor.

5. An elderly patient complains that he has been taking Motrin® for three days without experiencing much relief from his arthritis. What should the patient be told?
   a. Continue taking the drug since some patients have to take it for one or two weeks before they begin to feel its full effects.
   b. See the physician because the dosage probably needs to be increased.
   c. Stop taking the drug until pharmacy personnel ensure that the medication is not expired.
   d. Double the dose of the medication so the effects can be felt faster.

6. Gout is caused by:
   a. The defective metabolism of allantoin.
   b. The inflammation of connective tissue surrounding the body joints.
   c. Defective purine metabolism that causes sodium urate micro-crystals to be deposited in certain body joints.
   d. The incomplete elimination of uric acid from the body.

7. Sulfinpyrazone (Anturane®) is used in the treatment of:
   a. Rheumatism.
   b. Arthritis.
   c. Gout.
8. What should a patient who is taking Benemid® be told?
   a. This medication should not be taken with aspirin.
   b. This medication should not be taken with alcohol or other CNS depressants since Benemid® is a CNS depressant.
   c. This medication should not be taken on an empty stomach since it causes severe tissue irritation.
   d. This medication should be taken with antidiarrheals to lessen gastrointestinal irritation.

9. Select the use of pentazocine (Talwin®).
   a. Anti-gout agent.
   b. Anti-inflammatory agent.
   c. Antipyretic.
   d. Analgesic.

10. Match the drug name in Column A with its corresponding name in Column B.

   COLUMN A                  COLUMN B
   _______ Anturane®       a.  Ibuprofen
   _______ Benemid®        b.  Butazolidin®
   _______ Motrin®         c.  Aspirin, magnesium hydroxide, and aluminum hydroxide tablets
   _______ Cama®           d.  Probenecid
   _______ Allopurinol     e.  Zyloprim®
   _______ Allopurinol     f.  Colchicine

   g.  Sulfinpyrazone

Check Your Answers on Next Page
1. c A condition characterized by inflammation of connective tissue. (para 4-2d)
2. a A form of rheumatism in which the inflammation is limited to body joints. (para 4-2e)
3. d Discard the aspirin and obtain a fresh supply. (para 4-4b)
4. c This medication should not be taken with alcohol or other CNS depressants. (para 4-4d)
5. a Continue taking the drug since some patients have to take it for one to two weeks before they begin to feel its full effects. (para 4-6b)
6. c Defective purine metabolism that causes sodium urate microcrystals to be deposited in certain body joints. (para 4-7a,b)
7. c Gout. (para 4-8b)
8. a This medication should not be taken with aspirin because aspirin will decrease its effectiveness. (para 4-8d)
9. d Analgesic. (para 4-4f)
10. g Anturane®. (para 4-8b)
    d Benemid®. (para 4-8d)
    a Motrin®. (para 4-6b)
    c Cama®. (para 4-4c)
    e Allopurinol. (para 4-8c)

End of Lesson 4
LES SON ASSIGNMENT

LESSON 5
Review of Ocular and Auditory Anatomy and Physiology.

TEXT ASSIGNMENT
Paragraphs 5-1 through 5-13.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

5-1. Given the name of a part of the bulbus oculi and a group of statements, select the statement that best describes that part or its function.

5-2. Given the name of one of the structures associated with the bulbus oculi (the adnexa) and a group of statements, select the statement which best describes that part or its function.

5-3. Given the name of a disease/condition that affects the eye and a group of statements, select the statement that best describes that disease/condition.

5-4. From a list of possible methods, select the method(s) by which sound may be transmitted.

5-5. Given the name of one of the parts of the human ear and a group of statements, select the statement which best describes that part of the ear or its function.

5-6. Given a disorder/malfunction of the ear and a group of statements, select the statement that best describes that disorder/malfunction.

5-7. Given a group of statements, select the statement that best describes how the body maintains equilibrium (balance).

SUGGESTION
After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 5
REVIEW OF OCULAR AND AUDITORY ANATOMY AND PHYSIOLOGY

Section I. OCCULAR ANATOMY AND PHYSIOLOGY

5-1. BACKGROUND

a. Stimulus. Rays of light stimulate the receptor tissues of the eyeballs (bulbus oculi) to produce the special sense of vision. This includes both the sensation of vision or seeing and a variety of reactions known as the light reflexes. The actual reception of the light energy is a chemical reaction that in turn stimulates the neuron endings.

b. Sense Organ. The eyeball (bulbus oculi) is the special sense organ that contains the receptor tissues. The bulbus oculi is suspended in the orbit. The orbit is a skeletal socket of the skull that helps protect the bulbus oculi. Various structures associated with the functioning of the bulbus oculi are called the adnexa. The adnexa include the eyelids, the lacrimal system, and so forth.

5-2. THE BULBUS OCULI (Figure 5-1)

Figure 5-1. A focal-axis section of the bulbus oculi.
a. **Shape.** Normally the bulbus oculi is a spherical bulb-like structure. Its anterior surface, transparent and more curved, is known as the *cornea* of the bulbus oculi.

b. **Wall of the Bulbus Oculi.** The bulbus oculi is a hollow structure. Its wall is made up of three layers known as coats or tunics.

   1. **Sclera.** The outermost layer is white and very dense fibrous connective tissue (FCT). It is known as the *sclera*, *scleral coat*, or *fibrous tunic*. Its anterior portion is called the *cornea*. As already mentioned, the cornea is transparent and more curved than the rest of the sclera. The fixed curvature of the cornea enables it to serve as the major focusing device for the bulbus oculi.

   2. **Choroid.** The middle layer of the wall of the bulbus oculi is known as the *choroid*, *choroid coat*, or the *vascular tunic*. This layer is richly supplied with blood vessels. It is also pigmented with a black material. The black color absorbs the light rays and prevents them from reflecting at random.

   3. **Retina.** The inner layer of the wall of the bulbus oculi is known as the *retina*, *retinal coat*, or *internal tunic*. The actual photoreceptor elements are located in the retina at the back and sides of the bulbus oculi. These elements are the rods and cones. They constitute the nervous portion of the retina. In the anterior part of the bulbus oculi, the retina continues as a non-nervous portion.

c. **Internal Structures of the Bulbus Oculi.**

   1. **The nervous retina.**

      a. The photoreceptors of the nervous portion of the retina (Figure 5-2) contain chemicals known as visual pigments (rhodopsin). The cones are more concentrated in the center at the back of the bulbus oculi. The cones can perceive colors and are used for acute vision. However, cones require more intense light than do rods. The rods are distributed more toward the sides of the nervous retina. Although the rods are capable of perceiving less intense light, rods perceive only black and white.

      b. If you look directly at an object, light from the object will fall in the small depression of the retina called the *fovea centralis*. The fovea centralis is at the posterior end of the bulbus oculi, exactly opposite the centers of the cornea, pupil, and lens. The fovea centralis is found in a small yellow area of the retina called the *macula lutea*. The macula lutea is the area of the retina where vision is the sharpest.

      

      FOVEA = small depression  
      CENTRALIS = center  
      MACULA = spot  
      LUTEA = yellow
(c) Associated with the rods and cones are the beginnings of neurons of the optic nerve. These neurons pass out of the bulbus oculi at the posterior end (in a point medial and superior to the fovea centralis). At the point of exit, there are not rods or cones. Therefore, it is called the blind spot (optic papilla/optic disk).

(2) Ciliary body. The anterior end of the choroid layer thickens to form a circular “picture frame” around the lens of the bulbus oculi. This is also near the margin of the base of the cornea. The frame-like structure is called the ciliary body. It includes mostly radial muscle fibers, which form the ciliary muscle.

(3) Ligaments. The lens is suspended in place by ligaments. These ligaments connect the margin (equator) of the lens with the ciliary body.

(4) Crystalline lens. The crystalline lens is located in the center of the anterior of the bulbus oculi, just behind the cornea.

(a) The lens is biconvex. This means that it has two outwardly curved surfaces. The anterior surface is flatter (less curved) than the posterior surface.

(b) The lens is transparent and elastic. As one grows older, the lens becomes less and less elastic. The ligaments maintain a tension upon the lens. This tension keeps the lens flatter and allows the lens to focus on distant objects. When the ciliary muscle contracts, the tension on the lens is decreased. The decreased tension allows the lens to thicken. The greater thickness increases the anterior curvature and allows close objects to be seen clearly.
The process of focusing the crystalline lens for viewing close objects clearly is called accommodation. The process of accommodation is accompanied by a reduction in the pupil size as well as a convergence of the two central lines of sight (axes on bulbi oculi).

5. Iris. Another structure formed from the anterior portion of the choroid layer is the iris. The iris is located between the lens and the cornea.

(a) The pupil is the hole in the middle of the iris. Radial and circular muscles in the iris control the size of the pupil. The radial muscles are dilators. The circular muscles are the constrictors. By changing the size of the pupil, the iris controls the amount of light entering the bulbus oculi.

(b) The iris may have many different colors. Multiple genes determine the actual color.

6. Chambers. The space between the cornea and the lens is called the anterior cavity. The space between the cornea and the iris is referred to as the anterior chamber. The space between the iris and the lens is called the posterior chamber (see Figure 5-1). Both chambers of the anterior cavity are filled with a fluid called the aqueous humor. The aqueous humor is secreted into the chambers by the ciliary body. It drains into the encircling canal of Schlemm, located in the angle between the cornea and the iris. This angle is called the irioiocornealis angle.

7. Vitreous body. Behind the lens is a jelly-like material called the vitreous body. It fills the posterior cavity of the bulbus oculi.

5-3. THE ADNEXA

The adnexa are the various structures associated with the bulbus oculi.

a. Extrinsic Ocular Muscles. Among the adnexa are the extrinsic ocular muscles that move the bulbus oculi within the orbit (the cavity in the upper facial skull that contains the bulbus oculi).

b. Eyelids. Attached to the margins of the orbit, in front of the bulbus oculi, are the upper and lower eyelids. These have muscles for opening and closing the eyelids. The eyelashes (cilia) are special hairs of the eyelids that help protect these bulbus oculi. The margins of the eyelids have special oil to prevent the loss of fluids from the area. The inner lining of the eyelids is continuous with the conjunctiva, a membrane over the anterior surface of the bulbus oculi.

c. Lacrimal Apparatus. The conjunctiva must be kept moist and clean at all times. To do this, a lacrimal apparatus is associated with the eyelids. In the upper outer corner of the orbit is a lacrimal gland, which secretes a lacrimal fluid (tears) into the junction between the upper eyelid and the conjunctiva. The motion of the bulbus
oculi and the eyelids (blinking) moves this fluid moved across the surface of the conjunctiva to the medialinferior aspect. Here, the lacrimal fluid is collected and delivered into the nasal chamber by the nasal lacrimal duct.

d. **Eyebrow.** The eyebrow is a special group of hairs above the orbit. The eyebrow serves to keep rain and perspiration away from the bulbus oculi.

e. **Optic Nerve.** Neurons carry information from the photoreceptors of the nervous retina. They leave the bulbus oculi at the blind spot. At the optic nerve, or second cranial nerve, the neurons pass to the rear of the orbit. There, the optic nerve exits through the optic canal into the cranial cavity. Beneath the brain, the optic nerves from both sides join to form the optic chiasma, in which half of the neurons from each optic nerve cross to the opposite side. From the optic chiasma, the right and left optic tracts proceed to the brain proper.

5-4. DISEASES/CONDITIONS AFFECTING THE EYE

a. **Myopia ("Near-Sightedness").** In myopia the image from distant objects are focused in front of the retina. Myopia is caused by a lens that is too strong. Although the ciliary muscle is completely relaxed, the light rays entering the eye are not properly bent to be focused on the retina. This type of lens condition can be corrected by the use of a concave lens. Figure 5-3a illustrates this condition and correction with a concave lens.

b. **Hypermetropia (Hyperopia)("Far-Sightedness").** In hypermetropia, the parallel light rays entering the eye are not bent sufficiently by the lens and the image is focused behind the retina. In hypermetropia, the bulbus oculi is too short or the lens system is too weak when the ciliary muscle is relaxed. A convex lens is used to correct this condition. Figure 5-3b illustrates this condition and its correction with a convex lens.

c. **Astigmatism.** Astigmatism occurs when the light rays passing through an astigmatic lens are not all focused at the same point. A malformed lens or cornea causes astigmatism. A specially designed lens can be used to help correct this condition.

d. **Glaucoma.** Glaucoma is a common cause of blindness. In glaucoma, the intraocular pressure becomes too great and causes damage to the retina and optic nerve. The intraocular pressure of a normal person is approximately 15 to 20 mm Hg (millimeters of mercury), while the intraocular pressure of a person with glaucoma can reach from 80 to 90 mm Hg. As the intraocular pressure increases, damage is done to the delicate tissues of the eye. The retinal artery, which enters the bulbus oculi at the optic disk, becomes increasingly compressed. Hence, nutrition to the retina is reduced—damage to the retina and optic nerve follow. Glaucoma can be either of a sudden onset or of a slow onset. Glaucoma results from the high pressure caused by reduced drainage of a fluid (aqueous humor). Because of the decreased drainage and
continued fluid output, the high pressure develops. A variety of medications can be used to treat glaucoma. Pilocarpine, acetazolamide (Diamox®) and timolol (Timoptic®) are just three examples of such medications. These medications will be presented in later lessons.

e. **Cataracts.** A cataract is an irreversible and progressive clouding of the lens leading to blindness. Cataracts are surgically removed.

f. **Conjunctivitis.** Conjunctivitis is an inflammation of the conjunctiva.

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Figure 5-3. Myopia and Hypermetropia contrasted with normal vision.
Section II. AUDITORY ANATOMY AND PHYSIOLOGY

5-5. BACKGROUND

The human ear serves two major special sensory functions: hearing (auditory) and equilibrium (balance). The stimulus for hearing is sound waves. The stimulus for equilibrium is gravity.

a. Methods of Sound Transmission. The sound stimulus is transmitted in a variety of ways. Regardless of the actual transmission method, the sound stimulus is unchanged. Sound may be transmitted by:

(1) Airborne waves, which have frequency (pitch) and amplitude (loudness or intensity).

(2) Mechanical oscillations (vibrations) of structures.

(3) Fluid-born pressure pulses.

(4) Electrical impulses along the neurons to and in the brain.

b. Sections of the Human Ear (Figure 5-4). The human ear has three major parts. Each part serves a specific function in the transmission and reception of the sound stimulus. The three parts are known as the external (outer) ear, the middle ear, and the internal (inner) ear.

Figure 5-4. A frontal section of the human ear.
5-6. THE EXTERNAL EAR

The external ear begins on the outside of the head in the form of a funnel-shaped auricle (pinna). Actually serving as a funnel, the auricle directs airborne sound waves into the external auditory meatus. The external auditory meatus is a tubular canal extending into the temporal portion of the skull.

5-7. THE MIDDLE EAR

a. Tympanic Membrane. At the inner end of the external auditory meatus is a tympanic membrane. The tympanic membrane (eardrum) is a circular membrane separating the external auditory meatus from the middle ear cavity. The tympanic membrane vibrates (mechanically oscillates) in response to airborne sound waves.

b. Middle Ear Cavity. On the medial side of the tympanic membrane is the middle ear cavity. The middle ear cavity is a space within the temporal bone.

c. Auditory Ossicles. The auditory ossicles (OSSICLE = small bone) are three very small bones which form a chain across the middle ear cavity. They join the tympanic membrane with the medial wall of the middle ear cavity. In order, the ossicles are named as follows: malleus, incus, and stapes. The malleus is attached to the tympanic membrane. A sound stimulus is transmitted from the tympanic membrane to the medial wall of the middle ear cavity by way of the ossicles. The ossicles vibrate (mechanically oscillate) in response to the sound stimulus.

d. Auditory (Eustachian) Tube. The auditory tube is a passage connecting the middle ear cavity with the nasopharynx. The auditory tube maintains equal air pressure on the two sides of the tympanic membrane.

e. Association With Other Spaces. The middle ear cavity is associated with other spaces in the skull. The thin roof of the middle ear cavity is the floor of part of the cranial cavity. The middle ear cavity is continuous posteriorly with the mastoid air cells via the antrum (an upper posterior recess of the middle ear cavity).

5-8. THE INTERNAL EAR

a. Labyrinths (Figure 5-4).

(1) Bony labyrinth. The bony labyrinth (LABYRINTH = a maze) is a complex cavity within the temporal bone. It has three semi-circular canals, a vestibule (hallway), and a snail-shaped cochlear portion.

(2) Membranous labyrinth. The membranous labyrinth is a hollow tubular structure suspended within the bony labyrinth.
b. **Fluids of the Internal Ear.** The endolymph is a fluid filling the space within the membranous labyrinth. The perilymph is a fluid filling the space between the membranous labyrinth and the bony labyrinth.

\[ \text{ENDO} = \text{within} \]
\[ \text{PERI} = \text{around} \]

These fluids are continuously formed and drained away.

c. **The Cochlea.** The cochlea is a spiral structure associated with hearing. It has 2 1/2 turns. The snail-shaped portion of the bony labyrinth forms its outer boundaries.

1. The central column or axis of the cochlea is called the modiolus. Extending from this central column is a spiral shelf of bone called the spiral lamina. A fibrous membrane called the basilar membrane (or basilar lamina) connects the spiral lamina with the outer bony wall of the cochlea. The basilar membrane forms the floor of the cochlear duct, the spiral portion of the membranous labyrinth. Within the cochlear duct, there is a structure on the basilar membrane called the organ of Corti. The organ of Corti has hairs that are the sensory receptors for the special sense of hearing.

\[ \text{LAMINA} = \text{thin plate} \]

2. Within the bony cochlea, the space above the cochlear duct is known as the scala vestibuli and the space below is known as the scala tympani. Since the scala are joined at their apex, they form a continuous channel and the connection between them is called the helicotrema.

d. **Transmission.**

1. The sound stimulus is transferred from the stapes to the perilymph of the scala vestibuli. Here the stimulus is transmitted as a pressure pulse in the fluid.

2. In response, the basilar membrane of the cochlea vibrates (mechanically oscillates). Only selected portions of the basilar membrane vibrate at any one time, depending on the frequency of the sound stimulus.

3. The hair cells of the organ of Corti at that particular location are mechanically stimulated. This stimulation is transferred to the neurons of the acoustic nerve. The acoustic nerve passes out of the modiolus into the cranial cavity and goes to the brain.
5-9. DISORDERS OR MALFUNCTIONS OF THE EAR

a. **Deafness.** Deafness can be divided into two types. One type is caused by the inability of the middle ear mechanisms to transmit sounds into the cochlea. This is sometimes called conduction deafness. Another type, usually referred to as nerve deafness, is caused by the impairment of the auditory nerve or cochlea. As one might expect, if either the cochlea or auditory nerve is destroyed, the patient is permanently deaf. However, if the cochlea and auditory nerve are still capable of functioning and only the ossicular system has been destroyed, the patient can still hear because sound waves can be conducted into the cochlea by bone conduction.

b. **Tinnitus.** Tinnitus is ringing in the ears or the sensation of noise in the ears or head. Persons who take large doses of certain drugs (like aspirin) complain of tinnitus.

c. **Meniere’s Syndrome.** Meniere’s Syndrome is a disorder characterized by intermittent attacks of vertigo (dizziness), nausea, vomiting, and profuse sweating. It is a disorder of the membranous labyrinth of the inner ear.

d. **Swimmer’s Ear.** Swimmer’s ear is a fungal infection of the outer ear.

e. **Otitis Media.** Otitis media is the inflammation of the middle ear or eardrum.

f. **Otitis Externa.** Otitis externa is the inflammation of the outer ear.

Section III. ANATOMY AND PHYSIOLOGY OF EQUILIBRIUM (BALANCE)

5-10. BACKGROUND

a. **Posture.** Posture is the specific alignment of the body parts at any given time. Humans can assume an infinite variety of postures. However, the truly erect posture is unique to humans.

b. **Equilibrium.** Equilibrium is the state of balance of the body. An erect standing human has a highly unstable equilibrium. Therefore, the human can easily fall. Through a variety of sensory inputs (visual, and so forth) and postural reflexes, the body is maintained in its erect posture.

c. **Stimulus-Gravitational Forces.** A primary sensory input for equilibrium consists of gravitational forces. This input is received by the membranous labyrinth within the internal ear. The gravitational forces are of two types: static, when the body is standing still, and kinetic, when the body is moving in either linear (straight) or angular directions.
d. **Membranous Labyrinth.** The specific portions of the membranous labyrinth involved are the two sac-like structures--the sacculus and the utriculus. Each of these two structures has an area of special hair cells called the macula. In addition, there are three semi-circular ducts located within the osseous semi-circular canals of the temporal bone of the skull. Each semi-circular duct has a crista, a little ridge of hair cells across the axis of the duct.

e. **“Body Sense.”** All of the various sensory inputs related to the maintenance of equilibrium and posture are integrated within the brain as “body sense.” Correct information is sent to the muscles of the body by means of specific postural reflexes in order to maintain the proper posture.

**5-11. SACCUS AND UTRICULUS**

a. The sacculus and the utriculus are two sac-like portions of the membranous labyrinth. They are filled with endolymph.

b. On the wall of each sac is a collection of special hair cells known as the macula, which serves as a receptor organ for static and linear kinetic gravitational forces. The saccular macula and the utricular macula are oriented at more or less right angles to each other. For the pair of maculae in the membranous labyrinth of the right side, there is a corresponding pair in the labyrinth of the left side. Information from all of these maculae is sent into the brain for continuous sensing of the position of the head in space.

**5-12. SEMICIRCULAR DUCTS**

Extending from and opening into the utriculus are three hollow structures called the semicircular ducts. Since the utriculus completes the circle for each duct, the ducts act as if they were complete (Figure 5-5).

a. **Orientation.** Two of the ducts are vertically oriented (one anterior and one posterior). The third duct is essentially horizontal. The three ducts are all oriented at right angles to each other. In addition, the three ducts of one membranous labyrinth are matched or paired by the three ducts of the opposite membranous labyrinth.

b. **Ampullae and Cristae.** Each semi-circular duct ends with an enlargement where it opens into the utriculus. This enlargement or swelling is called an ampulla. The crista is at a right angle to the axis of the duct. Movement of the endolymph within the duct--caused by movement of the head in space--deforms (bends) the hairs of the crista in specific directions. These are responses to linear and/or angular kinetic gravitational forces.
5-13. THE VESTIBULAR NERVE

The vestibular nerve carries all this information from the maculae and cristae to the brain. The vestibular nerve is part of the auditory nerve. The auditory nerve (acoustic nerve) is a combination of the vestibular nerve (balance) and the otic nerve (hearing).

Continue with Exercises
EXERCISES, LESSON 5

INSTRUCTIONS: Answer the following exercises by marking the lettered response which best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. The sclera is best described as:
   a. The inner layer of the wall of the bulbus oculi where the rods and cones of the eye are located.
   b. The white and very dense fibrous connective tissue that is the outermost layer of the bulbus oculi.
   c. The middle layer of the wall of the bulbus oculi.
   d. The transparent layer that forms the outermost portion of the bulbus oculi.

2. The retina is:
   a. The middle layer of the bulbus oculi that is pigmented black to absorb light rays so they will not be reflected at random within the eye.
   b. The transparent portion of the bulbus oculi that serves as the major focusing device for the eye.
   c. The inner layer of the wall of the bulbus oculi where the photo-receptor elements of the eye are located.
   d. The non-nervous portion of the inner layer of the bulbus oculi.

3. The cones of the bulbus oculi function to:
   a. Perceive black and white.
   b. Perceive colors.
   c. Prevent random reflection of light rays within the eye.
   d. Provide vision in conditions of little or no light.
4. What is the blind spot?
   a. The blind spot is a place in the cornea where there are no cones.
   b. The blind spot is a place in the retina where the optic nerve enters the bulbus oculi.
   c. The blind spot is an area located in the center of the anterior of the bulbus oculi.
   d. The blind spot is the origin of the optic nerve where there are no rods or cones.

5. The vitreous body is best described as:
   a. The space between the cornea and the lens.
   b. The jelly-like material that fills the posterior cavity of the bulbus oculi.
   c. The group of muscles responsible for controlling the size of the pupil.
   d. The colored portion of the anterior part of the choroid layer that is between the lens and the cornea.

6. The function of the lacrimal apparatus of the eye is to:
   a. Produce oil to prevent the loss of fluids from the bulbus oculi.
   b. Keep rain and perspiration away from the bulbus oculi.
   c. Open and close the eyelids.
   d. Keep the eye clean and moist at all times.
7. Myopia is best defined as:
   a. A condition in which the image from a distant object is focused in front of the retina.
   b. A condition in which the light rays entering the eye are focused behind the retina.
   c. A condition characterized by increased intraocular pressure which can result in blindness.
   d. A condition characterized by an irreversible and progressive clouding of the lens.

8. What is the function of the auditory (Eustachian) tube?
   a. This tube transmits from the tympanic membrane to the middle ear cavity.
   b. This tube carries sound waves from the external ear to the auditory ossicles.
   c. This tube maintains equal air pressure on the two sides of the tympanic membrane.
   d. This tube carries the sound waves from the external ear to the tympanic membrane.

9. The cochlea of the internal ear is best described as:
   a. A complex cavity within the temporal bone.
   b. A spiral structure associated with hearing.
   c. A hollow tubular structure suspended within the bony labyrinth.
   d. A structure containing fluid which is located between the membranous labyrinth and the bony labyrinth.
10. Meniere’s Syndrome is best described as:
   a. An inflammation of the outer ear.
   b. An acute fungal infection of the outer ear.
   c. A disorder characterized by intermittent attacks of dizziness, nausea, vomiting, and profuse sweating.
   d. An inflammation of the middle ear or eardrum.

11. Conduction deafness is best described as:
   a. The type of deafness caused by the inability of the middle ear mechanisms to transmit sounds into the cochlea.
   b. The type of deafness caused by the impairment of the auditory nerve or cochlea.
   c. The type of deafness caused by the ossification of the tympanic membrane.

12. Which of the following statements best describes how the body maintains equilibrium?
   a. Information from the membranous labyrinth is sent to the brain.
   b. The semicircular ducts input energy to the brain.
   c. Movement of the endolymph within the semicircular duct provides all the equilibrium information to the brain.
   d. The brain receives sensory inputs from many sources and integrates this knowledge as “body sense.”

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 5

1. b The white and very dense fibrous connective tissue which is the outermost layer of the bulbus oculi. (para 5-2b(1))

2. c The inner layer of the wall of the bulbus oculi where the photoreceptor elements of the eye are located. (para 5-2b(3))

3. b Perceive colors. (para 5-2c(1)(a))

4. d The blind spot is the origin of the optic nerve where there are no rods or cones. (para 5-2c(1)(c))

5. b The jelly-like material which fills the posterior cavity of the bulbus oculi. (para 5-2c(7))

6. d Keep the eye clean and moist at all times. (para 5-3c)

7. a A condition in which the image from a distant object is focused in front of the retina. (para 5-4a)

8. c This tube maintains equal air pressure on the two sides of the tympanic membrane. (para 5-7d)

9. b A spiral structure associated with hearing. (para 5-8c)

10. c A disorder characterized by intermittent attacks of dizziness, nausea, vomiting, and profuse sweating. (para 5-9c)

11. a The type of deafness caused by the inability of the middle ear mechanisms to transmit sounds into the cochlea. (para 5-9a)

12. d The brain receives sensory inputs from many sources and integrates this knowledge into “body sense.” (para 5-10e)

End of Lesson 5
LESSON ASSIGNMENT

LESSON 6
Review of the Autonomic Nervous System.

TEXT ASSIGNMENT
Paragraphs 6-1 through 6-12.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

6-1. From a list, select the names of the two major divisions of the human nervous system.

6-2. From a list, select the names of the two divisions of the peripheral nervous system.

6-3. Given a group of statements, select the statement that best describes the autonomic nervous system.

6-4. Given a list, select the names of the two divisions of the autonomic nervous system.

6-5. Given a group of statements, select the statement that best describes the sympathetic nervous system.

6-6. Given a group of that best describes the statements, select the statement parasympathetic nervous system.

6-7. Given a group of statements, select the statement that best describes the physiology of the sympathetic nervous system.

6-8. Given a list of chemical substances, select the neurotransmitters of the sympathetic nervous system.

6-9. Given a group of statements and the name of one of the types of receptor sites of the sympathetic nervous system (alpha or beta), select the physiological effect produced by the stimulation of that receptor.

6-10. Given the name of a part of the body and a group of effects, select the effect produced on that part of the body by the sympathetic nervous system.

6-11. Given a group of statements, select the statement that best describes the physiology of the parasympathetic nervous system.
6-12. Given a list of chemical substances, select the chemical transmitter of the parasympathetic nervous system.

6-13. Given the name of a part of the body and a group of effects, select the effect produced on that part by the parasympathetic nervous system.

**SUGGESTION**

After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 6

REVIEW OF THE AUTONOMIC NERVOUS SYSTEM

Section I. INTRODUCTION

6-1. BACKGROUND

a. At some time in your life, you have faced a situation in which you have undergone a real scare. For example, have you ever been walking down a dark street at night and heard someone running toward you from behind? At that time, certain physiological changes took place in your body. Many of these changes directly involved the autonomic nervous system.

b. The autonomic nervous system (ANS) with its ability to make rapid internal adjustments is one of the most important systems present in the body in terms of the maintenance of body balance. The autonomic nervous system is very complex. Almost every organ of the body receives some type of effect produced by the autonomic nervous system.

c. Because of the wide distribution of the autonomic nervous system, many drugs produce definite effects upon it. This can occur as a blockade of natural activity or a direct effect mimicking natural stimulation. Many so-called side effects of drugs can also be traced to interference with normal autonomic function. Therefore, you must have an understanding of how the autonomic nervous system works and how various drugs can affect its operation. Many drugs used routinely and in emergencies are classified as autonomic nervous system drugs.

6-2. REVIEW OF THE HUMAN NERVOUS SYSTEM

a. The nervous system is divided into two major divisions—the central nervous system and the peripheral nervous system. As you will recall, the central nervous system is composed of the brain and spinal cord. The peripheral nervous system includes the parts of the nervous system other than the brain and spinal cord. Figure 6-1 illustrates the division of the human nervous system.

b. The peripheral nervous system has two divisions: the somatic nervous system and the autonomic nervous system. Figure 6-2 illustrates this division.

(1) Somatic nervous system. The somatic nervous system innervates skeletal muscle. It is under voluntary control and contains no ganglia. Acetylcholine is the chemical transmitter in the somatic nervous system (see lesson 2 of this subcourse).
(2) **Autonomic nervous system.** The autonomic nervous system is involuntary. It innervates smooth muscles, cardiac muscles, and gland cells. The autonomic nervous system aids the body in the fight or flight response.

![Diagram of the human nervous system]

**Figure 6-1.** Divisions of the peripheral nervous system.

![Diagram of the peripheral nervous system]

**Figure 6-2.** Divisions of the peripheral nervous system.

**Section II. THE AUTONOMIC NERVOUS SYSTEM**

**6-3. INTRODUCTION**

As was previously mentioned, the autonomic nervous system is one part of the peripheral nervous system. The autonomic nervous system is involuntary. It innervates smooth muscles, cardiac muscles, and gland cells. It aids the body in the fight or flight response. The autonomic nervous system helps to control urinary output, sweating, body temperature, arterial pressure, and gastrointestinal motility and secretion.

**6-4. CONTROL OF THE AUTONOMIC NERVOUS SYSTEM**

Centers located in the brain stem, hypothalamus, and spinal cord activate the autonomic nervous system.
6-5. ORGANIZATION OF THE AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system is divided into two divisions: the sympathetic and the parasympathetic. Figure 6-3 illustrates this division.

![Diagram of Autonomic Nervous System]

Figure 6-3. Divisions of the autonomic nervous system.

a. **Sympathetic Nervous System.** The sympathetic nervous system is frequently referred to as the adrenergic nervous system. Because of its transmitter epinephrine, which is more commonly known by its trade name "Adrenalin," it prepares the body for stress situations. Stimulation of the adrenergic nervous system has the general effect of expending energy. When a person is scared, this system prepares the body for the fight or flight response. In other words, it prepares the body to either fight or run. More information on this important system will be provided later in this lesson.

b. **Parasympathetic Nervous System.** The parasympathetic nervous system is usually referred to as the cholinergic nervous system. The cholinergic nervous system is responsible for bringing the body back to normal after the fight or flight response. The effects of the cholinergic nervous system are generally the opposite of those produced by the adrenergic nervous system. More information on the cholinergic nervous system will be provided later in this lesson.

Section III. THE SYMPATHETIC NERVOUS SYSTEM

6-6. INTRODUCTION TO THE SYMPATHETIC NERVOUS SYSTEM

You have already been told that the sympathetic nervous system is one component of the autonomic nervous system. Although this system is essential for a person in normal living, it is not crucial for a person to have this system if that individual is in a controlled environment (no stress, excitement, change in temperature, and so forth). Without the presence of this system, one's temperature would not adjust to the environmental temperature, one’s level of blood glucose would not increase during times of stress, and one’s resistance to fatigue would decrease.
6-7. PHYSIOLOGY OF THE SYMPATHETIC NERVOUS SYSTEM

a. The sympathetic nervous system is stimulated by the hypothalamus. The nerves of the sympathetic nervous system arise from the thoracolumbar section of the spinal cord. These nerves have short postganglionic fibers. These fibers synapse in the sympathetic chain ganglia that lie near the spinal cord. A ganglion is a joining of nerve fibers. Following synapse, the impulses travel down long postganglionic fibers and synapse at the effector organ.

b. The neurotransmitter at the preganglionic synapse is acetylcholine, while the neurotransmitters at the effector organ are norepinephrine and epinephrine. Norepinephrine and epinephrine are released by the adrenal medulla and circulate in the blood. Norepinephrine is also released by the postganglionic adrenergic neuron. The enzymes, catechol-o-methyltransferase (COMT) and monoamine oxidase (MAO) terminate transmission.

c. Circulating epinephrine and norepinephrine are destroyed by COMT. The norepinephrine, which is released by the neuron, is either reabsorbed by the neuron or destroyed in the synapse by MAO.

Figure 6-4. Sympathetic nervous system.
6-8. ALPHA AND BETA RECEPTOR SITES

It has been found that different effector organs have either alpha or beta predominant receptor sites.

a. **Alpha Receptors.** Alpha-receptors are associated mainly with increased contractibility of vascular smooth muscle and intestinal relaxation. Alpha-receptors have been classified into two types.

   (1) **Alpha_1**. Alpha_1 receptors are located at the postsynaptic effector sites to stimulate transmitter release in smooth muscle (that is, contracts smooth muscle of peripheral blood vessels.

   (2) **Alpha_2**. Alpha_2 receptors are located presynaptic on axon terminals to inhibit release of transmitter (norepinephrine). These predominate in the intestinal tract to cause relaxation.

b. **Beta Receptors.** Beta-receptors are associated with vasodilation and relaxation of nonintestinal smooth muscle and cardiac stimulation. Beta-receptors are divided into two types (example: bronchial dilation).

   (1) **Beta_1**. Beta_1 receptors cause cardiac stimulation and lipolysis.

   (2) **Beta_2**. Beta_2 receptors cause bronchodilatation, relaxation of blood vessels (usually skeletal muscles), and muscle glycogenolysis.

6-9. EFFECTS PRODUCED BY THE SYMPATHETIC NERVOUS SYSTEM

The sympathetic nervous system produces a variety of physiological effects upon the body. Listed below are some of these effects/responses:

a. **Eye (Pupil).** Mydriasis (dilation) of the pupil is produced by alpha stimulation.

b. **Heart.** Both an increase in heart rate and an increase in the contraction strength of the heart are produced by beta stimulation.

c. **Bronchi.** Relaxation of the bronchial muscle is produced by beta_2 stimulation.

d. **Blood Vessels.**

   (1) **Blood vessels in skeletal muscle.** Constriction or dilation is produced--over the usual concentration range of physiologically released and circulating epinephrine, the beta-receptor response (vasodilation) predominates in blood vessels of skeletal muscle and liver. The alpha-receptor response (vasoconstriction) is obtained in blood vessels of other abdominal organs.
(2) **Blood vessels in the skin and mucous membranes.** Constriction is produced by alpha stimulation.

e. **Salivary Glands.** Thick and viscous secretions are produced by alpha stimulation.

f. **Stomach.** The motility and tone of the stomach muscle is usually decreased (alpha_2 and beta? stimulation) and the stomach sphincters are contracted (alpha stimulation).

g. **Intestines.** The motility and tone of the intestinal muscles are decreased (alpha_2 and beta_2 stimulation) and secretions are inhibited.

h. **Urinary Bladder.** The wall of the bladder is usually relaxed (beta stimulation) and the sphincter of the bladder is contracted (alpha stimulation) by stimulation from the sympathetic nervous system.

**Section IV. THE PARASYMPATHETIC NERVOUS SYSTEM**

6-10. **INTRODUCTION TO THE PARASYMPATHETIC NERVOUS SYSTEM**

You have already been told that the parasympathetic nervous system is one component of the autonomic nervous system. The parasympathetic nervous system (also referred to as the cholinergic nervous system) is responsible for bringing the body back to normal after the fight or flight response. The effects of the cholinergic nervous system are generally the opposite of those produced by the sympathetic (adrenergic) nervous system. The parasympathetic nervous system is responsible for maintaining the daily functions performed within the body. This division of the autonomic nervous system serves to conserve energy—it is necessary for life. Without the presence of this nervous system, the absorption of necessary nutrients would be hindered, gastrointestinal motility would be decreased, gastrointestinal secretions would be increased, and the urinary bladder and rectum would fail to empty.

6-11. **PHYSIOLOGY OF THE PARASYMPATHETIC NERVOUS SYSTEM**

a. The parasympathetic nervous system is stimulated by the hypothalamus. It has long preganglionic fibers and short postganglionic fibers (Figure 6-5). The short postganglionic fibers are usually located within the effector organ.

b. The chemical transmitter at both the preganglionic synapse and at the effector organ is acetylcholine. As mentioned previously, acetylcholine is also the transmitter at skeletal muscle for the somatic nervous system; however, the receptors for the two nervous systems are different. Transmission of impulses is terminated by the destruction of acetylcholine by the enzyme acetylcholinesterase.
Acetycholinesterase is frequently referred to as cholinesterase. The general effects of parasympathetic stimulation are conservation and restoration of energy.

c. The parasympathetic nervous system does not have alpha and beta receptor sites.

![Diagram of the parasympathetic nervous system]

Figure 6-5. The parasympathetic nervous system.

6-12. EFFECTS PRODUCED BY THE PARASYMPATHETIC NERVOUS SYSTEM

The parasympathetic physiological activity on the organs is generally the opposite of the sympathetic with a few exceptions. The effect of the parasympathetic nervous system effects on some areas of the body are listed below:

a. **Eye (Pupil).** Contraction of the pupil (miosis) is produced by parasympathetic stimulation.

b. **Heart.** The parasympathetic nervous system produces a decrease in heart rate and a slight decrease in the contraction strength of the heart.

c. **Bronchi.** The bronchi are contracted by parasympathetic stimulation.
d. **Salivary Glands.** Parasympathetic nervous system stimulation of the salivary glands leads to profuse, watery secretions.

e. **Stomach.** Parasympathetic stimulation of the stomach leads to increased motility and tone and relaxed (usually) sphincters.

f. **Intestines.** Increased intestinal motility and tone and stimulated secretion of intestinal fluids are products of parasympathetic stimulation.

g. **Urinary Bladder.** Parasympathetic stimulation causes contraction of the bladder wall and relaxation of the sphincter.

*Continue with Exercises*
EXERCISES, LESSON 6

INSTRUCTIONS: Answer the following exercises by marking the lettered response that best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Select the names of the two major divisions of the human nervous system.
   a. The central nervous system and the somatic nervous system.
   b. The central nervous system and the peripheral nervous system.
   c. The central nervous system and the autonomic nervous system.
   d. The central nervous system and the parasympathetic nervous system.

2. Select the names of the two divisions of the peripheral nervous system.
   a. The central nervous system and the somatic nervous system.
   b. The autonomic nervous system and the parasympathetic nervous system.
   c. The somatic nervous system and the autonomic nervous system.

3. The autonomic nervous system is best described as:
   a. The part of the peripheral nervous system that is under voluntary control.
   b. The part of the peripheral nervous system that innervates skeletal muscle and which has acetylcholine as the chemical transmitter.
   c. The part of the peripheral nervous system that is involuntary and innervates smooth muscles, cardiac muscles, and gland cells.
   d. The part of the peripheral nervous system that is involuntary and is frequently referred to as the adrenergic nervous system.
4. Which statement best describes the sympathetic nervous system?
   a. The component of the autonomic nervous system that has acetylcholine as its primary transmitter.
   b. The component of the autonomic nervous system that has epinephrine as its chemical transmitter.
   c. The component of the autonomic nervous system which is responsible for bringing the body back to normal after the fight or flight response.
   d. The component of the autonomic nervous system which is not crucial for a person to have if they live in a controlled environment (no stress).

5. The parasympathetic nervous system is best described as the component of the autonomic nervous system which:
   a. Has acetylcholinesterase as its chemical transmitter.
   b. Has epinephrine as its chemical transmitter.
   c. Is not crucial for a person to have if he/she lives in a controlled environment (no stress).
   d. Is responsible for bringing the body back to normal after the fight or flight response.

6. The neurotransmitter of the sympathetic nervous system at the preganglionic synapse is ________________ while the neurotransmitters at the effector organ are ________________ and ________________.  
   a. Epinephrine, norepinephrine, and acetylcholine.
   b. Acetylcholine, norepinephrine, and epinephrine.
   c. Epinephrine, acetylcholine, and acetylcholinesterase.
   d. Acetylcholine, Catechol-o-methyltransferase, and monoamine oxidase.
7. Stimulation of beta-receptor sites results in:
   a. Vasodilation and relaxation of nonintestinal smooth muscle and cardiac stimulation.
   b. Increased contractility of vascular smooth muscle and intestinal relaxation.
   c. Contraction of smooth muscle.
   d. Vasocontraction of vascular smooth muscle.

8. Select the effect produced on the eye by the sympathetic nervous system.
   a. Mydriasis (dilation) of the pupil.
   b. Miosis (contraction) of the pupil.

9. Select the effect produced on the eye by parasympathetic stimulation.
   a. Mydriasis (dilation) of the pupil.
   b. Miosis (contraction) of the pupil.

10. Parasympathetic stimulation of the salivary glands leads to:
    a. Profuse, watery secretions.
    b. Thick and viscous secretions.
    c. None of the above.

11. Sympathetic stimulation of the intestines results in:
    a. Decreased motility and tone of the muscles.
    b. Increased motility and tone of the muscles.
    c. None of the above.
12. The chemical transmitter of the parasympathetic nervous system is:
   a. Epinephrine.
   b. Norepinephrine.
   c. Acetylcholinesterase.
   d. Acetylcholine.

13. Parasympathetic stimulation of the heart results in: (more than one response can be correct)
   a. Increased heart rate.
   b. Decreased heart rate.
   c. Increased contraction strength.
   d. Decreased contraction strength.

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 6

1. b The central nervous system and the peripheral nervous system. (para 6-2a)

2. c The somatic nervous system and the autonomic nervous system. (para 6-2b)

3. c The part of the peripheral nervous system that is involuntary and innervates smooth muscles, cardiac muscles, and gland cells. (para 6-2b(2))

4. b The component of the autonomic nervous system that has epinephrine as its chemical transmitter. (para 6-5a)

5. d Is responsible for bringing the body back to normal after the fight or flight response. (para 6-5b)

6. b Acetylcholine; norepinephrine and epinephrine. (para 6-7b)

7. a Vasodilation and relaxation of nonintestinal smooth muscle and cardiac stimulation. (para 6-8b)

8. a Hydriasis (dilation) of the pupil. (para 6-9a)

9. b Miosis (contraction) of the pupil. (para 6-12a)

10. a Profuse, water secretions. (para 6-12d)

11. a Decreased motility and tone of the muscles. (para 6-9g)

12. d Acetylcholine. (para 6-11b)

13. b Decreased heart rate. (para 6-12b)
    d Decreased contraction strength. (para 6-12b)

End of Lesson 6
LESSON ASSIGNMENT

LESSON 7
Adrenergic Agents.

TEXT ASSIGNMENT
Paragraphs 7-1 through 7-6.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

7-1. Given a group of statements, select the mechanism(s) of action of drugs which stimulate the sympathetic nervous system.

7-2. Given the name of one of the receptor sites of the adrenergic nervous system and a list of effects, select the effect produced by the stimulation of that receptor site.

7-3. Given the name of a certain part of the body and a group of effects, select the effect produced on that part of the body by adrenergic stimulation.

7-4. Given a group of statements, select the best definition of the term adrenergic (sympathomimetic) drug.

7-5. Given the trade and/or generic name of an adrenergic (sympathomimetic) drug and a list of pharmacological effects, indications for use, cautions and warnings, or side effects, select the effect(s), use(s), caution(s) and warning(s), or side effect(s) for that drug.

7-6. Given the trade or generic name of an adrenergic (sympathomimetic) drug and a group of trade and/or generic names of drugs, select the appropriate trade or generic name for that drug.

SUGGESTION
After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 7

ADRENERGIC AGENTS

7-1. BACKGROUND

The autonomic nervous system was discussed in lesson 6 of this subcourse. In
that lesson, you learned of the sympathetic division of this nervous system. Specifically, it
was stated that the sympathetic nervous system is frequently referred to as the
adrenergic nervous system because of its transmitter epinephrine that is more
commonly known by its trade name, "Adrenalin." The adrenergic nervous system
prepares the body for stress situations. Stimulation of the adrenergic nervous system has
the general effect of expending energy. When a person is scared, this system
prepares the body for the fight or flight response.

7-2. MECHANISMS OF ACTION OF AGENTS WHICH STIMULATE SYMPATHETIC
NERVOUS SYSTEM

Drugs that stimulate the sympathetic nervous system have a variety of
mechanisms of action. These include:

a. Mimicking the action of the transmitter norepinephrine. See figure 7-1 for a
diagrammatic representation of the sympathetic nervous system.

b. Rapidly displacing the transmitter from its storage site to activate the receptor.

c. Blocking the uptake of the transmitter into storage sites.

d. Inhibiting enzymes that break down the transmitter.

Figure 7-1. Diagrammatic representation of the sympathetic nervous system.
7-3. RECEPTOR SITE THEORY OF ADRENERGIC TRANSMISSION

Two types of receptor sites are theorized to explain adrenergic effects.

a. **Alpha-Receptors.** Alpha-receptors are associated mainly with increased contractibility of vascular smooth muscle and intestinal relaxation.

   (1) **Alpha\textsubscript{1}**. The alpha\textsubscript{1} is located at postsynaptic effector sites to stimulate transmitter release in smooth muscle. For example, the smooth muscle of peripheral blood vessels is contracted in alpha\textsubscript{1} stimulation.

   (2) **Alpha\textsubscript{2}**. The alpha\textsubscript{2} receptor site is located presynaptic on axon terminals to inhibit the release of norepinephrine (the transmitter). The effects of alpha\textsubscript{2} stimulation results in relaxation of the intestinal tract--motility and tone are decreased.

b. **Beta-Receptors.** Beta-receptors are associated with vasodilation and relaxation of nonintestinal smooth muscle and cardiac stimulation.

   (1) **Beta\textsubscript{1}**. Stimulation of beta\textsubscript{1} receptor sites results in cardiac stimulation and lipolysis.

   (2) **Beta\textsubscript{2}**. Stimulation of beta\textsubscript{2} receptor sites causes bronchodilation, relaxation of blood vessels (usually in skeletal muscles), and muscle glycogenolysis.

7-4. PHARMACOLOGICAL EFFECTS PRODUCED BY ADRENERGIC STIMULATION

a. **Certain Types of Smooth Muscle.** The adrenergic effect on certain types of smooth muscle--especially the blood vessels of the skin, mucous membranes, and salivary glands--is constriction. This is an alpha\textsubscript{1} effect.

b. **Other Types of Smooth Muscle.** The adrenergic effect on other types of smooth muscle varies according to the receptor site. The wall of the gut is relaxed through inhibition--this is an alpha\textsubscript{2} effect. The bronchial smooth muscle is dilated--this is a beta\textsubscript{2} effect. The blood vessels supplying skeletal muscle are dilated--this is a beta\textsubscript{2} effect.

c. **Cardiac Stimulation.** Cardiac stimulation is a beta\textsubscript{1} effect. Such stimulation results in increased heart rate and increased force of contraction by the heart.

d. **Metabolic Effects.** Beta\textsubscript{2} stimulation causes glycogenolysis in liver and muscle tissue. Beta\textsubscript{1} stimulation causes liberation of free fatty acids (lipolysis) from adipose tissue.
e. **Central Nervous System (CNS) Excitatory Actions.** Adrenergic stimulation results in respiratory stimulation, an increase in wakefulness, and in a reduction of appetite.

7-5. **ADRENERGIC (SYMPATHOMIMETIC) DRUGS**

Sympathomimetic drugs are agents which when administered will mimic (produce the same effects) normal adrenergic (sympathetic) stimulation. This normal adrenergic stimulation refers to the effects produced by epinephrine on the body. Two agents produce the adrenergic effects: epinephrine and norepinephrine. Epinephrine is the original model of the sympathomimetic agent. It has both Alpha and Beta activity. Figure 7-2 shows the chemical structure of epinephrine.

![Chemical structure of epinephrine.](image)

7-6. **SPECIFIC ADRENERGIC (SYMPATHOMIMETIC) AGENTS**

a. **Epinephrine (Adrenalin).**

(1) **Pharmacological effects.**

(a) **Blood pressure.** The blood pressure in the skin and mucosa is increased via vasopressor action of peripheral vessels.

(b) **Vascular effects.** Epinephrine constricts the blood vessels of mucosa and the skin (alpha effect). Physiological doses (0.5-1.0 milligram) administered subcutaneously causes dilatation of vessels in skeletal muscle tissue. This effect decreases peripheral resistance and overcomes the vasoconstriction of peripheral vessels so that blood pressure is not greatly affected (predominantly beta effect). Large doses of epinephrine increase blood pressure: Alpha-receptor stimulation in the skeletal muscles overcome beta stimulation and the blood pressure is increased.

(c) **Cardiac effects.** Epinephrine acts upon Beta₁ receptors to greatly increase heart rate and output.

(d) **Smooth muscle.** The effect upon smooth muscle by epinephrine varies according to the organ stimulated and the type of adrenergic receptor effected in the muscle.
(e) Gastrointestinal (G.I.) tract. Epinephrine decreases the motility and tone of the gastrointestinal tract (alpha$_2$ and beta$_2$ effects).

(f) Central nervous system (CNS). Epinephrine provides some stimulation; therefore, it may produce some restlessness, apprehension, headache, and tremor.

(2) Indications for the use of epinephrine.

(a) Relieve bronchospasm. Epinephrine is used to relieve bronchospasm as is seen with patients who have asthma. It opens the breathing pathways and allows for easier breathing.

(b) Prolong the action of local anesthetics. Epinephrine is sometimes combined with a local anesthetic (that is, lidocaine). Because epinephrine is a vasoconstrictor, it prolongs the effects of the local anesthetic by increasing the time the local anesthetic is in contact with the affected tissue (reduces blood flow to and from the area).

(c) Restore cardiac rhythm in cardiac arrest. Because of its effects upon the heart, epinephrine is administered to increase cardiac output and rate in persons who experience cardiac arrest.

(d) Stop bleeding on topical surfaces. Because it is a vasoconstrictor, epinephrine is sometimes applied to topical surfaces to reduce or stop bleeding.

(e) Treat allergic reactions. Epinephrine is the drug of choice for the treatment of anaphylactic shock. It overcomes the physiological effects of histamine (substance which causes the anaphylactoid reaction). It should be noted that epinephrine is not an antihistamine. One, epinephrine reverses the drop in blood pressure caused by the vasodilatation effect of histamine because epinephrine produces vasoconstriction. Two, the epinephrine reverses the bronchoconstriction produced by the anaphylaxis.

(3) Cautions and warnings associated with the use of epinephrine.

(a) Epinephrine can cause anxiety, tenseness, headache, and an awareness of a forceful, rapid heart beat.

(b) Epinephrine should be used cautiously in-patients who have hypertension (high blood pressure), hyperthyroidism, and heart disease (that is, angina).
b. **Norepinephrine, Levarterenol (Levophed®).** This adrenergic drug acts almost exclusively on alpha-receptors.

(1) **Pharmacological effects.**

(a) Peripheral vasoconstriction. Norepinephrine causes marked peripheral vasoconstriction.

(b) Constriction of blood vessels in skeletal muscles. Unlike epinephrine, norepinephrine produces constriction of blood vessels in skeletal muscles.

(c) Increase in blood pressure. Norepinephrine causes a net increase in blood pressure.

(2) **Indication for the use of norepinephrine.** Norepinephrine is used to restore blood pressure in selected hypotensive states (that is, when hypotension occurs during spinal anesthesia).

(3) **Cautions and warnings associated with the use of norepinephrine.**

(a) Norepinephrine can cause local necrosis due to vasoconstriction when it is injected intravenously. Therefore, it should be infused slowly into a rapidly flowing vein, and the site into which the drug solution is being administered should be changed every 12 hours.

(b) The drug can produce anxiety and transient headaches.

(c) Norepinephrine should be used cautiously with patients who have heart disease (that is, angina), hypertension, and hyperthyroidism.

c. **Isoproterenol (Isuprel®).** Isoproterenol produces a powerful action on both beta_1 and beta_2 receptors. It has no alpha activity. Injection or aerosol readily absorbs Isoproterenol; however, oral absorption of the drug is unreliable.

(1) **Pharmacological effects.**

(a) Cardiovascular effects. Isoproterenol produces increased cardiac output and decreased blood pressure. Beta_2 stimulation is responsible for the increase in heart rate and the increase in the force of contraction. Isoproterenol causes a reduction in blood pressure because of a decrease in peripheral resistance. Beta_2 receptors cause vasodilatation in skeletal muscle.

(b) Smooth muscle. Smooth muscle is relaxed by isoproterenol. This relaxation is most pronounced in the bronchi and gastrointestinal (G.I.) tract.
(c) Central nervous system (CNS). Isoproterenol produces some central nervous system stimulation.

(2) Indications for the use of isoproterenol. Isoproterenol is indicated in a variety of conditions. These include:

(a) Bronchodilator in respiratory disorders.

(b) Cardiac stimulant in instances of heart block and cardiogenic shock following myocardial infarction or septicemia.

(3) Side effects associated with isoproterenol. Side effects associated with the use of isoproterenol include palpitation, tachycardia, headache, and flushing of the skin.

(4) Cautions and warnings associated with isoproterenol. Isoproterenol is contraindicated in patients who have pre-existing cardiac arrhythmias associated with tachycardia.

d. **Dopamine (Intropin®).** Dopamine is a chemical compound in the body which is the immediate precursor (a substance from which another substance is formed) of norepinephrine.

(1) Pharmacological actions. Dopamine exerts both alpha and beta effects. When administered intravenously in doses of 1 to 10 micrograms per kilogram of body weight per minute, the drug acts primarily on beta and dopaminergic receptors. In higher doses, alpha-receptors are stimulated and the net effect of the drug is the result of alpha, beta, and dopaminergic stimulation. Dopaminergic receptors cause dilatation in renal and mesenteric vascular beds. Beta, effects result in an increase in cardiac output. Dopaminergic effects cause vasodilatation in mesenteric and renal beds.

(2) Indications for the use of dopamine. Dopamine is indicated in the treatment of shock syndrome, including cardiogenic shock, trauma, or hypovolemic shock.

(3) Cautions and warnings associated with the use of dopamine.

(a) Dopamine should not be used in the presence of uncorrected tachyarrhythmias or ventricular fibrillation.

(b) This drug should not be administered in the presence of hypovolemia (that is, to administer fluids).

(c) This drug should not be added to any alkaline dilution solution since the drug is inactivated in alkaline solutions.
e. **Metaproterenol (Alupent®).**

(1) **Pharmacological actions.** Because of its specificity for beta2 receptors, metaproterenol causes a relaxation of the bronchi and uterus—little effect upon the heart is seen.

(2) **Indication for the use of metaproterenol.** Metaproterenol is used as a bronchodilator for bronchial asthma. It improves pulmonary function for a period of from 1 to 5 hours.

(3) **Cautions and warnings associated with the use of metaproterenol:**

(a) This drug is contraindicated with patients who have pre-existing cardiac arrhythmias associated with tachycardia.

(b) This drug is contraindicated in children under six years of age.

(4) **Side effects associated with the use of this agent.** Central nervous system (CNS) stimulation and muscle tremors are commonly seen in patients who take this medication.

g. **Albuterol (Ventolin®).**

(1) **Pharmacological actions.** This drug is specific for beta2 receptors and causes relaxation of the bronchi and uterus. It has a longer duration of action than metaproterenol.

(2) **Indications.** Patients use albuterol as indicated for relief of broncho spasm with reversible obstructive airway disease and prevention of exercise-induced bronchospasm.

(3) **Cautions and warnings.**

(a) Safety and efficacy in children under age 12 have not been established.

(b) Use with caution in individuals with cardiovascular disorders.

(4) **Side effects.** Possible side effects associated with Albuterol include CNS stimulation and palpitations.

f. **Terbutaline (Brethine®, Bricanyl®).**

(1) **Pharmacological actions.** This drug is specific for beta2 receptors with resultant relaxation of bronchial smooth muscle and uterus.
(2) **Indication.** Terbutaline is indicated as a bronchodilator for persons who have bronchial asthma. Terbutaline is longer acting than metaproterenol.

(3) **Cautions and warnings associated with terbutaline.**

(a) This drug is contraindicated in patients who have preexisting cardiac arrhythmias associated with tachycardia.

(b) Terbutaline is not recommended for use with patients who are under 12 years of age.

(4) **Side effects.** Central nervous system (CNS) stimulation and muscle tremors are commonly seen in patients who take this drug.

h. **Amphetamine.**

(1) **Pharmacological actions.** Amphetamine is a powerful central nervous system (CNS) stimulant with both alpha and beta activity.

(a) **CNS effects.** Amphetamine causes the person to be awake and alert. Furthermore, the person feels a decreased sense of fatigue.

(b) **Cardiovascular effects.** Amphetamine increases cardiac input and increases blood pressure.

**NOTE:** Overdosing or repeated dosing can reverse the effects of amphetamine. This occurs because amphetamine promotes the release of norepinephrine from its storage sites. Thus, large amounts of amphetamine deplete the stores of norepinephrine and results in diminished or in no effect being produced (tachyphylaxis).

(2) **Indications for the use of amphetamine derivatives.** Amphetamine derivatives are used to treat a variety of conditions. They are as follows:

(a) **Obesity.** Amphetamine derivatives are sometimes prescribed to help an individual lose weight.

(b) **Narcolepsy.** Narcolepsy is a condition characterized by brief attacks of deep sleep. Amphetamine-like products are used to treat this condition because of their ability to stimulate the patient.

(c) **Hyperkinetic syndrome (attention deficient disorder) in children.** Amphetamine derivatives normally stimulate adults; however, in children, it produces a paradoxical (unexpected) effect of calming the patient, decreasing hyperactivity, and prolonging attention span.
NOTE: Amphetamine derivatives are Note R (Schedule II).

(3) Cautions and warnings.

(a) Patients taking amphetamine derivatives develop tolerance and psychological dependence with chronic use.

(b) Amphetamine derivatives should be used cautiously with patients who have arteriosclerosis, cardiovascular disease, glaucoma, hypertension, and hyperthyroid sin.

(4) Side effects. Side effects commonly seen in patients who take amphetamine-like products are restlessness, tremor, hyperactive reflexes, irritability, insomnia, euphoria, and confusion.

i. Ephedrine.

(1) Pharmacological effects. Ephedrine directly stimulates both alpha and beta-receptors and indirectly stimulates Alpha-receptors by causing release of norepinephrine. Ephedrine is similar to epinephrine; however, it is longer acting and produces more effect on the central nervous system (CNS). Ephedrine produces cardiovascular effects similar to those produced by epinephrine. Finally, the bronchial muscle relaxation produced caused by ephedrine is less intense, but more sustained than that caused by epinephrine.

(2) Indications. Ephedrine is most commonly used as a bronchodilator. It is also used as a nasal decongestant, as a treatment for narcolepsy, and as agent to control blood pressure in patients under the effects of spinal and epidural anesthesia.

(3) Caution and warning. Ephedrine is contraindicated in patients who have severe hypertension and chronic heart disease.

j. Metaraminol (Aramine®).

(1) Pharmacological effects. Metaraminol produces alpha stimulation with beta1 effects. The vasoconstriction produced by metaraminol is very pronounced. The beta1 effects produced by metaraminol are similar to epinephrine. Overall, metaraminol produces less potent and longer duration with more gradual onset than the effects produced by norepinephrine.

(2) Indications. Metaraminol is indicated in the treatment of hypotensive states (that is, shock); however, it must be used with caution because it increases the myocardium’s demand of oxygen.
(3) Cautions and warnings. Metaraminol may induce arrhythmias in large doses. Furthermore, the drug should be used with caution with patients who have heart disease, thyroid disease, hypertension, or diabetes.

k. Phenylephrine (Neo-Synephrine®).

(1) Pharmacological effects. Phenylephrine is a powerful alpha stimulator with little or no effect on beta-receptors.

(2) Indications. Phenylephrine has a variety of uses. These include:

(a) Nasal decongestant.

(b) Vasopressor. The drug is used as a vasopressor for hypotension associated with spinal anesthesia and neurogenic shock.

(c) Mydriatic. The drug is used to produce mydriasis (dilatation of the pupil).

(3) Cautions and warnings. The drug is contraindicated in hypertension and existing ventricular tachycardia. Phenylephrine can induce cardiac irregularities.

l. Tetrahydrozoline (Tyzine®).

(1) Indications. This drug is used as a nasal decongestant.

(2) Caution and warning. Prolonged use of this agent as a nasal decongestant may produce chemical rhinitis.

(3) Side effects. Tetrahydrozoline may cause sneezing, stinging or burning of the mucous membranes, insomnia, or tachycardia.

NOTE: Agents listed in m and n, below, are referred to as incomplete sympathomimetics. They produce topical vasoconstriction of the nasal mucosa or conjunctiva. They have no direct effect on the myocardium or on the smooth muscle of the bronchioles. However, they do relax the intestine. Remember, although both the intestine and the bronchi are smooth muscles, they are affected by different receptors. Intestinal relaxation is moderated by alpha₂ receptors and bronchi relaxation by beta₂ receptors.

m. Xylometazoline (Otrivin®).

(1) Indications. Xylometazoline is used as a nasal decongestant.

(2) Caution and warning. No significant caution and warning is associated with the drug.
(3) **Side effects.** Side effects associated with this drug include stinging or burning of the mucous membranes, dry nose, and rebound congestion.

n. **Oxymetazoline (Afrin®).**

(1) **Indications.** Oxymetazoline is used as a nasal decongestant.

(2) **Caution and warning.** No significant caution and warning is associated with the drug.

(3) **Side effects.** Side effects associated with oxymetazoline include rebound congestion, dryness of the nose, and stinging or burning of the mucous membranes.

*Continue with Exercises*
EXERCISES, LESSON 7

INSTRUCTIONS: Answer the following exercises by marking the lettered response which best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson, and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Select the mechanism(s) of action of drugs that stimulate the sympathetic nervous system.
   a. Mimicking the action of the transmitter acetylcholine.
   b. Rapidly displacing the transmitter from its storage site to activate the receptor.
   c. Increasing the uptake of transmitter into the storage sites.
   d. Helping the enzymes that break down the transmitter.

2. Stimulation of the beta2 receptor site results in:
   a. Intestinal relaxation.
   b. Decreased motility of the intestinal tract.
   c. Bronchodilation.
   d. Cardiac stimulation.

3. What is the effect upon the heart of adrenergic stimulation?
   a. No effect is known.
   b. Decreased cardiac output.
   c. Increased heart rate.
   d. Decreased force of contraction.
4. The pharmacological effect of epinephrine (Adrenalin®) upon the gastrointestinal (G.I.) tract is:
   a. Increases motility and tone.
   b. Decreases motility and tone.
   c. Increases secretions.
   d. None of the above.

5. What is the indication for the use of norepinephrine?
   a. To prolong the action of local anesthetics.
   b. To stop bleeding on topical surfaces.
   c. To treat allergic reactions.
   d. To restore blood pressure in selective hypotensive states.

6. Isoproterenol (Isuprel®) is used in a variety of conditions. It is used:
   a. To restore blood pressure in selected hypotensive states.
   b. As a bronchodilator in respiratory disorders.
   c. To stop bleeding on topical surfaces.
   d. As a local vasoconstrictor to prolong the effects of local anesthetics.

7. Metaproterenol (Alupent®) is indicated for use as a:
   a. Bronchodilator for bronchial asthma.
   b. Nasal decongestant.
   c. Treatment for narcolepsy.
   d. Cardiac stimulant.
8. Ephedrine is most commonly used as a (n):
   a. Cardiac stimulant.
   b. Bronchodilator.
   c. Peripheral vasoconstrictor.
   d. Intestinal stimulant.

9. Caution should be used if patients that use metaraminol have:
   a. Diabetes.
   b. Thyroid disease.
   c. Hypertension.
   d. All the above.

10. Tetrahydrozoline (Tyzine®) is commonly used as a:
    a. Nasal decongestant.
    b. Cardiac stimulant.
    c. Mydriatic.
    d. Vasopressor.

11. One side effect associated with oxymetazoline (Afrin®) is:
    a. Rebound congestion
    b. Loss of appetite.
    c. Cardiac arrhythmias.
    d. Hypertension.
12. Match the trade or generic name in Column A with its appropriate trade or generic name in Column B.

<table>
<thead>
<tr>
<th>Column A</th>
<th>Column B</th>
</tr>
</thead>
<tbody>
<tr>
<td>__________Xylometazoline®</td>
<td>a. Otrivin®</td>
</tr>
<tr>
<td>__________Levophed®</td>
<td>b. Metaraminol</td>
</tr>
<tr>
<td>__________Intropin®</td>
<td>c. Metaproterenol</td>
</tr>
<tr>
<td>__________Epinephrine</td>
<td>d. Dopamine</td>
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<tr>
<td>__________Aramine®</td>
<td>e. Terbutaline</td>
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<tr>
<td>__________Brethine®</td>
<td>f. Adrenalin</td>
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<tr>
<td>__________Neo-Synephrine®</td>
<td>g. Phenylephrine</td>
</tr>
<tr>
<td>__________Alupent®</td>
<td>h. Levarterenol</td>
</tr>
</tbody>
</table>

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 7

1. b Rapidly displacing the transmitter from its storage site to activate the receptor. (para 7-2b)

2. c Bronchodilation. (para 7-3b(2))

3. c Increased heart rate. (para 7-4c)

4. b Decreases motility and tone. (para 7-6a(1)(e))

5. d To restore blood pressure in selective hypotensive states. (para 7-6b(2))

6. b As a bronchodilator in respiratory disorders. (para 7-6c(2)(a))

7. a A bronchodilator for bronchial asthma. (para 7-6e(2))

8. b Bronchodilator. (para 7-6i(2))

9. d All the above. (para 7-6j(3))

10. a Nasal decongestant. (para 7-6l(1))

11. a Rebound congestion. (para 7-6n(3))

12. a Xylometazoline. (para 7-6m)
   h Levophed®. (para 7-6b)
   d Intropin®. (para 7-6d)
   f Epinephrine. (para 7-6a)
   b Aramine®. (para 7-6j)
   e Brethine®. (para 7-6g)
   g Neo-Synephrine®. (para 7-6k)
   c Alupent®. (para 7-6e)

End of Lesson 7
LESSON ASSIGNMENT

LESSON 8
Adrenergic Blocking Agents.

TEXT ASSIGNMENT
Paragraphs 8-1 through 8-5.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

8-1. Given a group of statements, select the statement that best describes one of the mechanisms of actions of adrenergic blocking agents.

8-2. Given one of the following categories of drugs: alpha-blockers or beta-blockers and a group of statements, select the statement that best describes the mechanism by which that category of drugs produces its effects.

8-3. Given the trade and/or generic name of an adrenergic blocking agent, classify that agent as either an alpha or beta blocker.

8-4. Given the trade and/or generic name of an adrenergic blocking agent and a group of pharmacological actions, indications/uses, and side effects, select the action(s), indication(s)/use(s), and side effect(s) associated with that agent.

8-5. Given the trade or generic name of an adrenergic blocking agent and a group of trade and generic names of drugs, select the appropriate trade or generic name for the stated drug.

SUGGESTION
After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 8
ADRENERGIC BLOCKING AGENTS

8-1. INTRODUCTION TO ADRENERGIC BLOCKING AGENTS

a. In the last lesson, the topic of adrenergic (sympathomimetic) agents was discussed. As you will recall, this group of drugs produces effects like those produced by epinephrine.

b. This lesson will focus on the topic of adrenergic blocking agents. This group of agents blocks or interferes with the types of responses typically caused by the transmitters of the adrenergic (sympathetic) nervous system. Adrenergic blocking agents are sometimes referred to as sympatholytic agents.

8-2. GENERAL MECHANISMS OF ACTION OF ADRENERGIC BLOCKING AGENTS

There are two basic categories of mechanisms of action demonstrated by adrenergic blocking agents.

a. Some adrenergic blocking agents inhibit the synthesis, storage, or release of norepinephrine. Therefore, less norepinephrine is available to the receptors to produce its effects (adrenergic stimulation).

b. Other adrenergic blocking agents inhibit the reaction between norepinephrine and the receptor.

8-3. PRINCIPAL TYPES OF ADRENERGIC RECEPTORS

a. **Alpha-Receptors.** Alpha-receptors produce salivation, sweating, and contraction of smooth muscle (except in the gastrointestinal tract).

b. **Beta-Receptors.** Beta-receptors increase the frequency and strength of the heartbeat and cause relaxation of smooth muscle (except in the gastrointestinal tract).
8-4. ALPHA ADRENERGIC BLOCKING AGENTS

Effects produced by these agents occur because the alpha-receptors are blocked while beta-receptors are still capable of producing their effects.

a. Phentolamine (Regitine®).

(1) Pharmacological actions.

(a) Phentolamine causes blockage of the alpha₁ receptors. This causes vasodilatation that results in decreased blood pressure.

(b) Phentolamine also causes blockage of alpha₂ receptors. This causes a release of norepinephrine. Since the normal effect of norepinephrine is blocked at the alpha₂ receptor, the effect of epinephrine on the cardiac beta-receptors occurs.

(2) Indication/use. Phentolamine is used to prevent or treat dermal necrosis and sloughing caused by the extravasation (administration outside the vein) of norepinephrine (levarterenol).

(3) Side effects. Phentolamine can cause side effects such as tachycardia, flushing, cardiac arrhythmias, and orthostatic hypotension.

b. Prazosin (Minipress®).

(1) Pharmacological actions. Prazosin is an antihypertensive agent that selectively blocks alpha₁ receptors. This drug produces vasodilation and reduces peripheral resistance, but it produces little effect upon cardiac output.

(2) Indications/uses. Prazosin is an antihypertensive agent.

(3) Cautions and warnings. This agent should be used caution with patients who have severe cardiac disease or a history of mental depression.

(4) Side effects. Side effects associated with the use of prazosin include dizziness, sudden fainting, drowsiness, and lack of energy.

c. Other alpha blockers include terazosin (Hytrin®) and doxazosin (Cardura®). They are used for hypertension.
8-5. BETA-ADRENERGIC BLOCKING AGENTS

Beta-adrenergic blocking agents block beta effects—cardiac rate and force of contraction, vasodilatation in skeletal muscles, hyperglycemia, and bronchodilatation.

a. Propranolol (Inderal®).

(1) Pharmacological action. Propranolol blocks both beta_1 and beta_2 receptors.

(2) Indications/uses. Propranolol is used to treat a variety of conditions. Its uses are listed below:

(a) Antianginal agent. It lessens the heart’s need for oxygen because it slows the heart rate. With a slower heart rate, there is decreased need for oxygen and the angina pain diminishes.

(b) Antiarrhythmic agent.

(c) Antihypertensive agent.

(d) Suppressant agent (in the treatment of migraine headaches)

(3) Cautions and warnings. Propranolol should not be administered to patients who have bronchial asthma, cardiogenic shock, or sinus bradycardia. It should be used in caution with patients who have a history of allergies, diabetes mellitus, congestive heart failure, and emphysema. It is important to note that the abrupt withdrawal of this agent with patients who have heart disease (that is, angina) can cause arrhythmias or myocardial infarction (heart attack). This occurs because the sympathetic tone is adjusted to the blockage (probably by producing extra amounts of norepinephrine); thus, when the blockage is withdrawn, the heart cannot tolerate the extra norepinephrine that is present.

(4) Side effects. Side effects that can be produced by propranolol include dizziness or lightheadedness, very slow pulse, mental confusion or depression, cold hands, and numbness of the toes or fingers.

b. Metoprolol Tartrate (Lopressor®).

(1) Pharmacological actions. Metoprolol is a somewhat selective beta_1 blocker.

(2) Indication. Metoprolol is used as an antihypertensive agent.

(3) Side effects. Side effects associated with this agent include dizziness or drowsiness, mental depression, and hallucinations.
c. **Atenolol (Tenormin®).**

   (1) **Pharmacological actions.** Atenolol is a selective beta1 blocker; its long half-life permits once daily dosing.

   (2) **Indications.** Atenolol is used as an antihypertensive agent and for the treatment of angina pectoris because of coronary atherosclerosis.

   (3) **Side effects.** Side effects include dizziness, drowsiness, and some mental depression, but less than that of other agents.

d. **Timolol (Timoptic®).**

   (1) **Pharmacological actions.** Timolol has both beta1 and beta2 blocking activity.

   (2) **Indications.** The oral tablets are used as an anti-hypertensive agent. The eye drops are used for glaucoma.

   (3) **Side effects.** Possible side effects include dizziness, drowsiness, hallucinations, fatigue, slow pulse, confusion, depression, and cold hands and feet.

*Continue with Exercises*
EXERCISES, LESSON 8

INSTRUCTIONS: Answer the following exercises by marking the lettered response which best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which of the following statements best describes one of the mechanisms of action of adrenergic blocking agents?
   a. The production of excessive levels of acetylcholinesterase.
   b. The inhibition of the reaction between norepinephrine and the receptor.
   c. The inhibition of the synthesis, storage, or release of acetylcholine.
   d. The production of substances that produce physiological effects the opposite of norepinephrine.

2. Select the statement that best describes how alpha-adrenergic blocking agents produce their effects.
   a. The alpha-receptors are blocked and this allows the parasympathetic nervous system to produce its effects.
   b. The alpha-receptors are blocked while the beta-receptors still produce their effects.
   c. The alpha-receptors as well as the beta1 receptors are blocked, but the beta2 receptors still produce their effects.
   d. The alpha-receptors are blocked and the effects of the beta-receptors are antagonized.
3. Prazosin is used as:
   a. An antianginal agent.
   c. An antihypertensive agent.
   d. A vasodilator.

4. Side effect(s) commonly associated with phentolamine (Regitine®) include:
   a. Bradycardia.
   b. Cardiac arrhythmias.
   c. Sudden fainting.
   d. Extremely slow pulse rate.

5. Select the side effect(s) commonly associated with propranolol.
   a. Very slow pulse.
   b. Mental confusion.
   c. Dizziness.
   d. All the above.

6. Metoprolol tartrate is used as a(n):
   a. Antianginal agent.
   b. Antihypertensive.
   c. Means to prevent or treat dermal necrosis and sloughing caused by the extravasation of norepinephrine.
7. The drug prazosin is classified as a(n):
   a. Alpha-blocker.
   b. Beta-blocker.

8. The trade name of prazosin is:
   a. Minipress®.
   b. Inderal®.
   c. Lopressor®.
   d. Prapressor®.

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 8

1. b The inhibition of the reaction between norepinephrine and the receptor.  
   (para 8-2)

2. b The alpha-receptors are blocked while the beta-receptors still produce their effects.  
   (para 8-4)

3. c An antihypertensive agent.  (para 8-4)

4. b Cardiac arrhythmias.  (para 8-4a(3))

5. d All the above.  (para 8-5a(4))

6. b Antihypertensive.  (para 8-5b(2))

7. a Alpha-blocker.  (para 8-4b)

8. a Minipress®.  (para 8-4b)

End of Lesson 8
LESSON ASSIGNMENT

LESSON 9

Cholinergic Agents.

TEXT ASSIGNMENT

Paragaphs 9-1 through 9-6.

LESSON OBJECTIVES

After completing this lesson, you should be able to:

9-1. Given a group of statements, select the statement that best describes the term cholinergic agent.

9-2. Given a group of chemical transmitters, select the name of the chemical transmitter that acts at both the preganglionic synapse and the effector organ in relation to the cholinergic nervous system.

9-3. Given the name of a part of the body and a group of effects, select the effect(s) produced on that part of the body by the cholinergic nervous system.

9-4. Given the name of one of the types of cholinergic agents and a group of statements, select the statement that best describes that type of agent.

9-5. From a group of statements, select the statement that best describes the difference between reversible cholinesterase inhibitors and irreversible cholinesterase inhibitors.

9-6. Given the trade and/or generic name of a cholinergic agent and a group of indications/uses, cautions and warnings, side effects, or patient warning statements, select the indication/use, caution and warning, side effect, or patient warning statement that applies to that drug.

9-7. Given the trade or generic name of a cholinergic drug and a group of trade and/or generic names of drugs, select the trade or generic name of the given drug.

SUGGESTION

After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 9

CHOLINERGIC AGENTS

9-1. INTRODUCTION

Cholinergic (parasympathomimetic) agents are drugs which when administered will mimic the action of acetylcholine or normal parasympathetic stimulation. As you will remember (lesson 6), the parasympathetic nervous system is responsible for bringing the body back to normal after the fight or flight response. The parasympathetic (cholinergic) nervous system is responsible for maintaining the daily functions performed within the body. This division of the autonomic nervous system serves to conserve energy.

9-2. REVIEW OF THE PHYSIOLOGY OF THE CHOLINERGIC (PARASYMPATHETIC) NERVOUS SYSTEM

The cholinergic (parasympathetic) nervous system is stimulated by the hypothalamus. This nervous system has long preganglionic fibers and short postganglionic fibers (see Figure 9-1). The short postganglionic fibers are usually located within the effector organ.

![Figure 9-1. The cholinergic (parasympathetic) nervous system.](image)
9-3. CHEMICAL TRANSMISSION IN THE CHOLINERGIC (PARASYMPATHETIC) NERVOUS SYSTEM

The chemical transmitter at both the preganglionic synapse and at the effector organ is acetylcholine. Transmission of impulses is terminated by the destruction of acetylcholine by the enzyme acetylcholinesterase.

9-4. EFFECTS PRODUCED BY THE CHOLINERGIC NERVOUS SYSTEM

The general effects of parasympathetic stimulation are conservation and restoration of energy. The specific effects of the cholinergic nervous system are listed below:

a. **Eye (Pupil)**. Contraction of the pupil (miosis) is produced by cholinergic stimulation.

b. **Heart**. A decrease in the heart rate and a slight increase in the contraction strength of the heart are cholinergic effects.

c. **Bronchi**. The bronchi are contracted by cholinergic stimulation.

d. **Blood Vessels**. The blood vessels of the skin and mucosa and skeletal muscles are dilated by stimulation by the cholinergic nervous system.

e. **Salivary Glands**. Cholinergic stimulation of the salivary glands leads to profuse, watery secretions.

f. **Stomach**. Cholinergic stimulation of the stomach leads to increased motility and tone and relaxed (usually) sphincters.

g. **Intestines**. Increased intestinal motility and tone and stimulated secretion of intestinal fluids are products of cholinergic stimulation.

h. **Urinary Bladder**. Contraction of the bladder wall and relaxation of the sphincter are products of cholinergic stimulation. The result is that urination is stimulated.

9-5. THERAPEUTIC USE OF CHOLINERGIC AGENTS

The cholinergic (parasympathomimetic) agents mimic the action of acetylcholine. These drugs represent a relatively small class of therapeutic agents with very specific clinical indications. For the most part, cholinergic agents are used in the treatment of glaucoma (see lesson 5) and in the treatment of certain urinary tract disorders (they help produce urination and the emptying of the bladder).
9-6. TYPES OF CHOLINERGIC AGENTS

a. Direct Acting Agents. Direct acting drugs have molecules that resemble acetylcholine molecules; thus, they have a direct action on the acetylcholine receptor sites of the postganglionic synapse. These drugs are usually specific in their site of action. An example of a direct acting agent is pilocarpine hydrochloride (Isopto-Carpine®).

(1) Pilocarpine hydrochloride (Isopto-Carpine®). Pilocarpine hydrochloride is a direct acting parasympathomimetic. It is used in the treatment of glaucoma. It causes the contraction of the iris sphincter muscle; this results in miosis (pupil constriction). Pilocarpine can produce the following side effects: muscle tremors, unusual increase in perspiration, unusual watering of the mouth, blurred vision, and eye pain. The patient instilling this medication into the eye should be informed that the drug could cause a change in his near or distant vision. Therefore, he should ensure that his vision is clear before he drives or does any jobs that require him to see well.

(2) Bethanecol chloride (Urecholine®). Bethanecol chloride is a direct acting parasympathomimetic. It is used in the treatment of non-obstructive urinary retention. Bethanecol can produce side effects such as shortness of breath, blurred vision, and dizziness. This drug should not be administered to patients who have bronchial asthma. Patients should be instructed to take the drug on an empty stomach (one or two hours before meals) in order to decrease the probability of having stomach upset.

b. Indirect Acting Agents. Indirect acting agents alter or inhibit the activity of acetylcholinesterase. Since the activity of acetylcholinesterase is inhibited or altered, the acetylcholine levels will increase causing cholinergic activity. The indirect acting agents form a complex with acetylcholinesterase. Based upon the type of complex they form, the agents are placed into two groups:

(1) Reversible cholinesterase inhibitors. These agents form a temporary complex with acetylcholinesterase.

(a) Neostigmine (Prostigmin®). Neostigmine is a reversible indirect acting acetylcholinesterase inhibitor. This drug is used in the treatment of myasthenia gravis, a condition characterized by muscle weakness and fatigue. The drug is also used to treat urinary bladder atony. Side effects associated with this agent are diarrhea, abdominal cramps, increased salivation, and increased bronchial secretions.

(b) Physostigmine (Eserine®). Physostigmine is a reversible indirect acting acetylcholinesterase inhibitor. It is used in the treatment of glaucoma. Side effects associated with the use of physostigmine include loss of bladder control, muscle weakness, unusual increase in perspiration, blurred vision or change in distant vision, and headache. The patient using this medication should be warned that it can cause a change in near or distant vision; therefore, the patient should ensure that his vision is clear before he drives or performs any job which requires that he see well.
(2) **Irreversible cholinesterase inhibitors.** These agents form a stable complex with acetylcholinesterase.

(a) Echothiophate Iodide (Phospholine Iodide®). Echothiophate iodide is an irreversible indirect acting acetylcholinesterase inhibitor. It is used in the treatment of glaucoma. The side effects associated with echothiophate include loss of bladder control, muscle weakness, and shortness of breath. You should note that this medication is supplied as a dry powder with diluent. The diluent and the dry powder must be mixed just before you dispense it. The shelf life of the prepared solution can be extended by refrigeration. Since echothiophate may cause changes in the patient’s vision, the patient should be warned to insure his vision is clear before he drives or performs any job that requires him to have clear vision.

(b) Demecarium bromide (Humorsol®). Demecarium bromide is an irreversible, indirect acting acetylcholinesterase inhibitor. It is used in the treatment of glaucoma. Side effects that can occur while taking this medication include loss of bladder control, muscle weakness, and shortness of breath. Since this medication may cause changes in the patient’s vision, the patient should be warned to ensure his vision is clear before he drives or performs any job which requires him to have clear vision.

*Continue with Exercises*
EXERCISES, LESSON 9

INSTRUCTIONS: Answer the following exercises by marking the lettered response which best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. Which statement best describes the term cholinergic agent?
   a. Drugs which when administered will mimic the action of epinephrine or normal parasympathetic stimulation.
   b. Drugs which when administered will mimic the action of acetylcholine or normal parasympathetic stimulation.
   c. Drugs that produce the same effects as the adrenergic blocking drug.
   d. Drugs that antagonize the effects of the adrenergic nervous system.

2. Select the effect of cholinergic stimulation upon the eye (pupil).
   a. No effect.
   b. Mydriasis.
   c. Miosis.

3. Select the effect of cholinergic stimulation on the bronchi.
   a. No effect.
   b. Dilation.
   c. Contraction.
4. Select the effect of cholinergic stimulation on the urinary bladder.
   a. No effect.
   b. Urination is stimulated.
   c. Urination is suppressed.

5. Which statement best describes direct acting cholinergic agents?
   a. These agents alter or inhibit the activity of acetylcholinesterase.
   b. These agents form a complex with acetylcholinesterase thus producing cholinergic activity.
   c. These agents reduce the activity of epinephrine in order to enhance the effects of cholinergic stimulation.
   d. These agents have molecules that resemble acetylcholine molecules and produce action on the acetylcholine receptor sites of the postganglionic synapse.

6. Pilocarpine hydrochloride is used in the treatment of:
   a. Nonobstructive urinary retention.
   b. Glaucoma.
   c. Myasthenia gravis.
   d. Obstructive urinary retention.

7. Neostigmine (Prostigmine®) is used in the treatment of:
   a. Nonobstructive urinary retention.
   b. Glaucoma.
   c. Myasthenia gravis.
   d. Obstructive urinary retention.
8. Select the side effect(s) associated with the use of physostigmine.
   a. Loss of bladder control.
   b. Unusual decrease in perspiration.
   c. Dryness of the mouth and other mucous membranes.
   d. All the above.

9. Match the trade or generic name in Column A with its appropriate trade or generic name in Column B.

<table>
<thead>
<tr>
<th>Column A</th>
<th>Column B</th>
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<tr>
<td>Urecholine®</td>
<td>a. Physostigmine</td>
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<td>Phospholine iodide®</td>
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<td>Eserine®</td>
<td>d. Floropryl®</td>
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<td></td>
<td>e. Humorsol®</td>
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<td></td>
<td>f. Pilocarpine hydrochloride</td>
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SOLUTIONS TO EXERCISES, LESSON 9

1. b Drugs which when administered will mimic the action of acetylcholine or normal parasympathetic stimulation. (para 9-1)

2. c Miosis. (para 9-4a)

3. c Contraction. (para 9-4c)

4. b Urination is stimulated. (para 9-4h)

5. d These agents have molecules which resemble acetylcholine molecules and produce action on the acetylcholine receptor sites of the postganglionic synapse. (para 9-6a)

6. b Glaucoma. (para 9-6a(1))

7. c Myasthenia gravis. (para 9-6b(1)(a))

8. a Loss of bladder control. (para 9-6b(1)(b))

9. c Urecholine®. (para 9-6a(2))
   e Demecarium bromide. (para 9-6b(2)(b))
   b Phospholine iodide®. (para 9-6b(2)(a))
   a Eserine®. (para 9-6b(1)(b))

End of Lesson 9
LESSON ASSIGNMENT

LESSON 10
Cholinergic Blocking Agents (Anticholinergic Agents).

TEXT ASSIGNMENT
Paragraphs 10-1--10-4.

LESSON OBJECTIVES
After completing this lesson, you should be able to:

10-1. From a list of statements, select the statement that best describes how the cholinergic blocking agents produce their effects.

10-2. Given a group of drug categories, select the alternate name sometimes given to cholinergic blocking agents.

10-3. Given the name of a part of the body and a list of pharmacological effects, select the effect of the cholinergic blocking agents on that part.

10-4. Given a list of clinical uses, select the clinical use(s) of the cholinergic blocking agents.

10-5. Given the trade and/or generic name of cholinergic blocking agent and a group of uses, side effects, cautions and warnings, or instructions to the patient, select the use(s), side effect(s), caution(s) and warning(s), and instruction(s) to the patient which are specific to the given drug.

10-6. Given the trade or generic name of a cholinergic blocking agent and a list of trade and/or generic names of drugs, select the trade or generic name for the given drug.

SUGGESTION
After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 10

CHOLINERGIC BLOCKING AGENTS (ANTICHOLINERGIC AGENTS)

10-1. INTRODUCTION

In the last lesson, the topic of cholinergic agents was discussed. Now the topic of cholinergic blocking agents (anticholinergic agents) will be discussed. Cholinergic blocking agents block or reduce normal parasympathetic innervation at the postganglionic synapse (see Figure 10-1). Drugs in this category are sometimes referred to as parasympatholytics.

Figure 10-1. The postganglionic synapse--the site of action of the cholinergic blocking agents.

10-2. PHARMACOLOGICAL EFFECTS OF THE CHOLINERGIC BLOCKERS

The cholinergic blockers produce specific effects on certain organs in the body. These effects are:

a. **Stomach/Intestines.** The effect of the cholinergic blockers on the stomach and intestines is decreased activity.

b. **Salivary Glands.** The cholinergic blockers produce a drying effect.

c. **Eye (Pupil).** The cholinergic blockers produce dilation of the pupil (mydriasis).
d. **Urinary Bladder.** The cholinergic blockers produce urinary retention.

e. **Heart.** Increased heart rate is the effect produced on the heart by the cholinergic blockers.

f. **Bronchi.** The cholinergic blockers dilate the bronchi.

### 10-3. CLINICAL USES OF THE CHOLINERGIC BLOCKERS

The clinical uses of these drugs are based upon their normal pharmacological actions. Their most common clinical uses are listed below:

a. **Antispasmodics.** Antispasmodics are used to slow the motility of the gastrointestinal (GI) tract and reduce gastric secretions. Antispasmodics are commonly prescribed with other types of medications for patients who have ulcers or other GI disorders.

b. **Mydriatics/Cycloplegics.** These agents are used to produce pupil dilation (mydriasis) and to paralyze the muscles of accommodation (cycloplegia). In other words, these drugs prevent the eye from focusing. Medications used for these purposes are commonly used following ocular surgery and for certain types of eye examinations.

c. **Antiparkinsonism Agents.** These drugs are used to treat Parkinsonism, a condition characterized by excessive cholinergic activity in the brain. This condition results in an inability to perform fine motor movements.

d. **Cold Preparations.** Many over-the-counter and legend cold preparations contain cholinergic blocking agents. These cholinergic blockers help to dry secretions (that is, help to “dry” a runny nose).

e. **Antidote for Nerve Gas Poisoning.** Some cholinergic blocking drugs are used as antidotes for persons who have been poisoned by nerve gases (irreversible cholinesterase inhibitors). Certain cholinergic blocking agents are also used as antidotes for certain insecticides (irreversible cholinesterase inhibitors).

f. **Treatment of Bradycardia (Slow Heart Rate).** Atropine sulfate, a cholinergic blocker, is sometimes administered to a patient following cardiac arrest to increase the heart rate. By blocking cholinergic innervation to the heart, sympathetic nerves are allowed to override and increase the rate of the heart.

g. **Preoperative Medication.** Certain cholinergic blockers are administered to patients immediately before their undergoing a surgical procedure. In this case, the cholinergic blockers help to dry secretions in the mucous membranes.
10-4. EXAMPLES OF CHOLINERGIC BLOCKING AGENTS

a. Atropine. Atropine is a classic example of the cholinergic blockers. It is found alone and in combination with a wide-variety of other drugs. As an ophthalmic preparation (Isopto-Atropine®), it is used as a cycloplegic and as a mydriatic. Side effects associated with the use of atropine are unsteadiness, hallucinations, unusual dryness of mouth, and increased sensitivity of eyes to light. Patients who have glaucoma should use caution when using this preparation.

b. Scopolamine. Scopolamine is another classic example of the cholinergic blockers. Like atropine, scopolamine is found in a variety of medications. It is found in some over-the-counter cold medications. It is present in these products because of the drying effect it produces. In its ophthalmic form it is used as a mydriatic and as a cycloplegic. Side effects that can be caused by this drug include unsteadiness, fever, flushing, or redness of the face, hallucinations, and increased sensitivity of the eyes to light. Patients who have glaucoma should use this preparation with caution.

c. Homatropine Hydrobromide (Isopto-Homatropine®). This ophthalmic preparation is used as a mydriatic and as a cycloplegic. The side effects associated with this drug are the same as those associated with atropine and scopolamine (above). Patients who have glaucoma should use this preparation with caution.

d. Cyclopentolate (Cyclogyl®). This cholinergic blocker is used as a mydriatic and as a cycloplegic. Cyclopentolate can produce side effects such as unsteadiness, fever, redness of the face, hallucinations, or increased thirst. Patients who have glaucoma should use Cyclopentolate with caution.

e. Belladonna Alkaloids with Phenobarbital (Donnatal®). This preparation is used as an antispasmodic. Side effects associated with this agent are eye pain (from increased intraocular pressure), constipation, drowsiness, and dryness of the mouth. Patients taking this preparation should be informed of several things. Do not drink alcohol while taking Donnatal® (because of central nervous system depression). Never take this preparation within one hour of taking antacid (the effectiveness of the Donnatal® will be reduced). This drug may cause drowsiness in some patients; therefore, know how the drug will affect him before he drives or performs any job that requires alertness. Belladonna alkaloids sometimes make patients perspire less (this results in increased body temperature); therefore, do not become overheated because of excessive exercise or hot weather.

f. Propantheline Bromide (Pro-Banthine®). This agent is used in the treatment of peptic ulcers. Side effects associated with this drug include constipation, difficult urination (because of decreased muscle tone of the urinary bladder), eye pain (from increased intraocular pressure), and dizziness. Patients taking this medication should be informed of several things. Propantheline can produce drowsiness in some patients; therefore, they should ensure they know how the medicine will affect them before they drive or perform activities that require mental alertness. Sometimes
patients taking this medication perspire less; therefore, they should ensure they do not become overheated because of excessive exercise or hot weather. Patients that have glaucoma or severe heart disease should use this drug with caution.

g. **Belladonna Tincture.** This preparation is used for its antispasmodic effect on the gastrointestinal tract (effect produced chiefly by its atropine content). Side effects associated with this agent include dryness of the mouth, dizziness, and constipation.

h. **Dicyclomine (Bentyl®).** This preparation is used to relieve smooth muscle spasm of the gastrointestinal tract. Side effects that can be caused by this drug include constipation (caused by decreased peristalsis), difficult urination, and dizziness. Persons taking this drug should be cautioned against taking alcohol or other central nervous system (CNS) depressants.

i. **Trihexyphenidyl (Artane®).** This drug is used in the treatment of parkinsonism. Side effects that can be caused by trihexyphenidyl include constipation, difficult urination, dizziness, dry mouth, and reduced perspiration. Patients taking this preparation should be told several things. Do not take with alcohol or other central nervous system depressants. Some patients perspire less; therefore do not become overheated because of exercise or hot weather.

j. **Benztropine (Cogentin®).** Benztropine is used in the treatment of parkinsonism. The side effects and patient instructions for trihexyphenidyl (Artane®), above, also apply to benztropine.

**IMPORTANT NOTE:** Sometimes trihexyphenidyl (Artane®) and benztropine (Cogentin®) will be prescribed with certain phenothiazine tranquilizers to help reduce some of the centrally induced side effects produced by the tranquilizers.

**NOTE:** Drugs listed in k and l below are both antiparkinsonism drugs; however, they are NOT cholinergic blockers.

k. **Levodopa (Larodopa®).** This drug is used in the treatment of parkinsonism. Side effects associated with this agent include depression, difficult urination, unusual and uncontrolled movements of the body (that is, face, tongue, and arms), and mood changes. Patients taking this drug should be informed of several things. Take this medication with solid food to decrease the possibility of stomach upset. This drug may cause drowsiness in some patients; therefore, know how the drug will affect him before he drives or performs any job that requires alertness. This drug may cause dizziness or fainting in some patients; therefore, persons taking the drug should get up slowly from a lying or sitting position.
I. Carbidopa and Levodopa (Sinemet®). This preparation is used in the treatment of parkinsonism. Side effects that can be caused by this medication include mental depression, mood changes, unusual and uncontrolled movements of the body (that is, face, tongue, arms), and difficult urination. Patients taking this product should be informed of several things. Patients need to take this medication with solid food to decrease the possibility of stomach upset. This drug may cause drowsiness in some patients; therefore, know how the drug will affect him before he drives or performs any job that requires alertness. This drug may cause dizziness or fainting, persons taking the drug should get up slowly from a lying or sitting position.

Continue with Exercises
EXERCISES, LESSON 10

INSTRUCTIONS: Answer the following exercises by marking the lettered response which best answers the question.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers. For each exercise answered incorrectly, reread the material referenced with the solution.

1. The cholinergic blocking agents produce their effects by:
   a. Forming a stable complex with acetylcholine.
   b. Blocking or reducing normal parasympathetic innervation at the postganglionic synapse.
   c. Increasing the level of epinephrine or norepinephrine at the receptor site.
   d. Preventing the acetylcholinesterase from destroying the acetylcholine at the receptor site.

2. What other name is sometimes given to the cholinergic blocking agents?
   a. Parasympathomimetics.
   b. Para-adrenerlytics.
   c. Parasympatholytics.
   d. Paracholinomimetics.

3. The effect of the cholinergic blockers on the urinary bladder is:
   a. Urinary concentration.
   b. Urinary stimulation.
   c. Urinary retention.
4. The effect of the cholinergic blockers on the eye (pupil) is:
   a. Miosis (contraction of the pupil).
   b. Mydriasis (dilation of the pupil).

5. Select the clinical use(s) for the cholinergic blocking agents.
   a. Drying agents (in cold preparations).
   b. Antiparkinsonism agents.
   c. Antispasmodics.
   d. All the above.

6. Select the clinical use of Isopto-Atropine®.
   a. Antispasmodic.
   b. Cycloplegic.
   c. Treatment of peptic ulcer.
   d. Treatment of parkinsonism.

7. Persons who take belladonna alkaloids with phenobarbital (Donnatal®) should be cautioned:
   a. Not to take the medication within one hour of taking antacid.
   b. Not to exercise while taking the drug.
   c. Not to take the medication with food or milk.
   d. Not to take other medications while they are taking this product.
8. The product Bentyl® (dicyclomine) is used in the treatment of:
   a. Peptic ulcers.
   b. Glaucoma.
   c. Parkinsonism.
   d. Muscle spasms in the GI tract.

9. Select the side effect(s) associated with the use of trihexphenidyl.
   a. Loss of bladder control.
   b. Unusual increase in perspiration.
   c. Dry mouth.
   d. Muscle weakness.

10. Persons taking levodopa (Larodopa®) should be informed that:
    a. They should arise slowly from a sitting or lying position since the drug may cause fainting.
    b. They should take the drug on an empty stomach (one or two hours before meals) to decrease the likelihood of stomach upset.
    c. They should not take the drug with milk or antacid.
11. Match the trade or generic name of Column A with its appropriate trade or generic name in Column B.

<table>
<thead>
<tr>
<th>Column A</th>
<th>Column B</th>
</tr>
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<tbody>
<tr>
<td>Trihexyphenidyl</td>
<td>a. Cyclopentolate</td>
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<td>Bentyl®</td>
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<td>Cyclogyl®</td>
<td>c. Cogentin®</td>
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<td>Benztrapine</td>
<td>d. Dicyclomine</td>
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<td>Sinemet®</td>
<td>e. Artane®</td>
</tr>
</tbody>
</table>

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 10

1. b  Blocking or reducing normal parasympathetic innervation at the postganglionic synapse.  (para 10-1)

2. c  Parasympatholytics.  (para 10-1)

3. c  Urinary retention.  (para 10-2d)

4. b  Mydriasis (dilation of the pupil).  (para 10-2c)

5. d  All the above.  (paras 10-3a, c, and d)

6. b  Cycloplegic.  (para 10-4a)

7. a  Not to take the medication within one hour of taking antacid.  (para 10-4e)

8. d  Muscle spasms in the G.I tract.  (para 10-4h)

9. c  Dry mouth.  (para 10-4i)

10. a  They should arise slowly from a sitting or lying position since the drug may cause fainting.  (para 10-4k)

11. e  Trihexyphenidyl  (para 10-4i)
      d  Bentyl®  (para 10-4h)
      a  Cyclogy®  (para 10-4d)
      c  Benztropine.  (para 10-4j)
      b  Sinemet®.  (para 10-4l)

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End of Lesson 10
This Drug Pronunciation Guide was developed to help you to learn how the trade and generic names of commonly prescribed medications are frequently pronounced. Not all the drugs in the guide are discussed in this subcourse. Remember, it is not enough to be able to know the uses, indications, cautions and warnings, and contraindications for a drug—you must also know how to pronounce that drug's name.

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<td>Probenecid (Pro-ben’-eh-sid)</td>
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<td>Bonine (Bo’-neen)</td>
<td>Meclizine (Mek’-li-zeen)</td>
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<td>Ergotamine (Er-got’-a-meen) and Caffeine (Kaf’-feen)</td>
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<td>Calamine (Kal’-a-mine)</td>
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<td>Catapres (Kat’-a-press)</td>
<td>Clonidine (Klo’-ni-deen)</td>
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<td>CeeNu (See’-new)</td>
<td>Lomustine (Lo-mus’-teen)</td>
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<td>Chlorpheniramine  (Klor-fen-it’-a-meen)</td>
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<td>Clomid (Klo’-mid)</td>
<td>Clonaphene (Klo’-mi-feen)</td>
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<td>Clonopin (Klo-o-pin)</td>
<td>Clonazepam (Klo-na’-ze-pam)</td>
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<td>Codeine (Ko’-deen)</td>
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<td>Cogentin (Ko-jen’-tin)</td>
<td>Benztropine (Benz’-tro-pee)</td>
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<td>Colace (Ko’-lace)</td>
<td>Dioctyl(Di-ok’-til) Sodium (So’-dee-um)</td>
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<td>Sulfosuccinate (Sul-fo-suk’-si-nate)</td>
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<td>Compazine (Kom’-pa-zeen)</td>
<td>Prochlorperazine  (Pro-klor-per’-a-zeen)</td>
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<td>Cordran (Kor’-dran)</td>
<td>Flurandrenolide (Floor-an-dren’-o-lide)</td>
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<td>Coumadin (Koo’-mah-din)</td>
<td>Warfarin (War’-fah-rin)</td>
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<td>Cloroquine (Klor’-o-kwin) and Primaquine (Prim’-a-kwin)</td>
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<td>Cyclopentolate (Si-klo-pen’-to-late)</td>
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<td>Liothyronine (Li-o-thy-ro-nee)</td>
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<td>Cyclophosphamide (Si-klo-fos’-fa-mide)</td>
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<td>Propoxyphene (Pro-pok’-se-feen) and Acetaminopen (As-et-am’-ino-fen)</td>
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<td>Propoxyphene (Pro-pok-se-feen)</td>
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<td>Dexamethasone (Dek-sa-meth’-ah-sone)</td>
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<td>Prednisone (Pred’-ni-sone)</td>
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<td>Meperidine (Meh-pair’-i-deen)</td>
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<td>Dextroamphetamine (Deks-tro-am-fet’-a-meen)</td>
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<td>Diabinese (Di-ab’-i-nees)</td>
<td>Chlorpropamide (Klor-prop’-a-mide)</td>
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<td>Diethylstilbestrol (Di-eth-il-stil-bes’-trol)</td>
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<td>Dilantin (Di-lan’-tin)</td>
<td>Phenytoin (Fen’-i-toin)</td>
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<td>Dilaudid (Di-law’-did)</td>
<td>Hydromorphone (Hy-dro-more’- fon)</td>
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<td>Dimetane (Di’-meh-tane)</td>
<td>Brompheniramine (Brom-fen-ir’-a-meen)</td>
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<td>Dimetapp (Di'-meh-tap)</td>
<td>Brompheniramine (Brom-fen-ir’a-meen) and Phenylephrine (Fen-il-ef’-rin) and Phenylpropanolamine (Fen-il-pro-pan-ol’a-meen)</td>
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<td>Dexbrompheniramine (Deks-brom-fen-ir’a-meen) and Pseudoephedrine (Soo-do-e-fed’-rin)</td>
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<td>Methadone (Meth’a-done)</td>
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<td>Aluminum (Ah-loo’-mi-num) and Acetate (As’e-tate)</td>
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<td>Donnatal (Don’-na-tal)</td>
<td>Belladonna (Bel-la-don’-na) and Alkaloids (Al’-ka-loids) and Phenobarbital (Feen-o-barb’-i-tal)</td>
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<td>Bisacodyl (Bis-a’-ko-dil)</td>
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<td>Triamterene (Tri-am’-ter-een) and Hydrochlorothiazide (Hy-dro-klor-o-thi’-a-zide)</td>
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<td>Acetohexamide (As’e-to-heks’-a-mide)</td>
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<td>Triamterene (Tri-am’-ter-een)</td>
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<td>Fluorouracil (Flo-ro-ur’-ah-sil)</td>
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<td>Amitriptyline (Am-i-trip’-til-een)</td>
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<td>Elixir Terpin (Ter’-pin) Hydrate</td>
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<td>Codeine (Ko’-deen) and Aspirin (As’e-per-in)</td>
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<td>Erythromycin (E-rith-ro-mie’-sin)</td>
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<td>Equanil (Ek’-wa-nil)</td>
<td>Meprobamate (Me-pro-bam’-ate)</td>
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<td>Ergotamine (Er-got’a-meen)</td>
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<td>Ergonovine (Er-go-no’-veen)</td>
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<td>Hyrochlorothiazide (Hy-dro-klor-o-thi’-a-zide)</td>
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<td>Ferrous (Fer’-rus) and Gluconate (Glu’-con-ate)</td>
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<td>Metronidazole (Me-tro-ni'-dah-zole)</td>
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<td>Cyclobenzaprine (Si-klo-benz'-a-preen)</td>
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<td>Griseofulvin (Griz-e-o-ful'-vin)</td>
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<td>Suiphamethoxazole (Sul-fah-meth-oks'-ah-zole)</td>
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<td>Griseofulvin (Griz-e-o-ful'-vin)</td>
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<td>Ergotamine (Er-got'-a-meen)</td>
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<td>Haloperidol (Hal-o-pair'-i-dol)</td>
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<td>Hydrochlorothiazide (Hy-dro-klor-thi'-a-zide)</td>
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<td>Erythromycin (Er-ith-ro-mi'-sin)</td>
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<td>Estolate (Es'-to-late)</td>
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<td>Indomethacin (In-do-meth'-a-sin)</td>
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<td>Insulin (In'-sul-in)</td>
<td>Isoniazid (I-so-ni'-a-zid)</td>
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<td>Ismelin (Is'-meh-lin)</td>
<td>Cromolyn (Kro'-mo-lin)</td>
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<td>Cephalexin (Sef-ah-lek'-sin)</td>
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<td>Levodopa (Le-o-do'-pa)</td>
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<td>Amoxicillin (Ah-moks'-i-sil-in)</td>
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<td>Chlorambucil (Klor-ram'-bu-sil)</td>
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<td>(Klor-die-az-eh-pok'-side)</td>
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<td>Lidex (Lie'-deks)</td>
<td>Fluocinolone (Flo-o-sin'-o-nide)</td>
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<td>Diphenoxylate (Die-fen-ok'-si-late)</td>
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<td>Metoprolol (Met-o-pro'-lol)</td>
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<td>Mandelate (Man'-deh-late)</td>
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<td>Amethopterin (Ah-meth-op'-ter-in)</td>
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<td>Prazosin (Pra'-zo-sin)</td>
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<td>Minocycline (Mi-no-si'-kleen)</td>
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<td>Ethambutol (Eth-am'-bu-tol)</td>
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<td>Myleran (My-le-r-an)</td>
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<td>Primidone (Pri'-mi-done)</td>
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<td>Mysoline (My'-so-leen)</td>
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<td>Pentobarbital (Pen-to-barb'-i-tal)</td>
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<td>Phenylephrine (Fen-il-eh'-frin)</td>
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<td>Nitroglycerin (Ni-tro-gli'-ser-in)</td>
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<td>Chloral Hydrate (Klor'-al- Hy'-drate)</td>
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<td>Orphenadrine Citrate (Or-fen'-a-dreen)</td>
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<td>Norpace (Nor'-pace)</td>
<td>Disopyramide (Di-so-peer'-a-mide)</td>
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<td>Guaifenesin (Gwi-fen’-eh-sin), Phenylpropanolamine (Fen-il-pro-pan-o’-f-a-me'en), and Codeine (Ko’-deen)</td>
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<td>Nitro glycerin (Ni-tro-gli’-ser-in)</td>
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<td>Dibucaine (Die’-bu-kain)</td>
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<td>Hydrochlorothiazide (Hy-dro-klor-thi’-a-zide)</td>
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<td>Tolbutamide (Tol-bu’-tah-mide)</td>
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<td>Ornade (Or’-nade)</td>
<td>Chlorpheniramine (Klor-fen-ir’-a-me'en), Triprolidine (Tri-pro-li-deen) and</td>
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<td>Pseudoephedrine (Su-do-eh-fed’-rin)</td>
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<td>Chlorzoxazone (Klor-zok’-sa-zone)</td>
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<td>Oxytocin (Ok-see-tow’-sin)</td>
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<td>Tetracaine (Teh’-tra-kain)</td>
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<td>Estrogens (Es-tro-jens)</td>
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<td>Imipramine (Im-ip’-rah-me'en)</td>
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<td>Propantheline (Pro-pan’-the-leen)</td>
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<td>Phenazopyridine (Fen-ahs-o-per’-i-deen)</td>
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<td>Rifampin (Rie-fam’-pin)</td>
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<td>Magaidrate (Mag’-al-drade)</td>
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ANNEX -- Drug Pronunciation Guide | | A-1 |

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LESSON ASSIGNMENT

LESSON 1
The Respiratory System and Respiratory System Drugs.

ASSIGNMENT

Paragraphs 1-1--1-20.

TASKS
081-824-0001, Perform Initial Screening of a Prescription.

081-824-0026, Evaluate a Prescription.

081-824-0027, Evaluate a Completed Prescription.

081-824-0028, Issue Outpatient Medications.

LESSON OBJECTIVES
After you finish this lesson you should be able to:

1-1. Given a group of statements and one of the following terms: respiration, external respiration, or internal respiration, select the statement which best defines the given term.

1-2. Given a diagram of the human respiratory system and a list of names of the parts of the human respiratory system, match the name of its part with its proper location.

1-3. Given the name of one of the components of the human respiratory system and a group of statements, select the statement that best describes that component or its function.

1-4. From a group of statements, select the statement which best describes either costal (thoracic) or diaphragmatic (abdominal) breathing.

1-5. Given the name of a condition affecting the respiratory system and a group of statements, select the statement that best describes the given condition.
1-6. Given the name of a type of respiratory system drug (that is, antitussive agent) and a group of statements, select the statement that best describes that type of agent.

1-7. Given the trade or generic name of a respiratory system drug and a group of indications, uses, side effects, or patient precautionary statements, select the indication(s), use(s), side effect(s), or patient precautionary statement(s) for the given drug name.

1-8. Given the trade or generic name of a respiratory system drug and a group of trade and/or generic names, select the given drug’s corresponding trade or generic name.

SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 1
THE RESPIRATORY SYSTEM AND RESPIRATORY SYSTEM DRUGS

Section I. THE RESPIRATORY SYSTEM

1-1. INTRODUCTION

a. Respiration. Respiration is the exchange of gases between the atmosphere and the cells of the body. It is a physiological process. There are two types of respiration—external and internal. External respiration is the exchange of gases between the air in the lungs and blood. Internal respiration is the exchange of gases between the blood and the individual cells of the body.

b. Breathing. Breathing is the process that moves air into and out of the lungs. It is a mechanical process. There are two types of breathing in humans—costal (thoracic) and diaphragmatic (abdominal). In costal breathing, the major structure causing the movement of the air is the rib cage. In diaphragmatic breathing, interaction between the diaphragm and the abdominal wall causes the air to move into and out of the lungs.

1-2. COMPONENTS AND SUBDIVISIONS OF THE HUMAN RESPIRATORY SYSTEM

NOTE: See Figure 1-1 for an illustration of the human respiratory system.

a. Components. The components of the human respiratory system consist of air passageways and two lungs. Air moves from the outside of the body into tiny sacs in the lungs called alveoli (pronounced al-VE-oh-lie).

b. Main Subdivisions. The main subdivisions of the respiratory system may be identified by their relationship to the voice box or larynx. Thus, the main subdivisions are as follows:

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<th>FUNCTION</th>
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<tr>
<td>(1) SUPRALARYNGEAL STRUCTURES</td>
<td>cleanse, warm, moisten, and test inflowing air</td>
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<tr>
<td>(su-prah-lah-RIN-je-al)</td>
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<td>(2) LARYNX (voice-box)</td>
<td>controls the volume of inflowing air; produces selected pitch</td>
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<tr>
<td>(LARE-inks)</td>
<td>(vibration frequency) in the moving column of air</td>
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(3) **INFRALARYNGEAL STRUCTURES**  
(in-frah-lah-RIN-je-al)  
distribute air to the alveoli of the lung where the actual external respiration takes place.

Figure 1-1. The human respiratory system.
1-3. SUPRALARYNGEAL STRUCTURES (See Figure 1-2.)

a. External Nose. The external nose is the portion projecting from the face. Primarily cartilages support it. It has a midline divider called the nasal septum, which extends from the internal nose. Paired openings (nostrils lead to paired spaces (vestibules). Guard hairs in the nostrils filter inflowing air.

![Figure 1-2. Supralaryngeal structures.](image)

b. Nasal Chambers (Internal Nose). Behind each vestibule of the external nose is a nasal chamber. The two nasal chambers together form the internal nose. These chambers too are separated by the nasal septum.

(1) Mucoperiosteum. The walls of the nasal chambers are lined with a thick mucous-type membrane known as the mucoperiosteum. It has a ciliated epithelial surface and a rich blood supply, which provides warmth and moisture. At times, it may become quite swollen.

CILIATED = Provided with cilia (hair like projections that move fluids to the rear)
(2) **Conchae.** The lateral wall of each chamber has three scroll-like extensions into the nasal chamber, which help to increase the surface area exposed to the inflowing air. These scroll-like extensions are known as conchae.

CONCHA = sea shell  
CONCHA (singular), CONCHAE (plural)  
(pronounced KON -kah)

(3) **Olfactory epithelium.** The sense of smell is because of special nerve endings located in the upper areas of the nasal chambers. The epithelium containing the sensory endings is known as the olfactory epithelium.

(4) **Paranasal sinuses.** There are air “cells” or cavities in the skull known as paranasal sinuses. The paranasal sinuses are connected with the nasal chambers and are lined with the same ciliated mucoperiosteum. Thus, these sinuses are extensions of the nasal chambers into the skull bones. For this reason, they are known as paranasal sinuses.

c. **Pharynx.** The pharynx (FAIR-inks) is the common posterior space for the respiratory and digestive systems.

(1) **Nasopharynx.** That portion of the pharynx specifically related to the respiratory system is the nasopharynx. It is the portion of the pharynx above the soft palate. The two posterior openings (nares) of the nasal chambers lead into the single space of the nasopharynx. The auditory (eustachian) tubes also open into the nasopharynx. The auditory tubes connect the nasopharynx with the middle ears (to equalize the pressure between the outside and inside of the eardrum). Lying in the upper posterior wall of the nasopharynx are the pharyngeal tonsils (adenoids). The soft palate floor of the nasopharynx is a trap door that closes off the upper respiratory passageways during swallowing.

(2) **Oropharynx.** The portion of the pharynx closely related to the digestive system is the oropharynx. It is the portion of the pharynx below the soft palate and above the upper edge of the epiglottis. (The epiglottis is the flap that prevents food from entering the larynx (discussed below) during swallowing.)

(3) **Laryngopharynx.** That portion of the pharynx that is common to the respiratory and digestive systems is the laryngopharynx. It is the portion of the pharynx below the upper edge of the epiglottis. Thus, the digestive and respiratory systems lead into it from above, and lead off from it below.

1-4. **LARYNX**

The larynx, also called the Adam’s apple or voice box, connects the pharynx with the trachea. The larynx, located in the anterior neck region, has a box-like shape. See Figure 1-3 for an illustration. Since the voice box of the male becomes larger and heavier during puberty, the voice deepens. The adult male’s voice box tends to be
located lower in the neck; in the female, the larynx remains higher and smaller and the voice is of a higher pitch.

a. **Parts and Spaces.** The larynx has a vestibule ("entrance hallway") that can be covered over by the epiglottis. The glottis itself is the hole between the vocal cords. Through the glottis, air passes from the vestibule into the main chamber of the larynx (below the cords) and then into the trachea. The skeleton of the larynx is made up of a series of cartilages.
b. **Muscles.** The larynx serves two functions and there are two sets of muscles—one for each function.

(1) One set controls the size of the glottis. Thus, it regulates the volume of air passing through the trachea.

(2) The other set controls the tension of the vocal cords. Thus, it produces vibrations of selected frequencies (variations in pitch) of the moving air to be used in the process of speaking.

**1-5. INFRALARYNGEAL STRUCTURES**

a. **Trachea and Bronchi.** The respiratory tree (Figure 1-4) is the set of tubular structures that carry the air from the larynx to the alveoli of the lungs. Looking at a person UPSIDE DOWN, the trachea is the trunk of the tree and the bronchi are the branches. These tubular parts are held open (made patent) by rings of cartilage. Their lining is ciliated to remove mucus and other materials that get into the passageway.

b. **Alveoli.** The alveoli (alveolus, singular) are tiny spherical (balloon-like) sacs that are connected to the larger tubes of the lungs by tiny tubes known as alveolar ducts and bronchioles. The alveoli are so small that there are millions in the adult lungs. This very small size produces a maximum surface area through which external respiration takes place. External respiration is the actual exchange of gases between the air in the alveolar spaces and the adjacent blood capillaries through their walls.

c. **Lungs.** A lung is an individual organ composed of tubular structures and alveoli, bound together by fibrous connective tissue (FCT). In the human, there are two lungs, right and left. Each lung is supplied by a primary or mainstem bronchus leading off from the trachea. The right lung is larger in volume than the left lung. The left lung must leave room for the heart. The right lung is divided into 3 pulmonary lobes (upper, middle and lower) and 10 bronchopulmonary segments (2 + 3 + 5). The left lung is divided into 2 pulmonary lobes (upper and lower) and 8 bronchopulmonary segments (4 + 4). A pulmonary lobe is a major subdivision of a lung marked by fissures (deep folds). Each lobe is further partitioned into bronchopulmonary segments. Each lobe is supplied by a secondary or lobar bronchus. A tertiary or segmental bronchus, a branch of the lobar bronchus supplies each segment.

d. **Pleural Cavities.** Each serous cavity has inner and outer membranes. In the case of the lungs, the inner membrane, is known as the visceral pleura which very closely covers the surface of the lungs. The outer membrane is known as the parietal pleura, forming the outer wall of the space. The pleural spaces are the potential spaces between the inner and outer membranes. The opening between the pleural layers contains a slick fluid called pleural fluid. The pleural fluid serves as a lubricant and allows the lungs to move freely with a minimum of friction.
Section II. BREATHING AND BREATHING MECHANISMS IN HUMANS

1-6. INTRODUCTION

   a. Boyle’s law tells us that as the volume (V) of a gas-filled container increases, the pressure (P) inside decreases; as the volume (V) of a closed container decreases, the pressure (P) inside increases. When two connected spaces of air have different pressures, the air moves from the space with greater pressure to the one with lesser pressure. In regard to breathing, we can consider the air pressure around the human body to be constant. The pressure inside the lungs may be greater or less than the pressure outside the body. Thus, a greater internal pressure causes air to flow out; a greater external pressure causes air to flow in.

   b. We can compare the human trunk to a hollow cylinder. This cylinder is divided into upper and lower cavities by the diaphragm. The upper is the thoracic cavity and is essentially gas-filled. The lower is the abdominopelvic cavity and is essentially water-filled.
1-7. COSTAL (THORACIC) BREATHING

a. Inhalation. Muscles attached to the thoracic cage raise the rib cage. A typical rib might be compared to a bucket handle, attached at one end to the sternum (breastbone) and at the other end to the vertebral column. The “bucket handle” is lifted by the overall movement upward and outward of the rib cage. These movements increase the thoracic diameters from right to left (transverse) and from front to back (A-P). Thus, the intrathoracic volume increases. Recalling Boyle’s law, the increase in volume leads to a decrease in pressure. The air-pressure outside the body then forces air into the lungs and inflates them.

b. Exhalation. The rib cage movements and pressure relationships are reversed for exhalation. Thus, intrathoracic volume decreases. The intrathoracic pressure increases and forces air outside the body.

1-8. DIAPHRAGMATIC (ABDOMINAL) BREATHING

The diaphragm is a thin, but strong, dome-shaped muscular membrane that separates the abdominal and thoracic cavities. The abdominal wall is elastic in nature. The abdominal cavity is filled with soft, watery tissues.

a. Inhalation. As the diaphragm contracts, the dome flattens and the diaphragm descends. This increases the depth (vertical diameter) of the thoracic cavity and thus increases its volume. This decreases air pressure within the thoracic cavity. The greater air pressure outside the body then forces air into the lungs.

b. Exhalation. As the diaphragm relaxes, the elastic abdominal wall forces the diaphragm back up by pushing the watery tissues of the abdomen against the underside of the relaxed diaphragm. The dome extends upward. The process of inhalation is thus reversed.

Section III. CONDITIONS AFFECTING THE RESPIRATORY SYSTEM

1-9. INTRODUCTION

Many conditions affect the respiratory system. Some of the conditions are lifethreatening, while many are chronic conditions which affect thousands of patients. Many of the patients who suffer from these conditions will be standing in front of the outpatient pharmacy in order to receive prescriptions to obtain some relief.

1-10. PNEUMONIA

Pneumonia is caused by an infection of the lung. This infection is caused by either bacteria (like the pneumococcus bacterium) or viruses. In pneumonia the walls of
the alveoli become inflamed and filled with fluid and the air spaces in the alveoli become filled with blood and fluid. As you might expect, the exchange of gases in the alveoli becomes impaired. Death can result from pneumonia.

1-11. ASTHMA

Asthma, a condition usually caused by allergic reactions to substances in the environment, affects many people. The allergic reactions cause the bronchioles to spasm. Hence, the flow of air into and out of the lungs becomes impaired. For some unknown reason, the flow of air out of the lungs is more impeded than the flow of air into the lungs. Hence, the person with asthma often finds it more difficult to expire (expel the air) than to inspire. Furthermore, such labored breathing, after many years, often results in the asthma-sufferer having a barrel-shaped chest.

1-12. STATUS ASTHMATICUS

Status asthmaticus is a very sudden, continuous, and intense asthmatic attack.

1-13. EMPHYSEMA

Emphysema is a condition in which the patient has large portions of the alveolar walls destroyed. Consequently, the patient finds it necessary to breathe faster and more deeply in order to obtain the oxygen needed to live. Emphysema is often associated with smoking. Emphysema may also be referred to as Chronic Obstructive Pulmonary Disease (COPD).

1-14. PULMONARY EDEMA

Pulmonary edema is a condition in which fluid collects in the interstitial spaces of the lungs and in the alveoli. Obviously, the exchange of gases in the alveoli becomes impaired. Pulmonary edema is usually caused when the left side of the heart fails to pump efficiently; when this happens blood backs up into the pulmonary circulation and causes fluid in the lungs.

Section IV. RESPIRATORY SYSTEM DRUGS

1-15. INTRODUCTION

Drugs affecting the respiratory system have been in use for years. In the first part of this century, for example, various members of the morphine family (that is, heroin) were used in the treatment of coughs. In the 1980s, people are using both legend and over-the-counter cough preparations. At certain times of the year you will see many prescriptions for cough medicines and expectorants. You have probably
seen such increases when winter arrives. This section of the subcourse will discuss some respiratory systems medications commonly seen in the pharmacy.

1-16. ANTITUSSIVE AGENTS

a. Background. Antitussives are agents that relieve or prevent coughing. These agents, in general, act on the central nervous system to depress the cough reflex center in the medulla of the brain. Antitussives are used to reduce respiratory irritation. Such reduction of respiratory irritation results in the patient's being able to rest better at night because he is not kept awake by his coughing.

b. Antitussive Agents.

(1) Codeine. Codeine is considered to be the most useful narcotic antitussive agent. Codeine aids in relieving the pain (that is, producing analgesia) associated with a hacking cough. The main side effects associated with codeine include drowsiness, nausea, vomiting, and constipation. When a preparation containing codeine is dispensed to a patient that patient should be told that the product may cause drowsiness, and that he should not drink alcohol while taking the medication. Codeine is a Note R drug alone and cannot be refilled. It is a Note Q item when it is found in combination products (for example: Robitussin A-C Syrup). The usual oral dosage of codeine alone is 15 milligrams (1/4 grain) every 4 to 6 hours as needed for cough. The dosage can be increased but should not exceed 120 milligrams in 24 hours because of its central nervous system (CNS) depressant effects.

(2) Benzonatate (Tessalon®). Benzonatate is a nonnarcotic antitussive that produces its effect through a CNS depressant effect similar to codeine. Furthermore, it produces a local anesthetic effect on the stretch receptors in the lower respiratory tract, which control coughing. Benzonatate is usually given in 100 milligram doses—three to six times daily. This drug has few side effects except that it will numb the mouth, tongue, and pharynx if the capsules are chewed (this is because of its topical anesthetic effect). Benzonatate is available in the form of 100 milligram capsules.

(3) Dextromethorphan, DM (Pertussin CS®). Dextromethorphan is another non-narcotic antitussive. It is found alone or in combination—usually with expectorants. The most common side effect associated with this drug is gastrointestinal (G.I.) upset. Dextromethorphan is a non-legend drug, which may be written as a prescription drug or as a hand-out item depending on the local policy of your hospital. The usual oral dosage of this drug is 10 to 30 milligrams, every four to eight hours. Do not exceed 120mg in 24 hours. There are many products on the market, which contain dextromethorphan in combination. Examples of such products include Robitussin-DM® and Baytussin-DM®.
1-17. EXPECTORANT AGENTS

a. **Background.** Expectorants are agents, which facilitate the removal of secretions of the bronchopulmonary mucous membrane. Most of the expectorants discussed below act reflexively by irritating the gastric mucosa. This, in turn, stimulates secretions in the respiratory tract. Expectorants are used to remove bronchial secretions which are purulent (containing pus), viscid (thick), or excessive. The loosened material is then moved toward the pharynx through ciliary motion and coughing.

b. **Expectorant Agents.**

   (1) **Guaifenesin (Robitussin®, Baytussin®).** Guaifenesin is the most commonly used expectorant today. This nonlegend drug has the side effect of gastrointestinal (G.I.) upset. Guaifenesin may be found alone as a syrup (100 milligrams per 5 milliliters), tablet 600 mg (Humibid® L.A.), or in many combination products such as Robitussin-DM®.

   (2) **Saturated Solution of Potassium Iodide.** Saturated Solution of Potassium Iodide (SSKI) is an expectorant administered as 300 milligrams (10 drops) in a glass of water or fruit juice every three or four times daily. SSKI has a very unpleasant taste. Overdoses of this product may lead to a condition known as iodism that produces an acne-type rash, fever, and rhinitis or runny nose. Patient compliance with this product may be low because of its unpleasant taste. Consequently, when the medication is dispensed you should tell the patient to place the required amount of SSKI in fruit juice in order to mask its taste. This drug is available in a saturated solution of 1 gram per milliliter in 30 milliliter containers.

   (3) **Elixir of Terpin Hydrate.** Elixir of Terpin Hydrate (ETH) is an expectorant, which works directly on the bronchial secretory cells in the lower respiratory tract to facilitate the removal of bronchial secretions. It is usually given in doses, which range from 85 to 170 milligrams (1 or 2 teaspoonsful) 3 or 4 times daily. The side effects of this drug are related to its alcohol content (42 percent or 84 proof). If enough ETH is consumed it will produce significant CNS depression. Even with the high alcohol content, ETH is an Over the Counter (OTC) product. It is available as a syrup (85 milligrams per 5 milliliters) in 120 milliliter containers.

   **NOTE:** Terpin Hydrate is no longer approved for use as an expectorant; it is used mainly as a vehicle for cough mixtures.

1-18. ANTITUSSIVE-EXPECTORANT COMBINATION PRODUCTS

The antitussive-expectorant combinations are used for a hyperactive nonproductive cough. The side effects of these drugs, of course, will be dependent on the antitussive-expectorant combination used. Some typical combination products used
by the military are Robitussin-DM®, Robitussin® A-C Syrup, and Novahistine®
Expectorant Liquid.

1-19. MUCOLYTICS

a. Background. Mucolytics are respiratory drugs that dissolve mucous in the
respiratory tract. They are used by inhalation in an attempt to reduce the viscosity
(thickness) of respiratory tract fluid. The loosened material can then be moved toward the
pharynx more easily by ciliary motion and coughing. Like the expectorants, the
mucolytics are used in the treatment of respiratory disorders in which the secretions are
purulent (contain pus), viscid, or excessive. Consequently, the mucolytics represent an
alternative to the oral use of expectorants.

b. Mucolytic Agents.

(1) Acetylcysteine (Mucomyst®). This is a mucolytic given by inhalation or
nebulization. Nebulization is treatment by spray. Two to twenty milliliters of a 10
percent drug solution or 1 to 10 milliliters of a 20 percent Mucomyst® solution is
nebulized into a face mask or mouth piece every two to six hours daily. Acetylcysteine
has an unpleasant (like rotten eggs) smell. Side effects associated with this agent
include nausea and vomiting and broncho-spasms with higher concentrations (with the
20 percent solution). This medication is only dispensed for inpatient use—usually to the
respiratory therapy clinic or to the nursing station. The sterile solution should be
covered, refrigerated, and used within 96 hours after the vial is opened. It is available in
10 percent and 20 percent solutions in containers of 4, 10, or 30 milliliters.

(2) Sodium Chloride Solution U.S.P. (0.9 percent sodium chloride solution).
This agent is used alone or in combination with other mucolytic agents. Sodium
chloride solution increases the respiratory fluid volume by osmosis, which tends to
decrease the viscosity of the respiratory fluid. It is also administered by inhalation in a
nebulized form as a dense mist in a tent or delivered through a face mask or mouth
piece. The main side effect seen with sodium chloride solution occurs after prolonged
inhalation. This will cause localized irritation of the bronchial mucosa. Sodium chloride
solution for this purpose is for inpatient use by respiratory therapy personnel or by
nursing personnel. Concentrated Sodium Chloride (23.4%) is used by respiratory
therapy to induce sputum production (sputum induction procedure).

1-20. BRONCHODILATOR AGENTS

a. Background. The bronchodilators are agents that cause expansion of the air
passages of the lungs. This allows the patient to breathe more easily and are of value in
overcoming acute bronchospasms. They are employed as adjuncts in prophylactic and
symptomatic treatment of the individual complications of obstructive pulmonary
diseases such as asthma, bronchitis, and emphysema. Most of these agents have
been discussed in other lessons of the pharmacology series.
b. **Bronchodilator Agents (Sympathomimetics).** Sympathomimetic bronchodilators act by relaxing contractions of the smooth muscle of the bronchioles. These agents are often referred to as “Beta agonists”.

(1) **Albuterol (Proventil®, Ventolin®).** Albuterol is a short acting beta-agonist or bronchodilator. It is used in the relief and prevention of bronchospasm and in the prevention of exercise-induced bronchospasm. Albuterol is available as an inhalation aerosol, inhalation solution, inhalation capsules, regular and sustained release tablets, and syrup. Other than the sustained release products, it is prescribed every 4 to 6 hours. Albuterol is often used as “rescue therapy” due to its quick onset of action.

(2) **Salmeterol (Serevent®).** Salmeterol is indicated for the same conditions as albuterol, however its distinct advantage is that it is administered twice daily. It is available as an inhalation aerosol. Salmeterol CANNOT be used for “rescue therapy”; a short acting beta agonist such as albuterol must be used.

(3) **Epinephrine (Adrenalin®).** Epinephrine is used as a bronchodilator because of its beta effects on the bronchi and a pharmacologic antagonist of histamine. Epinephrine is employed for the treatment of acute attacks of bronchospasms associated with emphysema, bronchitis, or anaphylaxis. The inhalation route is not the preferred route of administration, however, it may be used. Epinephrine is usually administered subcutaneously when used and is fairly effective at reducing bronchospasms.

(4) **Metaproterenol (Alupent®, Metaprel®).** This is an adrenergic agent that has primary beta2 activity. That is, its main effect is to relax the bronchioles. It has the same indications as epinephrine. It may be used for the prevention of bronchospasms associated with chronic obstructive pulmonary diseases. Inhalation of metaproterenol may be used in the treatment of mild bronchospasm attacks. Metaproterenol is somewhat more effective than inhaled isoproterenol. Metaproterenol’s duration of action is substantially longer than that of isoproterenol.

(5) **Ephedrine.** Ephedrine has actions of those similar to those of epinephrine. Ephedrine is not frequently used because of the availability of other more suitable agents. Ephedrine is administered orally. It is used to treat mild bronchospasm attacks and prophylactically to prevent bronchospasm attacks. Ephedrine is not as suitable as epinephrine for the treatment of severe attacks of bronchial asthma because its bronchodilator action is weaker.

(6) **Isoproterenol (Isuprel®).** Isoproterenol is an adrenergic agent used to treat asthma, bronchitis, and emphysema. Like metaproterenol, isoproterenol is administered by inhalation for the treatment of mild bronchospasms. Isoproterenol may be administered intravenously with great caution to treat status asthmaticus.

(7) **Other sympathomimetic bronchodilators include terbutaline (Brethine®), pirbuterol (Maxair®), and bitolterol mesylate (Tornalate®).**
c. **Bronchodilator Agents (Xanthine derivatives).** The methylxanthines (theophylline and derivatives) directly relax the smooth muscle of the bronchi and pulmonary blood vessels. They may also reduce the fatigability and thereby improve contractility in patients with chronic obstructive airway disease. Xanthine derivatives are often used in the treatment of apnea and bradycardia of prematurity in infants.

   (1) Aminophylline. Aminophylline is a xanthine derivative containing ~80% theophylline. It is prescribed as a bronchodilator to treat asthma. It will also relieve bronchospasms associated with emphysema and bronchitis. Aminophylline may be administered orally or rectally to prevent severe attacks of bronchial asthma but is generally administered intravenously (I.V.) to relieve acute bronchospasms or status asthmaticus resistant to adrenergic drugs.

   (2) Theophylline (Theolair®, Slo-Phyllin®, Theodur®). Theophylline is often prescribed as the xanthine of choice for oral administration (tablets, capsules, elixir, syrup, or solution). One must take care when dispensing theophylline products. Each different brand varies in the actual amount of theophylline contained in the product and in the duration of action. Theophylline is a drug with a very narrow therapeutic index (the treatment dose is very close to the toxic dose). For this reason, patients should have their theophylline blood levels monitored on a routine basis.

d. **Miscellaneous Respiratory Agents.**

   (1) Cromolyn (Intal®). Cromolyn is a unique product that works by inhibiting the release of histamine and other spasm-causing compounds from mast cells located in the lungs and prevents bronchoconstriction. It is used mainly for the treatment or prevention of mild bronchospasms associated with asthma. It is available as an inhalation aerosol and nebulization solution.

   (2) Leukotriene modifiers. The production of leukotrienes (immunologic proteins) and the binding of leukotriene receptors appears to be responsible for airway edema, smooth muscle constriction and altered inflammatory processes contributing to the signs and symptoms of asthma. For this reason, several new agents have been developed.

      (a) Zafirlukast (Accolate®), montelukast (Singulair®). Both of these agents are leukotriene receptor antagonists which cause inhibition of bronchoconstriction. Zafirlukast is available as a tablet prescribed twice daily. Montelukast is prescribed as a once daily tablet.

      (b) Ziluton (Zyflo®), Ziluton works a little differently in that it inhibits the formation of leukotrienes to prevent bronchoconstriction. Ziluton is administered four times daily.

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**Continue with Exercises**
1. External respiration is ___________________.
   a. The exchange of gases between the atmosphere and the cells of the body.
   b. The exchange of gases between the blood and the individual cells of the body.
   c. The exchange of gases between the air in the lungs and blood.
   d. The aeration of the lungs.

2. Bronchi are ____________________________.
   a. Tubes that lead from the larynx to the lungs.
   b. Tubes that warm and humidify the air as it enters the lungs.
   c. Tubes that extend into the nasal chamber in order to increase the surface area exposed to inflowing air.
   d. Tubes that lead from the trachea to the lungs.

3. Select the statement that best describes the paranasal sinuses.
   a. Air cells or cavities in the skull that are connected with the nasal chambers and lined with ciliated mucoperiosteum.
   b. Special nerve endings located in the upper areas of the nasal chambers.
   c. The portion of the pharynx that is common to both the respiratory and digestive systems.
   d. The vestibules that are covered by the epiglottis.
REFER TO THE FIGURE BELOW AS YOU ANSWER QUESTIONS 4 AND 5.

4. Which letter in the illustration above refers to the bronchi?
   a. a
   b. b
   c. c
   d. d

5. Which letter in the illustration above refers to the pleural space?
   a. a
   b. b
   c. c
   d. d
6. Which of the statements below best describes abdominal breathing?

   a. Breathing which occurs because of the contractions of the small intestine and other abdominal organs.
   b. Breathing which occurs because of changes in the intrathoracic volume.
   c. Breathing which occurs because of the contraction and relaxation of the diaphragm.
   d. Breathing which occurs because of changes in the position of the rib cage.

7. Pneumonia is best described as ____________________.

   a. A condition in which fluid collects in the interstitial spaces of the lungs caused by the left heart’s inability to pump efficiently.
   b. An infection of the lungs caused by bacteria or viruses in which the walls of the alveoli become inflamed.
   c. A condition in which the patient has large portions of the walls of the alveoli destroyed.
   d. A state of impaired breathing caused by spasms of the bronchi.

8. Mucolytic agents are drugs which ____________________.

   a. Relieve bronchospasms.
   b. Dissolve mucous in the respiratory tract.
   c. Are used to irritate the gastric mucosa.
   d. Relieve or prevent coughing.
9. Acetylcysteine is used as a(n) _________________________.
   a. Antitussive agent.
   b. Mucolytic agent.
   c. Expectorant agent.
   d. Bronchodilator.

10. Elixir of Terpin Hydrate is used as a(n) ________________.
    a. Expectorant.
    b. Antitussive.
    c. Mucolytic.
    d. Bronchodilator.

11. Match the drug name in Column A with its corresponding trade name in Column B.

    Column A                          Column B
    ____ Acetylcysteine.            a.  Isuprel®.
    ____ Metaproterenol.            b.  Alupent®.
    ____ Guaifenesin.               c.  Tessalon®
    ____ Cromolyn.                  d.  Mucomyst®.
    ____ Isoproterenol.             e.  Intal®.
    ____ Benzonatate.               f.  Baytussin®.

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 1

1. c  The exchange of gases between the air in the lungs and blood.  (para 1-1a)

2. d  Tubes which lead from the trachea to the lungs.  (para 1-5a)

3. a  Air cells or cavities in the skull which are connected with the nasal chambers and lined with ciliated mucoperiosteum.  (para 1-3b(4))

4. d  (Figure 1-1)

5. a  (Figure 1-1)

6. c  Breathing which occurs because of the contraction and relaxation of the diaphragm.  (para 1-8)

7. b  An infection of the lungs caused by bacteria or viruses in which the walls of the alveoli become inflamed.  (para 1-10)

8. b  Dissolve mucous in the respiratory tract.  (para 1-19a)

9. b  Mucolytic agent.  (para 1-19b(1))
10. a Expectorant. *(para 1-17b(3))*

11. COLUMN A                                           COLUMN B
   ____d___ Acetylcysteine. *(para 1-19b(1))*   a. Isuprel®.
   ____b___ Metaproterenol. *(para 1-20b(4))*  b. Alupent®.
   ____f___ Guaifenesin. *(para 1-17b(1))*     c. Tessalon®.
   ____e___ Cromolyn. *(para 1-20d(1))*        d. Mucomyst®.
   ____a___ Isoproterenol. *(para 1-20b(6))*   e. Intal®.
   ____c___ Benzonatate. *(para 1-16b(2))*    f. Baytussin®.

*End of Lesson 1*
LESSON ASSIGNMENT

LESSON 2
The Human Cardiovascular and Lymphatic Systems.

LESSON ASSIGNMENT
Paragraphs 2-1--2-22.

TASKS
081-824-0001, Perform Initial Screening of a Prescription.

081-824-0026, Evaluate a Prescription.

081-824-0024, Fill a Prescription for a Controlled/Non-Controlled Drug.

081-824-0027, Evaluate a Completed Prescription.

081-824-0028, Issue Outpatient Medications.

LESSON OBJECTIVES
After you finish this lesson you should be able to:

2-1. Given a group of statements, select the statement that best explains the need for circulatory systems.

2-2. Given a group of systems, select the two circulatory systems in the human body.

2-3. Given the name of one of the major components of the human circulatory system and a group of statements, select the statement that best describes that component.

2-4. Given a group of components, select the components of blood.

2-5. From a group of statements, select the statement that best describes either the plasma or the formed elements of the blood.

2-6. Given a group of statements and the names of one of the formed elements of the blood, select the statement that best describes the given formed elements.
2-7. From a group of functions, select the function(s) of the blood.

2-8. Given a group of statements and one of the types of blood vessels, select the statement that best describes that type of blood vessel.

2-9. Given the steps of blood clotting in an unsequential order and several selections of varying sequence, select the sequence of blood clotting as the steps actually occur.

2-10. From a group of statements, select the definition of the term blood pressure, systolic blood pressure, and diastolic blood pressure.

2-11. Given a group of medical problems and one of the following conditions: hypertension and hypotension, select the medical problem(s) associated with the given condition.

2-12. Given a group of statements and the name of a disorder which may affect the circulatory system, select the statement that best describes the disorder.

2-13. Given a drawing of either the anterior or the interior view of the human heart and a list of names of parts of the heart, match the name of each part of the heart with its location.

2-14. From a group of statements, select the statement that best describes the property of inherent rhythmicity.

2-15. Given one of the following: sinoatrial node, atrioventricular node, Bundle of HIS, or Purkinje fibers and a group of statements; select the statement that best describes the role of the given heart structure in the heartbeat.

2-16. Given one of the following electrolytes: sodium, potassium, or calcium and a group of statements, select the statement which best describes the effect(s) of abnormal amounts of that electrolyte on the myocardium.
2-17. Given the name of a cardiac disorder and a group of statements, select the statement that best describes that disorder.

2-18. Given the name of one of the structures of the human lymphatic system and a group of statements, select the statement that best describes that structure.

**SUGGESTION**

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 2
THE HUMAN CARDIOVASCULAR AND LYMPHATIC SYSTEMS

Section I. INTRODUCTION

2-1. NEED FOR CIRCULATORY SYSTEMS

a. The need for circulatory systems is based on two criteria:

   (1) Number of cells. Multicellular animals are animals with great numbers of cells.

   (2) Size. In larger animals, most cells are too far away from sources of food and oxygen for simple diffusion to provide sufficient amounts. Also, distances are too great for simple removal of wastes.

b. Because of these criteria, we need a system (or systems) to carry materials to all cells. To get food and oxygen to the cells and to remove waste products, we need a transport system, or circulatory system. Human circulatory systems are so effective that few cells are more than the width of two cells away from a capillary.

2-2. BASIC COMPONENTS OF ANY CIRCULATORY SYSTEM

The four basic components of any circulatory system are a vehicle, conduits, a motive force, and exchange areas.

a. Vehicle. The vehicle is the substance that actually carries the materials being transported.

b. Conduits. A conduit is a channel, pipe, or tube through which a vehicle travels.

c. Motive Force. If we say that a force is motive, we mean that it produces movement. Systems providing a motive force are often known as pumps.

d. Exchange Areas. Since the materials being transported must eventually be exchanged with a part of the body, special areas are developed for this purpose. They are called exchange areas.

2-3. CIRCULATORY SYSTEMS IN THE HUMAN BODY

a. The cardiovascular system is the circulatory system involving the heart and blood vessels.
b. The lymphatic system is a drainage-type circulatory system involved with the clear fluid known as lymph.

c. There are other minor circulatory systems in the human body, such as the one involved with cerebrospinal fluid.

Section II. THE HUMAN CARDIOVASCULAR SYSTEM

2-4. GENERAL

The human cardiovascular system is a collection of interacting structures designed to supply oxygen and nutrients to living cells and to remove carbon dioxide and other wastes. Its major components are the:


b. Blood Vessels. Blood vessels are the conduits, or channels, through which the blood is moved.

c. Heart. The heart is the pump that provides the primary motive force.

d. Capillaries. The capillaries, minute (very small) vessels, provide exchange areas. For example, in the capillaries of the lungs, oxygen is added and carbon dioxide is removed from the blood.

2-5. BLOOD

Blood is the vehicle for the human cardiovascular system. Its major subdivisions are the plasma, a fluid containing proteins, and the formed elements, including red blood cells, white blood cells, and platelets.

a. Plasma.

(1) Plasma makes up about 55 percent of the total blood volume. It is mainly composed of water. A variety of materials are dissolved in plasma. Among the most important of these are proteins.

(2) After the blood clots, the clear fluid remaining is called serum. Serum does not contain the proteins used for clotting. Otherwise, it is very similar to plasma.

b. Formed Elements. The formed elements make up about 45 percent of the total blood volume. The formed elements are cellular in nature. While the red blood cells (RBCs) and white blood cells (WBCs) are cells, the platelets are only fragments of cells.
(1) **Red blood cells (erythrocytes).** Red blood cells (RBCs) are biconcave discs. That is, they are shaped something like an inner tube from an automobile tire, but with a thin middle portion instead of a hole. There are approximately 5,000,000 RBCs in a cubic millimeter of normal adult blood. Red blood cells contain hemoglobin, a protein that carries most of the oxygen transported by the blood.

(2) **White blood cells (leukocytes).** There are various types of WBCs, but the most common are neutrophils and lymphocytes. Neutrophils phagocytize (swallow up) foreign particles and organisms, and digest them. Lymphocytes produce antibodies and serve other functions in immunity. In normal adults, there are about 5,000 to 11,000 WBCs per cubic millimeter of blood.

(3) **Platelets.** Platelets are about half the size of erythrocytes. They are fragments of cells. Since they are fragile, they last only about 3-5 days. Their main function is to aid in clotting by clumping together and by releasing chemical factors relating to clotting. There are 150,000-350,000 platelets in a cubic millimeter of normal blood.

c. **Some General Functions of the Blood.**

(1) Blood serves as a vehicle for oxygen nutrients, carbon dioxide and other wastes, hormones, antibodies, heat, and so forth.

(2) Blood aids in temperature control. Beneath the skin, there is a network of vessels that functions much like a radiator. To avoid accumulation of excess heat in the body, the flow of blood to these vessels can be increased greatly. Here, aided by the evaporative cooling provided by the sweat glands, large amounts of heat can be rapidly given off. The flow of blood also keeps the outer parts of the body from becoming too cold.

(3) The blood aids in protecting our bodies by providing immunity. Some WBCs phagocytize (swallow up) foreign particles and microorganisms. Other WBCs produce antibodies. The blood transports antibodies throughout the body.

(4) **Blood clotting** is another function of blood. Not only does this prevent continued blood loss; it also helps prevent invasion of the body by microorganisms and viruses by sealing the wound opening.

2-6. **BLOOD VESSELS**

The blood is conducted or carried through the body by tubular structures known as blood vessels. Since at no time does the whole blood ever leave a blood vessel of some sort, we refer to this system as a closed system.
a. **General Construction.** The blood vessels in general are tubular and have a three-layered wall.

   (1) **Intima.** A layer of smooth epithelium known as the intima lines the lumen (hollow central cavity).

   (2) **Media.** A middle layer of smooth muscle tissue is called the media.

   (3) **Adventitia.** The adventitia is the outer layer of fibrous connective tissue that holds everything together.

b. **Types of Blood Vessels.** See Figure 2-1 for a diagram of the human circulatory system. We recognize three types of blood vessels:

   (1) The **arteries** carry blood away from the chambers of the heart.

   (2) The **veins** carry blood to the chambers of the heart.

   (3) **Capillaries** are extremely thin-walled vessels having only the intimal layer through which exchanges can take place between the blood and the tissue cells.

c. **Relationships.** Arteries and veins are largest where they are closest to the heart. Away from the heart, they branch into smaller and smaller and more numerous vessels. The branching continues until the smallest arteries (arterioles) empty into the capillaries. The capillaries in turn are drained by the venules of the venous system.

d. **Valves.** Within the heart and the veins are structures known as valves. Valves function to insure that the blood flows in only one direction.

**2-7. BLOOD CLOTTING**

Blood clotting is a process that is dependent on several different factors. This process is also known as **hemostasis.** There are three general mechanisms involved in blood clotting: vascular spasm, the platelet plug, and the clotting mechanism.

a. **Vascular Spasm.** When a blood vessel is cut, the vascular spasm causes rapid constriction of the cut blood vessel. This decreases the amount of blood lost. The mechanism by which this mechanism occurs is not fully known, but it appears to be a reflex response initiated by pain. It is interesting to note that when a vessel is cut by crushing, the vascular spasm response seems to occur more rapidly and more intensely than if the vessel is quickly cut (as with a knife). After the vascular spasm has occurred, the second mechanism involved with the clotting process—the platelet plug—occurs.
b. **Platelet Plug.** The blood platelets circulate freely in the blood until they reach a blood vessel that has been severed. Platelets then adhere to the ruptured point of the blood vessel. After a period of time, the platelets partially plug the severed vessel.

c. **Clotting Mechanism.** The third mechanism involves the formation of the blood clot. The clot forms within three to six minutes after the rupturing of the blood
vessel. In about 30 minutes the clot shrinks; thus pulling the end of the severed vessel in to close the diameter of the vessel even further.

2-8. MECHANISMS OF BLOOD CLOTTING

The actual clotting mechanisms involve several steps—each step is essential to clotting:

STEP 1: The blood platelets release a substance that is known as thromboplastin.

STEP 2: Thromboplastin reacts with calcium and another substance, prothrombin, to form thrombin. Vitamin K is necessary for the proper formation of prothrombin.

STEP 3: The thrombin formed acts as an enzyme to convert fibrinogen to fibrin threads that eventually form the blood clot.

NOTE: For a more in-depth discussion of blood clotting you should locate and read a physiology text that is appropriate to your level of understanding.

2-9. BLOOD PRESSURE

a. Introduction. Blood pressure is the force exerted by the blood as it is pumped throughout the circulatory system. Blood pressure is needed by the body for the perfusion and distribution of nutrients throughout the body. Blood pressure is expressed in numerical values with the use of an instrument such as the sphygmomanometer. Blood pressure is expressed as systolic blood pressure over diastolic blood pressure (for example, 120/70). Systolic blood pressure is the pressure of blood as it is being pumped from the heart. When the heart contracts, it is said to be in systole. Diastolic pressure is the residual pressure of the blood because of the elasticity of the blood vessels (when the heart is at rest).

b. Regulation. In order to regulate blood pressure to meet the immediate needs of the body, the body is equipped with various systems that can change the blood pressure both by a change in the size of the openings of the various blood vessels and by a change in the volume of the blood (that is, blood plasma).

(1) Baroreceptors. Baroreceptors are located in the aortic arch of the aorta and in the internal carotid arteries. Baroreceptors are really a series of specialized neurons that function as rapidly acting blood pressure regulators. They sense changes in blood pressure and act in a reflex manner to change both the rate and force of the contraction of the heart and the size of the openings of the blood vessels.

(2) Chemoreceptors. Chemoreceptors are receptors which sense changes in the oxygen content of the blood. They are located in high numbers in the aortic arch.
and internal carotid arteries. The chemoreceptors have a dual purpose in that they help to regulate blood pressure in addition to the regulation of blood pressure. The change in blood pressure they produce is due mainly to the change in heart rate. Working in conjunction with the chemoreceptors is a mechanism known as the CNS ischemic response. The CNS ischemic response senses an increase in carbon dioxide and lactic acid (both waste products of metabolism) in the blood and reacts to increase or decrease heart rate to maintain these products within normal amounts. The CNS ischemic response generally decreases the heart rate so that blood spends a longer time in the lungs thereby allowing for an increased exchange of oxygen and carbon dioxide.

c. **Correction of Blood Pressure.** Blood pressure is corrected by changing blood vessel tone and cardiac output. The baroreceptors eventually adapt to whatever pressure level to which they are exposed. Therefore, prolonged regulation of arterial pressure requires other control systems. Kidney malfunctions, fluid shifts, and electrolyte imbalances will eventually occur if this condition is not corrected. These are also known as long term regulators.

d. **Renal Fluid-Volume Mechanism.** The renal fluid-volume mechanism is one of the long-term regulators located in the kidneys. This mechanism works by causing changes in the amount of water reabsorbed by the kidneys. An increase in water reabsorption leads to an increase in blood pressure and a decrease in water reabsorption leads to a corresponding decrease in the blood pressure. The secretion of certain hormones also affects blood pressure. Aldosterone, a hormone secreted by the adrenal cortex, leads to an increase in sodium retention. This increase in sodium retention leads to a corresponding increase in water retention with an overall effect of higher blood pressure.

**2-10. ABNORMAL BLOOD PRESSURE**

a. **Hypertension.** Hypertension is characterized by a persistent increase in blood pressure. It should be noted that there are always periodic increases in blood pressure due to times of stress or physical exertion. However, if the blood pressure remains at these high levels serious complications could result. Some of the effects of hypertension on the body are frequent nosebleeds, strokes, hypertrophy of the myocardium, and arteriosclerosis. Hypertension is one of the easiest disorders to treat if it is detected early. Drug therapy consists of diuretics and other antihypertensives. It is essential for the patient who has controlled his blood pressure by the use of medication to continue to take that medication even after the outward signs and symptoms subside.

b. **Hypotension.** Hypotension is defined as persistent and abnormal low blood pressure. This condition is not usually fatal in itself; however, the hypotensive patient is much more susceptible to shock in case of a rapid loss of blood. Many times low blood pressure is observed in persons who exercise a great deal. When hypotension becomes serious, it can be treated by drug therapy. Effects of hypotension
on the body include general fatigue and weakness and decreased kidney function. An increase in the susceptibility to orthostatic hypotension (that is, the patient faints when arising too quickly from a bed or chair) or fainting is also seen.

2-11. DISORDERS WHICH AFFECT THE BLOOD SYSTEM

As with any other system of the body, some disorders may affect the blood system. Usually these disorders are types of anemias, but there are other disorders involved.

a. Iron Deficiency Anemia. Iron deficiency anemia is due to a deficiency of elemental iron in the blood. Iron is essential for the proper functioning of hemoglobin. In iron deficiency anemia, the blood cannot transport as much oxygen. Therefore, the tissues of the body are deprived of the much-needed oxygen. Furthermore, the presence of iron deficiency anemia affects the formulation of blood cells. Treatment of iron deficiency anemia requires the administration of iron either orally or parenterally.

b. Hemolytic Anemia. Hemolytic anemia is a general term referring to anemias caused by weakened red blood cell membranes. There are several types of hemolytic anemias that are often classified according to their cause. Some of the causes of hemolytic anemia are drugs (such as primaquine or the sulfonamides), heredity, or lack of either vitamin B12 or folic acid. In hemolytic anemia, the red blood cells are weak and lyse (break apart) as they squeeze through the small capillaries or spleen. The treatment of the hemolytic anemias is obviously dependent on the particular cause. Splenectomies, discontinuance of the causative agent, or the administration of folic acid or vitamin B12 are some of the treatment possibilities.

c. Sickle Cell Anemia. Sickle cell anemia is a serious anemia that is predominant in people of black race. The erythrocytes of a person who has sickle cell anemia become sickle-shaped and, therefore, are not efficient carriers of gases or nutrients. The sickle-shaped cells also increase the viscosity of the blood that leads to decreased circulation in the small arteries and capillaries. Symptoms of sickle-cell anemia include pain of certain organs, bone and joint pain, fever, and cerebral thrombosis. The spleen is not usually enlarged. Complications associated with sickle cell anemia are leg ulcers, osteomyelitis, and occasionally, cardiac enlargement. The treatment for sickle cell anemia is usually symptomatic as the actual cause of the condition is unknown. Blood transfusions are usually involved in most treatment regimens.

d. Aplastic Anemia. Aplastic anemia is a very serious and usually fatal condition that affects about four out of every one million people. It is characterized by a progressive degeneration of the bone marrow that is rarely reversible. The usual cause appears to be toxins or drugs and excessive use of X-rays. The prognosis of this severe bone marrow depression is generally poor.
e. **Hemophilia.** Hemophilia is usually a hereditary disease characterized by a lack of one of the factors necessary for the clotting of the blood. Hemophilia is a disease that occurs more commonly in men than women. Patients who have hemophilia do not usually develop massive hemorrhages, but rather slow oozing or trickling of blood. The primary danger with hemophiliac patients is trauma involving severe bleeding. In these cases, the patient may soon die because of a severe loss of blood that will occur if the missing clotting factor is not soon administered.

f. **Leukemia.** Leukemia is a disease of the white blood cell forming tissue. It is characterized by an abnormally high white blood cell count. During the progression of the disease, the white blood cells gradually crowd out the erythrocytes and in some cases the leukocytes phagocytize (engulf) the red blood cells.

g. **Mononucleosis.** Mononucleosis is an extremely contagious disease characterized by an abnormally large number of one type of white blood cells (the monocytes). The disease affects the lymph tissue and is characterized by fever, sore throat, and inflamed lymph nodes. The spleen may become enlarged and lassitude (general tired feeling) on the part of the patient is not uncommon. Mononucleosis is thought to be a disease of viral origin that usually strikes people between the ages of ten and thirty-five. The treatment of mononucleosis is symptomatic. The disease usually runs its complete course in about four to six weeks.

h. **Pernicious Anemia.** Pernicious anemia is caused by the inability of the body to absorb vitamin B₁₂ from the intestine. This failure to absorb vitamin B₁₂ is caused by a lack of the intrinsic factor that is normally secreted by the parietal cells in the stomach. The presence of this intrinsic factor is needed in order to absorb vitamin B₁₂. Pernicious anemia rarely affects persons under the age of thirty-five. It is more common in persons of English, Scandinavian, and Irish descent. It may be difficult to detect this condition because there are few outwardly visible signs associated with it. As with all anemias, fatigability is usually the first noticeable symptom. The red blood cells are large and oval. The treatment of pernicious anemia centers on the parenteral administration of vitamin B₁₂ (cyanocobalamin) which must be continued for the remainder of the patient’s life.

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2-12. **DISORDERS ASSOCIATED WITH THE CIRCULATORY SYSTEM**

**NOTE:** Two rather acute disorders that affect the circulatory system are a thrombus and an embolus. They are not considered diseases, but acute disorders.

a. **Thrombus.** A thrombus is a clot formed in a blood vessel that remains attached to the wall of the vessel. A thrombus can conceivably occur in any blood vessel. However, they are of primary concern when they occur in vessels serving vital organ systems such as the liver, kidneys, brain, and heart. Thrombi frequently get larger within the vessel and, if untreated, may eventually lead to complete blockage of the vessel. Such a blockage could lead to an infarction, an area of necrosis in a tissue or organ that results from the obstruction of circulation to that area.
b. **Embolus.** If the thrombus becomes dislodged from the wall of the vessel, it becomes an **embolus.** The usual treatment for an embolus is anticoagulant therapy in an effort to decrease the possibility of any future clotting. If necessary, certain enzymes may be administered to the patient in order to dissolve the existing clot. Treatment of an embolus is nearly impossible until it becomes an embolism. When the embolism has been identified, the treatment usually involves bed rest, anticoagulant therapy, and the possible administration of fibrinolytic enzymes.

2-13. **VASCOULAR DISORDERS**

Vascular disorders comprise some of the most common disorders in humans. Usually symptoms of vascular disorders are not seen until the condition reaches a point where it is considered serious. Several vascular disorders are discussed below:

a. **Arteriosclerosis.** A loss of elasticity or hardening of the arterial walls characterizes arteriosclerosis. The result is a decrease in the ability of these arteries to change their diameter. A complication that usually accompanies arteriosclerosis is **atherosclerosis.** Atherosclerosis is a condition in which lipid (fat) deposits form on the inside of the arteries causing a decrease in the flow of blood through the arteries. Both these conditions show a higher incidence in diabetics and in overweight individuals. Surgery and antihyperlipidemic drugs are used to treat these conditions.

b. **Varicose Veins.** A varicose vein is a condition that is probably because of excessively prolonged pooling of blood in the lower extremities (for example: legs). Varicose veins are especially common in people who are required to stand for prolonged periods of time with little or no exercise.

c. **Peripheral Vascular Disease.** Peripheral vascular disease is characterized by vasoconstriction of the arteries (especially in the extremities). Decreased blood flow to the extremities and corresponding hypothermia are some of the usual signs of this condition.

2-14. **BONE MARROW DEPRESSION**

Bone marrow depression is a condition characterized by a decrease in the function of the bone marrow that leads to a reduction in the cellular components of the blood. The overall effect of bone marrow depression is anemia and susceptibility to infection. The most common cause of bone marrow depression seems to be the toxicity of drugs. If detected early, the reversal of the disease may be accomplished by the removal of the causative agent (for example, the drug).
2-15. THE HEART

Through the action of its very muscular walls, the heart produces the primary motive force to drive the blood through the arterial system. In humans, the heart is located just above the diaphragm, in the middle of the thorax, and extending slightly to the left. It is said that the heart of an average individual is about the size of that individual’s clenched fist.

a. General Construction of the Human Heart. See Figure 2-2 for an illustration of the human heart.

(1) Chambers. The heart is divided into four cavities known as the chambers. The upper two chambers are known as the atria, right and left. Each atrium has an ear-like projection known as an auricle. The lower two chambers are known as ventricles, right and left. Between the two atria is a common wall known as the interatrial septum. Between the two ventricles is a common wall known as the interventricular septum.

<table>
<thead>
<tr>
<th>Term</th>
<th>Meaning</th>
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<tbody>
<tr>
<td>ATRIUM</td>
<td>hall</td>
</tr>
<tr>
<td>AURICLE</td>
<td>ear-like flap</td>
</tr>
<tr>
<td>VENTER</td>
<td>belly</td>
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<td>SEPTUM</td>
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</table>

(2) Wall layers. The walls of the chambers are in three general layers. Lining the cavity of each chamber is a smooth epithelium known as the endocardium. (Endocarditis is an inflammation of the endocardium.) The middle layer is made up of cardiac muscle tissue and is known as the myocardium. The outer layer of the heart is another epithelium known as the epicardium.

(3) Relationship of wall thickness to required pressure levels. A cross-section of the chambers shows that the atrial walls are relatively thin. The right ventricular wall is much thicker. The left ventricular wall is three to five times thicker than that of the right. These differences in wall thickness reflect the amount of muscle tissue needed to produce the amount of pressure required of each chamber.
Figure 2-2. The human heart.

(4) Cardiac valves (Figure 2-3).

(a) Between the atrium and ventricle of each side is the atrioventricular (A-V) valve. Each A-V valve prevents the blood from going back into the atrium from the ventricle of the same side. The right A-V valve is known as the tricuspid valve. The left A-V valve is known as the mitral valve. (“Might is never right.”). The mitral valve is sometimes called the bicuspid valve. The leaflets (flaps) of the A-V valves are prevented from being pushed back into the atria by fibrous cords. These fibrous
cords are attached to the undersides (the ventricular side) of the leaflets and are called chordae tendineae. At their other ends, the chordae tendineae are attached to the inner walls of the ventricles by papillary muscles.

(b) A major artery leads away from each ventricle: the pulmonary trunk from the right ventricle and the aortic arch from the left ventricle. A semilunar valve is found at the base of each of the pulmonary trunk and the aortic arch. These semilunar valves prevent blood from flowing back into the ventricles. The pulmonary (semilunar) valve and the aortic (semilunar) valve are each made up of three semilunar ("pocket-like") cusps.
b. **Coronary Arteries and Cardiac Veins.** We may say that the heart deals with two different kinds of blood flow: “functional” blood and “nutritive” blood. “Functional” blood is the blood that the heart works on, or pushes with its motive force. However, the walls of the heart require nutrition that they cannot get directly from the blood within the chambers. “Nutritive” blood is supplied to these walls by the coronary arteries, right and left. The coronary arteries arise from the base of the aortic arch and are distributed over the surface of the heart. This blood is collected by the cardiac veins and empties into the right atrium of the heart. Should a coronary artery, or one of its branches, become closed for whatever reason, that part of the heart wall formerly supplied nutrient blood by the closed vessel will very likely die.

c. **Pericardial Sac.** The average heart contracts in what is known as a heart beat, about 70-80 times a minute. To reduce the frictional forces that would be applied to its moving surfaces, the heart is enclosed in a special serous sac known as the pericardium (“around the heart”).

### 2-16. THE PROPERTY OF INHERENT RHYTHMICITY

a. The heart muscle (myocardium), like other muscles, is dependent upon electrical energy for its proper contraction. One property of cardiac muscle that cannot be found in any other muscle is inherent rhythmicity. Inherent rhythmicity is the property of the cardiac muscle that allows cardiac muscle cells to beat separately without any stimulation. If a cardiac muscle cell is placed in a saline (salt) bath containing the required amount of essential electrolytes the muscle cell will contract and relax rhythmically with no external stimulation. Furthermore, if another cardiac cell is placed in the same bath it, too, will beat at its own separate rate. It is interesting that when the two cardiac cells are placed together (in contact) the two cells will begin to beat as a unit. The property of inherent rhythmicity allows the myocardium to beat together with a minimal amount of nervous stimulation.

b. Instead of initiating the contractile process, nervous stimulation functions rather to govern the rate of the heartbeat. The property of inherent rhythmicity appears to be embryonic in origin. That is, the heart begins beating and systemic circulation occurs before any nervous tissue is formed.

### 2-17. THE HEARTBEAT

a. Initiation of the Cardiac Impulse. The initiation of the cardiac impulse begins in a highly specialized node of nervous tissue known as the sinoatrial node (also known as the SA node). As the name implies, the sino-atrial node is located in one of the atrias specifically the right atrium. The SA node initiates the electrical impulse that spreads out over both the atria causing the atrial muscles to contract. The fact that the SA node is located within the right atrium explains why the right atrium contracts 0.08 seconds before the left atrium contracts—although the contraction of the atria can still be considered to be simultaneous. As the atrial, muscle contracts the impulse travels through the atrial muscle to the atroventricular (AV) node.
b. **Atrioventricular Node.** The AV node is located between the right atrium and the right ventricle. The AV node is responsible for the contraction of both the ventricles. From the atrioventricular node, the impulse travels through the Bundle of HIS to the purkinje fibers of the ventricles.

c. **Bundle of HIS.** The Bundle of HIS is a collection of cardiac fibers through which the impulse travels on its way to the Purkinje fiber system. The Bundle of HIS is located at the uppermost portion of the ventricular septum. The ventricular septum is the thick muscular membrane that separates the right ventricle from the left ventricle.

d. **Purkinje Fibers.** The Purkinje fibers transverse and branch off within the ventricular septum branching to supply both ventricles near the bottom of the septum. By branching close to the bottom of the ventricular septum, the contractions of the ventricles go in an upward direction that is necessary for proper blood flow. Consequently, the contraction of the ventricles forces the blood upward to the aorta and pulmonary arteries.

e. **Control of the SA Node and AV Node.** Both the SA and the AV node are controlled by the autonomic nervous system. Parasympathetic stimulation, supplied by the vagus nerve tends to decrease both the rate and force of contraction of the heart. Sympathetic stimulation, from the cervical sympathetic ganglia, serves to increase both the rate and force of contraction of the heart. The predominant sympathetic receptor is a beta-receptor although it has been shown that a small amount of alpha-receptors are present in the heart.

### 2-18. ELECTROLYTES OF SIGNIFICANCE IN HEART FUNCTIONING

As with all muscle and nervous tissue, a proper concentration of electrolytes is essential for normal heart function. The three electrolytes essential for proper cardiac function are potassium, calcium, and sodium.

a. **Potassium.** An increase in the level of potassium in the extra-cellular fluid causes a decrease in the heart rate as well as a decrease in the force of contraction. The heart becomes dilated and flaccid. An extremely large increase in potassium can block nervous conduction through the atrioventricular bundle. If potassium levels are increased two or three times above normal, the atrioventricular blockade is usually so severe that death occurs. Potassium depletion also causes a decrease in the heart rate and an increase in the force of contraction. This is of concern, especially in the patient who has been taking digitalis. As you will remember, digitalis is valuable in the treatment of heart failure because it decreases the heart rate as well as increases the force of contraction, thus the efficiency of the heart is increased. If potassium levels are depleted at too great a degree, digitalis intoxication can result in which case the heart rate might decrease to too slow a rate.

b. **Calcium.** Calcium is primarily involved with the contractile processes of the myocardium. An increase in calcium levels may cause over contraction of the heart and
a decrease in calcium levels may cause cardiac flaccidity. It should be noted that calcium level alterations rarely reach the point where these effects can be seen.

c. **Sodium.** Sodium is another essential electrolyte involved in cardiac function. However, sodium imbalances are usually manifested in some of the other systems before cardiac problems arise. If sodium levels are increased above normal depressed cardiac function occurs. Sodium levels are of concern in congestive heart failure because of the edema that can certainly aggravate congestive heart failure. Persons having congestive heart failure must carefully monitor their sodium intake in that too much sodium can cause an excessive fluid accumulation in the tissues. This fluid accumulation causes the heart to work harder in order to compensate for the water.

d. **Magnesium.** Magnesium is an essential electrolyte involved as a cofactor in many enzyme systems. It is also closely linked to regulating intracellular potassium and calcium content. High magnesium levels may affect heart rate, cardiac conduction, and blood pressure. Hypotension, vasodilation, bradycardia, heart block, and cardiac arrest can occur with increasing levels. Low magnesium may cause cardiac arrhythmias and may play an important role in atypical ventricular tachycardia (torsades de pointes). Attempting to replace potassium is difficult if an existing magnesium or calcium deficiency is also present.

2-19. CARDIAC DISORDERS

Cardiac disorders are some of the top killers in the United States. A variety of medications are used in the treatment of these conditions.

a. **Bradycardia.** Bradycardia is a slow heart rate. Generally, bradycardia refers to a heart rate less than 60 beats per minute. This condition is sometimes referred to as sinus bradycardia because the decrease in heart rate is usually attributed to a decrease in the activity of the sinoatrial node. An increase in vagal tone is probably the cause of most cases of bradycardia. In most cases, bradycardia is not serious. Bradycardia is often observed in sleeping persons and in young athletes. There are no symptoms of bradycardia unless it is severe. For simple bradycardia, no treatment is usually needed; however, severe bradycardia may be treated with atropine.

b. **Tachycardia.** Tachycardia means a rapid heart rate. Generally, tachycardia refers to a heart rate more than 100 beats per minute. Tachycardia can be caused by a number of disorders (for example, hyperthyroidism, vagal suppression, sympathetic nervous system stimulation, emotional responses, and exercise). The usual treatment of tachycardia is aimed at removing its cause.

c. **Arrhythmia.** Arrhythmia is a term that is used to refer to any abnormal heartbeat (that is, missed beats or extra beats). There are two types of arrhythmias that will be discussed in this subcourse: flutter and fibrillation.
(1) **Flutter.** Flutter is a very rapid heart rate with rhythm present. Usually the heart rate is much faster than in simple tachycardia (between 200 to 400 beats per minute).

(2) **Fibrillation.** Fibrillation is a term which refers to an extremely rapid heart rate with no rhythm. This condition is treated with an electric defibrillator that reverses fibrillation with the use of an electric shock.

d. **Angina Pectoris.** Angina pectoris is an acute condition in which one or more of the coronary arteries becomes blocked. A sharp burning pain in the chest that may be felt also in the neck and left arm characterizes angina. The coronary arteries may become partially occluded (closed) by an embolism or thrombus, or a simple increase in oxygen demand when exercising, but is usually attributed to a result of atherosclerotic obstruction of the coronary arteries. The heart muscle cells are thus deprived of oxygen because of the decreased flow of blood and death of the myocardial cells may result if the condition is not remedied. Acute management of angina pectoris is usually achieved with the use of a rapid acting vasodilator such as nitroglycerin or amyl nitrite.

e. **Myocardial Infarction.** A myocardial infarction is similar to angina pectoris, but it is usually more serious. During angina pectoris the coronary arteries are usually only partially blocked; however, during a myocardial infarction complete blockage of one of the coronary arteries results. The symptoms are essentially the same as angina pectoris, but are not usually relieved by vasodilators. Complete bed rest is essential for the patient. Death of cardiac muscle cells often results unless another vessel is able to carry blood to the affected area.

f. **Congestive Heart Failure.** Congestive heart failure is defined as a decrease in the efficiency of the pumping of the heart. This condition usually leads to pulmonary edema, a complication attributed to the fluid back up. Because of decreased blood flow, there is a decrease in renal circulation that can further aggravate the associated edema because of both decreased glomerular filtration rate and increased sodium retention. Vasodilators that belong to a class of drugs called Angiotensin Converting Enzyme Inhibitors (ACE inhibitors) are the first line drug of choice for treatment of congestive heart failure. If a patient cannot tolerate ACE inhibitors, they may be placed on a nitrate (Isordil®) and hydralazine instead. As heart failure worsens and edema increases, diuretics are used to decrease edema. Digitalis glycosides (digoxin) used to be the drug of choice for heart failure, however due to many drug-drug interactions and narrow therapeutic index, it is reserved for acute symptomatic heart failure or in patients with heart failure and atrial fibrillation. Digoxin works by increasing the efficiency of the heart as a pump by decreasing both the size of the heart and the rate of the heart while at the same time increasing the force of contraction. As heart failure worsens, treatment may involve the addition of beta-adrenergic blockers (carvedilol, metoprolol) and spironolactone (potassium-sparing diuretic).
g. **Cardiac Arrest.** A cardiac arrest is simply the sudden cessation (stoppage) of the heartbeat. The cause of the stoppage may or may not be known. Treatment of the cardiac arrest is dependent upon the cause of the arrest.

h. **Rheumatic Fever.** Rheumatic fever is a streptococcal infection which many times attacks the valves of the heart. The result is a deformed or weakened valve that results in a heart murmur.

i. **Endocarditis.** Endocarditis is an inflammation of the membrane that lines the heart. Bacteria that repeatedly enter the bloodstream usually cause endocarditis. The bacteria which causes the endocarditis may enter the bloodstream following a tooth extraction and, on occasion, is associated with unsanitary intravenous injection techniques. Diagnosis of endocarditis usually involves the presence of a low fever and a soft, muffled heart murmur. The valves of the heart are also affected and if not detected and treated early endocarditis may cause irreversible damage. The treatment of endocarditis usually centers on bed rest and long term (4-6 weeks) antibiotic therapy.

j. **Heart Block.** A heart block is defined as a condition in which the cardiac excitation is slowed or interrupted somewhere in the normal pathway where conduction takes place. The two primary types of heart block usually seen are the SA or sinoatrial block and the atrioventricular or AV block. The term "heart block" is somewhat ambiguous. Usually the block only occurs occasionally and the result is manifested in only a skipped beat. Generally, the SA block requires no treatment; however, the prognosis is dependent on the cause and frequency of the block. During the AV block several or all impulses from the SA node are delayed or blocked in the AV node or bundle. Obviously, this type of block is much more serious than the SA block. Treatment of AV block depends upon the cause and the severity of the block. Digitalis toxicity may cause AV block on occasion.

2-20. **CARDIOVASCULAR CIRCULATORY PATTERNS**

See Figure 2-4 for an illustration depicting cardiovascular circulatory patterns.

a. **General.** The human cardiovascular system is described as a closed, twocycle system.

(1) It is **closed** because at no place is the blood as whole blood ever outside the system.

(2) It is **two-cycle** because the blood passes through the heart twice with each complete circuit of the body. In the pulmonary cycle, the blood passes from the right heart, through the lungs, and to the left heart. In the systemic cycle, the blood passes from the left heart, through the body in general, and returns to the right heart.

(3) It is common for an area of the body to be supplied by more than one blood vessel, so that if one is damaged, the others will continue the supply. This is
known as **collateral circulation**. However, there are situations, such as in the heart and the brain, where a single artery supplies a specific part of a structure. Such an artery is called an **end artery**. When an end artery is damaged, that area supplied by it will usually die, as in the case of the coronary artery above, or the cause of a “stroke” in the brain.

b. **Pulmonary Cycle.** The pulmonary cycle begins in the right ventricle of the heart. Contraction of the right ventricular wall applies pressure to the blood. This forces the tricuspid valve closed, and the closed valve prevents blood from going back into the right atrium. The pressure forces blood past the semilunar valve into the pulmonary trunk. Upon relaxation of the right ventricle, backpressure of the blood in the pulmonary trunk closes the pulmonary semilunar valve. The blood then passes into the lungs through the pulmonary arterial system. Gases are exchanged between the alveoli. This blood, now saturated with oxygen, is collected by the pulmonary veins and carried to the left atrium of the heart. This completes the **pulmonary cycle**.

![Figure 2-4. Cardiovascular circulatory pattern.](image-url)
c. **Systemic Cycle.**

1. **Left ventricle of the heart.** The oxygen-saturated blood is moved from the left atrium into the left ventricle. When the left ventricular wall contracts, the pressure closes the mitral valve, which prevents blood from returning to the left atrium. The contraction of the left ventricular wall therefore forces the blood through the aortic semilunar valve into the aortic arch. Upon relaxation of the left ventricular valve, the back pressure of the aortic arch forces the aortic semilunar valve closed.

2. **Arterial distributions.** The blood then passes through the various arteries to the tissues of the body. See Figure 2-5 for an illustration of the main arteries of the human body.
   - (a) The carotid arteries supply the head. The neck and upper members are supplied by the subclavian arteries.
   - (b) The aortic arch continues as a large single vessel known as the aorta passing down through the trunk of the body in front of the vertebral column. It gives off branches to the trunk wall and to the contents of the trunk.
   - (c) At the lower end of the trunk, the aorta divides into right and left iliac arteries, supplying the pelvic region and lower members.

3. **Capillary beds of the body tissues.** In the capillary beds of the tissues of the body, materials (such as food, oxygen, and waste products) are exchanged between the blood and the cells of the body.

4. **Venous tributaries.** See Figure 2-6 for an illustration of the main veins of the human body.
   - (a) The blood from the capillaries among the tissues is collected by a venous system parallel to the arteries. This system of deep veins returns the blood back to the right atrium of the heart.
   - (b) In the subcutaneous layer, immediately beneath the skin, is a network of superficial veins draining the skin areas. These superficial veins collect, and then join the deep veins in the axillae (armpits) and the inguinal region (groin).
   - (c) The superior vena cava collects the blood from the head, neck, and upper members. The inferior vena cava collects the blood from the rest of the body. As the final major veins, the venae cavae empty the returned blood into the right atrium of the heart.
   - (d) The veins are generally supplied with valves to assist in making the blood flow toward the heart. It is of some interest to note that the veins from the head do not contain valves.
Figure 2-5. Main arteries of the human body.
Figure 2-6. Main veins of the human body.
From that portion of the gut where materials are absorbed through the walls into the capillaries, the blood receives a great variety of substances. While most of these substances are useful, some may be harmful to the body. The blood carrying these substances is carried directly to the liver by the hepatic portal venous system. This blood is specially treated and conditioned in the liver before it is returned to the general circulation by way of the hepatic veins.

Section IV. THE HUMAN LYMPHATIC SYSTEM

2-21. GENERAL

Between the cells of the body are spaces filled with fluid. This is the interstitial (or tissue) fluid, often referred to as intercellular fluid. There are continuous exchanges between the intracellular fluid, the interstitial fluid, and the plasma of the blood. The lymphatic system returns to the bloodstream the excess interstitial fluid, which includes proteins and fluid derived from the blood.

2-22. STRUCTURES OF THE HUMAN LYMPHATIC SYSTEM

See Figure 2-7 for an illustration of the human lymphatic system.

a. **Lymphatic Capillaries.** Lymphatic capillaries are located in the interstitial spaces. Here, they absorb the excess fluids.

b. **Lymph Vessels.** A tributary system of vessels collects these excess fluids, now called lymph. Like veins, lymphatic vessels are supplied with valves to help maintain a flow of lymph in one direction only. The lymphatic vessels, to a greater or lesser extent, parallel the venous vessels along the way. The major lymph vessel in the human body is called the thoracic duct. The thoracic duct passes from the abdomen up through the thorax and into the root of the neck in front of the vertebral column. The thoracic duct empties into the junction of the left subclavian and jugular veins.

c. **Lymph Nodes.** Along the way, lymphatic vessels are interrupted by special structures known as lymph nodes. These lymph nodes serve as special filters for the lymph fluid passing through.

d. **Tonsils.** Tonsils are special collections of lymphoid tissue, very similar to a group of lymph nodes. These are protective structures and are located primarily at the entrances of the respiratory and digestive systems.
Figure 2-7. The human lymphatic system.

Continue with Exercises
EXERCISES, LESSON 2

REQUIREMENT: The following exercises are to be answered by marking the lettered response that best answers the question; or by completing the incomplete statement; or by writing the answer in the space provided at the end of the question.

After you have completed all the exercises, turn to “Solutions to Exercises,” at the end of the lesson, and check your answers with the solutions.

1. Which of the following statements best explain the need for circulatory systems?
   a. To protect the body from invading bacteria.
   b. To get food and oxygen to the cells.
   c. To remove waste products from the cells.
   d. To provide a means of cell reproduction.

2. Which of the following are circulatory systems in the human body?
   a. The sinoatrial system.
   b. The lymphatic system.
   c. The diastolic system.
   d. The cardiovascular system.

3. Capillaries are best described as ___________________
   a. Vehicles for nutrients, oxygen, and wastes.
   b. Very large conduits or channels through which the blood is moved.
   c. Very small vessels that provide exchange areas.
   d. The component of the cardiovascular system that serves as the primary motive force of blood movement.
4. Select the components of the blood.
   a. Plasma.
   b. Formed elements (red blood cells, white blood cells, and platelets).
   c. Both a and b.

5. Plasma is best described as ______________________
   a. The protein material that carries dissolved oxygen in the blood.
   b. The liquid portion of the blood that is responsible for blood clotting.
   c. The clear fluid that remains after the blood has clotted.
   d. The clear fluid portion of the blood that accounts for approximately 55 percent of the total blood volume.

6. Red blood cells (RBCs) are best described as _______________
   a. Fragments of cells that aid in the clotting of blood by clumping together and by releasing certain chemical factors related to clotting.
   b. The formed elements of the blood that phagocytize (swallow up) foreign particles and organisms.
   c. Biconcave discs that contain hemoglobin, a protein responsible for carrying most of the oxygen transported by the blood.
   d. The formed elements of the blood that produce antibodies and serve other functions in immunity.

7. Which of the following statements best describes veins?
   a. The blood vessels that carry blood to the chambers of the heart.
   b. The blood vessels that carry blood away from the chambers of the heart.
   c. Extremely thin-walled blood vessels that act as exchange areas.
   d. Blood vessels that always carry deoxygenated blood.
8. Below are the steps involved in the clotting of blood. Select the arrangement of steps that best reflects their sequential order in the clotting process.

I. Thromboplastin reacts with calcium and another substance, prothrombin, to form thrombin.

II. The blood platelets release a substance that is known as thromboplastin.

III. The thrombin formed acts as an enzyme to convert fibrinogen to fibrin threads that eventually form the blood clot.

   a. I, II, and III.
   b. III, II, and I.
   c. II, III, and I.
   d. II, I, and III.

9. Blood pressure is best described as _____________________.

   a. The residual pressure of the blood due to the elasticity of the blood vessels.
   b. The force exerted by the blood as it is pumped throughout the circulatory system.
   c. The pressure the blood exerts as it is pumped from the heart.
   d. The pressure the blood exerts when the heart is resting.

10. Select the medical problems associated with high blood pressure.

    a. Frequent nosebleeds.
    b. Arteriosclerosis.
    c. Strokes.
    d. Hypertrophy of the myocardium.
    e. All of the above.
11. Hemophilia is __________________________.

   a. A very serious type of anemia characterized by a progressive degeneration of the bone marrow.
   
   b. A hereditary disease characterized by a lack of one of the factors necessary for the clotting of the blood.
   
   c. A general term that refers to a group of anemias caused by weakened red blood cell membranes.
   
   d. A type of anemia caused by a deficiency of elemental iron in the blood.

12. Leukemia is ________________________.

   a. A very serious and usually fatal condition characterized by the excessive production of red blood cells.
   
   b. A serious type of anemia predominant in older people because they tend to have red blood cells with weakened membranes.
   
   c. A disease of the white blood cell forming tissue characterized by an abnormally high white blood cell count.
   
   d. A disease of the red blood cell forming tissue which results in the production of excessive numbers of red blood cells which phagocytize the other cells in the blood.

13. Arteriosclerosis is ____________________________.

   a. A condition characterized by a loss of elasticity or hardening of the arterial walls.
   
   b. A condition characterized by vasoconstriction of the arteries in the extremities.
   
   c. A condition that occurs when a clot is formed in a blood vessel.
   
   d. A serious condition that affects the arteries and causes them to lose vital fluids.
14. Which of the following statements best describes the property inherent rhythmicity?

   a. The property of cardiac cells which allows them to beat without the presence of any electrolytes.

   b. The property of the heart cells that allows them to initiate each contractile process instead of requiring them to govern the rate of the heart beat.

   c. The property of the myocardium to continue pumping blood after the individual has died.

   d. The property of the cardiac muscle that allows cardiac muscle cells to beat separately without any stimulation.

15. Match the name of each part of the heart with its respective structure.

   _____ Left atrium.

   _____ Right atrium.

   _____ Left ventricle.

   _____ Right ventricle.
16. Which statement best describes the role of the Bundle of HIS in the heartbeat?

   a. The Bundle of HIS is responsible for the contraction of both the ventricles.

   b. The Bundle of HIS is a collection of cardiac fibers through which the impulse travels on its way to the Purkinje fibers.

   c. The Bundle of HIS provides nervous stimulation so that the ventricles go in a downward direction, which is necessary for proper blood flow.

   d. The Bundle of HIS is responsible for initiating the cardiac impulse.

17. Select the effect of excessive levels of calcium in the extracellular fluid.

   a. Cardiac flaccidity.

   b. Cardiac edema.

   c. Spastic condition of the heart.

   d. A decrease in the force of contraction of the heart beat.

18. Congestive heart failure is best described as ____________________.

   a. An acute condition in which one or more of the coronary arteries become blocked.

   b. A complete blockage of one or more of the coronary arteries which results in damage to the cardiac muscle.

   c. An inflammation of the membrane that lines the heart.

   d. A decrease in the efficiency of the pumping of the heart which usually leads to pulmonary edema.
19. A lymph node is ______________________.

   a. A special structure that filters the lymph fluid.
   
   b. A structure located in the interstitial spaces which absorbs excess extracellular fluids.
   
   c. The major lymph vessel in the body.
   
   d. A special collection of lymphoid tissue which serves as the major site of red blood cell destruction in the body.

**Check Your Answers on Next Page**
1.  b  To get food and oxygen to the cells.  (para 2-1b)  
    c  To remove waste products from the cells.  (para 2-1b)  
2.  b  The lymphatic system.  (para 2-3b)  
    d  The cardiovascular system.  (para 2-3a)  
3.  c  Very small vessels that provide exchange areas.  (para 2-4d)  
4.  c  Both a and b.  (para 2-5)  
5.  d  The clear fluid portion of the blood which accounts for approximately 55 percent of the total blood volume.  (para 2-5a)  
6.  c  Biconcave discs which contain hemoglobin, a protein responsible for carrying most of the oxygen transported by the blood.  (para 2-5b(1))  
7.  a  The blood vessels which carry blood to the chambers of the heart.  (para 2-6b(2))  
8.  d  II, I, and III.  (para 2-8)  
9.  b  The force exerted by the blood as it is pumped throughout the circulatory system.  (para 2-9a)  
10.  e  All the above.  (para 2-10a)  
11.  b  A hereditary disease characterized by a lack of one of the factors necessary for the clotting of the blood.  (para 2-11e)  
12.  c  A disease of the white blood cell forming tissue characterized by an abnormally high white blood cell count.  (para 2-11f)  
13.  a  A condition characterized by a loss of elasticity or hardening of the arterial walls.  (para 2-13a)  
14.  d  The property of the cardiac muscle which allows cardiac muscle cells to beat separately without any stimulation.  (para 2-16a)
15.  _____b____ Left atrium.  (Figure 2-2)
    _____a____ Right atrium.  (Figure 2-2)
    _____c____ Left ventricle.  (Figure 2-2)
    _____d____ Right ventricle.  (Figure 2-2)

16.  b  The Bundle of HIS is a collection of cardiac fibers through which the
     impulse travels on its way to the Purkinje fibers.  (para 2-17c)

17.  c  Spastic condition of the heart.  (para 2-18b)

18.  d  A decrease in the efficiency of the pumping of the heart, which
     usually leads to pulmonary edema.  (para 2-19f)

19.  a  A special structure which filters the lymph fluid.  (para 2-22c)

*End of Lesson 2*
LESSON ASSIGNMENT

LESSON 3 Cardiac Drugs.

LESSON ASSIGNMENT Paragraphs 3-1--3-15.

TASKS

081-824-0001, Perform Initial Screening of a Prescription.

081-824-0026, Evaluate a Prescription.

081-824-0002/3, Fill a Prescription For a Controlled/Non-Controlled Drug.

081-824-0027, Evaluate a Completed Prescription.

081-824-0028, Issue Outpatient Medications.

OBJECTIVES After you finish this lesson you should be able to:

3-1. From a group of statements, select the best description of congestive heart failure.

3-2. Given a group of statements, select the statement which best describes the primary pharmacological property of digitalis and related cardiac glycosides.

3-3. Given a group of statements, select the statement which best describes digitalizing dose.

3-4. From a group of statements, select the statement that best describes the difference between the digitalizing dose and the maintenance dose of digitalis.

3-5. Given the trade and/or generic name of a cardiac drug and a group of uses, side effects, or patient precautionary statements, select the use(s), side effect(s), or patient precautionary statement(s) for that drug.

3-6. Given the trade or generic name of a cardiac agent and a group of drug names (trade and/or generic), select the corresponding trade or generic name for the given drug.
3-7. Given a group of statements and one of the following terms: cardiac arrhythmia flutter or fibrillation, select the statement which best defines the given term.

SUGGESTION

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
3-1. INTRODUCTION

Heart disease is the number one killer in the United States today. Two people succumb to conditions related to heart disease every minute of the day. However, it must be remembered that heart disease can be treated. Discoveries of new ways to use existing drugs and improved surgical techniques translate into longer and more productive lives for persons who have heart disease. In lesson 2 of this subcourse, various disease states that can affect the circulatory system were discussed. In this lesson, some of these conditions will be reviewed. The primary focus of this lesson will be the drug used to treat these conditions.

3-2. REVIEW OF CONGESTIVE HEART FAILURE

Congestive heart failure may be defined as nonefficient pumping of the heart. This inefficiency in pumping the heart leads to an increase in the size of the heart and an increase in the heart rate. This increase in heart size and heart rate result because of the heart's attempt to compensate for the poor efficiency in pumping blood to other parts of the body. Consequently, the kidneys improperly function. Improperly functioning kidneys result in edema of the extremities due to improper excretion (removal) of sodium and waste products in the urine. If a patient's congestive heart failure becomes acute, he may have pulmonary edema due to poor kidney function.

3-3. TREATMENT OF CONGESTIVE HEART FAILURE

Rest and restriction of sodium (that is, sodium chloride) intake are important aspects of the non-pharmacologic treatment of congestive heart failure. Drug treatment includes ACE Inhibitors, diuretics (see Lesson 8), digitalis and the related cardiac glycosides, beta adrenergic blockers, and spironolactone.

3-4. ANGIOTENSIN-CONVERTING ENZYME INHIBITORS (ACE INHIBITORS)

a. Angiotensin-converting enzyme inhibitors (ACE inhibitors) belong to a unique class of vasodilators. ACE inhibitors block a specific enzyme (angiotensin converting enzyme) that converts angiotensin I to angiotensin II. Angiotensin II is one of the most potent vasodilators in the body. The mechanism of action of ACE inhibitors in the treatment of congestive heart failure relies on the ability to cause both arterial and venous vasodilation through this inhibition, thereby decreasing the workload on the heart. Hemodynamic effects associated with long term use include increased cardiac function and decreased blood pressure and heart rate. Significant improvements are
seen in exercise tolerance and left ventricular size. ACE inhibitors are well tolerated and have been shown to decrease hospitalizations and deaths. For these reasons, agents in this class are first line pharmacologic treatment for congestive heart failure.

b. ACE Inhibitors are often initiated immediately after a heart attack or when a patient still has mild symptoms of heart failure. The starting dose is low and titrated (gradually increased) up to the maximum tolerated dose (based on heart rate and blood pressure). The most bothersome side effect is a dry cough which develops in some patients. Other side effects include angioedema (facial swelling) and elevated potassium levels.

c. Agents included in this class include captopril (Capoten®), enalapril (Vasotec®), lisinopril (Prinivil®, Zestril®), and ramipril (Altace®)

3-5. DIGITALIS AND THE RELATED GLYCOSIDES

a. The mechanisms of action of digitalis and related cardiac glycosides in the treatment of congestive heart failure are not fully understood. The main pharmacological property of these drugs is their ability to increase the force of myocardial contraction (the heart muscle’s contraction) by a direct action on the ventricular heart muscles. Conduction is also slowed somehow between the SA node and the AV node, resulting in a decrease in heart rate. Because of the slower heart rate and increase in the force of the myocardial contraction, the heart has more time to adequately fill with venous blood. The secondary changes seen as a result of the first three mechanisms of action will be a decrease in heart size and a decrease in heart rate due to more efficient pumping of the heart. Because of the slower heart rate, cardiac glycosides are also used in the treatment of atrial flutter or atrial fibrillation.

b. Because of improved circulation to the kidneys, an increase in urinary output (diuresis) within 24 to 48 hours following administration of cardiac glycosides will also be seen. Digitalis toxicity is enhanced in patients who have low serum potassium (hypokalemia), so potassium supplements may be given based upon periodic blood test analysis.

c. Digitalis and related glycosides have very narrow therapeutic indices (the treatment dose is very close to the toxic dose) and many drug-drug interactions. The dose must also be adjusted in renal failure, which is common in CHF patients. For these reasons digitalis is reserved for acute symptomatic heart failure or in those patients with CHF and atrial fibrillation.

3-6. DIGITALIZING DOSE

a. The digitalizing dose of a cardiac glycoside is the initial large dose of the drug that is given to the patient in order to relieve the symptoms of congestive heart failure or to render the patient asymptomatic as it is commonly referred to. Often the digitalization is accomplished by administering relatively large doses of digitalis preparations within a
18-24 hours to the patient. This type of intensive administration of “loading” doses can cause toxic reactions since digitalis preparations have only a moderate safety margin.

b. Although a patient’s condition may have responded to digitalization, he may have to continue to take a digitalis product for a long period. The physician must determine the amount of drug the patient must take on a daily basis in order for the patient’s heart to perform at its optimal level. **Maintenance doses** are ordered which are just enough to replace the amount of digitalis eliminated since the administration of the last dose. The maintenance dose is then taken each day to maintain the quantity of drug required to keep the patient’s heart beating efficiently. Although these daily maintenance doses are much lower than the original digitalizing doses, the risk of toxicity remains.

### 3.7. DIGITALIS PRODUCTS

a. **Digoxin (Lanoxin®)**. Digoxin is the most common cardiac glycoside used to treat congestive heart failure. The drug is usually administered intravenously (IV) for digitalization in a total dosage of from 1 to 1.5 milligrams. This drug may be given orally if the physician desires. The maintenance dose ranges from 0.125 milligram to 0.5 milligram daily, but normally 0.25 milligram of digoxin is given each day to the patient. The side effects of digoxin include anorexia (loss of appetite), arrhythmias, nausea and vomiting, and yellowish-green vision. Digoxin should be used with caution in patients who have kidney problems because the kidneys are the primary route of excretion for this agent. This drug should be used with caution in patients who have low serum potassium. Digoxin is available in 0.125 milligram, 0.25 milligram, and 0.5 milligram tablets; 0.05 milligram, 0.1 milligram and 0.2 mg liquid filled capsules; or in an injectable solution of 0.1 milligram per milliliter in 1 milliliter containers and 0.25 milligram per milliliter in 2 milliliter containers. It is also available in a 0.05 milligram per milliliter pediatric elixir. The bioavailability is improved with the liquid filled capsules such that 0.1mg of the capsule is equivalent to 0.125 mg of the tablet. Many times the physician will prescribe the pediatric elixir with directions for the patient to take a certain total daily dose (e.g., 0.125 milligram). You must interpret this as milliliters (or cubic centimeterscc’s) in order for the patient to dose himself with the calibrated dropper supplied with the preparation. As you probably realize, you might have to use your pharmaceutical calculation skills to calculate the dose of the drug solution.

b. **Digitoxin (Crystodigin®)**. Digitoxin is another cardiac glycoside obtained from Digitalis purpurea. Although rarely used, you must be aware of this agent as it can be confused with digoxin. This product must be used with caution in patients with liver problems since this drug is excreted primarily in the bile and consequently, has a long half-life (5 to 7 days). The drug is available as a 0.1 mg and 0.2 mg tablet.
3-8. OTHER AGENTS USED IN CONGESTIVE HEART FAILURE

a. **Beta Adrenergic Blocking Agents.** The stimulation of beta-1 receptors in cardiac tissue causes an increased heart rate often causing an increase in workload of the heart. As heart failure worsens, the body compensates by stimulating beta receptors to make the heart pump faster and faster. Consequently, the faster the heart pumps, the less time the ventricles have to fill and pump efficiently. Beta adrenergic blocking agents work by blocking this stimulation and allowing less work by the heart by decreasing the heart rate. Doses are initiated very low and titrated very slowly (over weeks to months). Large initial doses of beta blockers will actually worsen and produce heart failure. The most common agents used in the treatment of heart failure include carvedilol (Coreg®) and metoprolol (Lopressor®).

b. **Spironolactone (Aldactone®).** Spironolactone is a potassium sparing diuretic that works by inhibiting aldosterone and causing diuresis. It is useful in the treatment of edema common in CHF patients.

c. **Amiodarone (Cordarone®).** Amiodarone is an agent used in the treatment of atrial and ventricular arrhythmias. However, when used in patients who have CHF and arrhythmias, it has been shown to improve exercise tolerance, decrease hospitalizations, and improve pump function.

Section II. THE ANTIARRHYTHMIC AGENTS

3-9. REVIEW OF CARDIAC ARRHYTHMIAS

Disorders of impulse information, impulse conduction, or a combination of these factors produces cardiac arrhythmias (or abnormal heartbeats). These are two types of arrhythmias that we will consider: flutter and fibrillation.

a. **Flutter.** Flutter is a very rapid heart rate with rhythm present. Usually the heart rate is much faster in flutter than it is in simple tachycardia. In flutter, the heart can beat from 200 to 400 beats per minute.

b. **Fibrillation.** Fibrillation occurs when there is a very rapid heart beat with no rhythm.

3-10. THE USE OF ANTIARRHYTHMIC DRUGS

The term antiarrhythmic drugs refer to the agents that suppress abnormal beats or restore normal cardiac rhythm by depressing various properties of the myocardium (heart muscle). This is a general mechanism of action for all these drugs. The toxicity of the drugs will be discussed with each individual drug since it varies with each agent.
3-11. SPECIFIC ANTIARRHYTHMIC DRUGS

a. **Quinidine (Quiniglute®, Quinidex®).** Quinidine is an antiarrhythmic agent used in the treatment of atrial fibrillation and ventricular arrhythmias. It is given orally in a usual dose of 200 to 400 milligrams every 6-8 hours. The side effects associated with quinidine include hypersensitivity reactions, gastrointestinal (GI) disturbances (nausea, vomiting, and diarrhea) and a group of symptoms known as cinchonism. Some symptoms associated with cinchonism are tinnitus (ringing in the ears), vertigo (dizziness), and headaches.

b. **Procainamide (Pronestyl®).** Procainamide is used in the treatment of atrial and ventricular arrhythmias in an oral dosage range of from 250 to 500 milligrams four times daily. Procainamide is similar in chemical structure to procaine. It retains the quinidine like actions of procaine, but it is not rapidly hydrolyzed and its action persists long enough so that it is active even after oral as well as parenteral administration. Pharmacologically, procainamide is equivalent to quinidine. Procainamide may cause anorexia, nausea and vomiting, and drug hypersensitivity.

c. **Propranolol (Inderal®).** Propranolol is an agent that is used in the treatment of hypertension, angina pectoris, and cardiac arrhythmias. It is especially useful in the treatment of ventricular arrhythmias. The normal dosage of this drug for antiarrhythmic purposes is 10 to 40 milligrams given three or four times daily. As you might expect, the dose of the drug can be adjusted to meet the individual needs of the patient. The side effects associated with propranolol include bradycardia, bronchoconstriction, and congestive heart failure (CHF). These arise because of the beta blocking effects of the drug. The drug should be used with caution in persons who have asthma. Other beta blocking agents commonly used include Metoprolol (Lopressor®) and Atenolol (Tenormin®) and Sotalol (Betapace®).

d. **Phenytoin (Dilantin®).** Phenytoin is an agent that may be administered intravenously to reverse digitalis-induced arrhythmias. Rapid intravenous administration may cause bradycardia, hypotension, and cardiac arrest (rarely).

e. **Lidocaine (Xylocaine®).** Lidocaine is an agent that may be given intravenously in the treatment of ventricular arrhythmias. Large intravenous doses may produce convulsions, coma, and respiratory depression. You should be aware that not all lidocaine solutions are to be administered intravenously. *Lidocaine for intravenous use is clearly marked as such on the container.*

f. **Amiodarone (Cordarone®).** Amiodarone is an agent that is used to treat life-threatening ventricular arrhythmias and occasionally atrial arrhythmias. It is administered as an IV loading dose over 24 hours followed by oral maintenance. Use of amiodarone is associated with hepatic, ophthalmic, thyroid, and pulmonary side effects.

g. **Diltiazem (Cardizem®).** Diltiazem is used intravenously (5-20 mg/hr) to control ventricular rate in atrial flutter or fibrillation. The oral dosage is 240 mg to 320
mg per day in divided doses 1 to 4 times daily. Side effects include hypotension, bradycardia, congestive heart failure (CHF), edema, and dermatitis.

Section III. ANTIHYPERLIPIDEMIC AGENTS

3-12. REVIEW OF ATHEROSCLEROSIS

Atherosclerosis is a condition in which lipid (fat) deposits form on the inside of the arteries causing a decrease in the flow of blood through the arteries. The make up of these deposits is mostly cholesterol as a consequence of genetic and dietary factors which result in too much cholesterol. The arteries of most concern are the coronary arteries (those that supply the heart) and the carotid arteries (those that supply the brain). Hyperlipidemia is a condition of high levels of cholesterol, triglycerides, and /or lipoprotein in the blood. The higher the levels in the blood, the greater the risk that they will deposit on the inside of arteries. Several studies have shown a correlation between cholesterol levels and premature heart disease. Studies have shown that each 1% reduction in serum cholesterol correlates with a 2% decline in the risk of myocardial infarction. For example, a 25% reduction in cholesterol will reduce the risk of myocardial infarction by 50%. Diet, exercise, antihyperlipidemic drugs, and surgery are the most common treatments. If a patient has high cholesterol only, and no evidence of atherosclerosis, the treatment of the hyperlipidemia is referred to as primary prevention. If the patient already has atherosclerosis, treatment is known as secondary prevention.

3-13. DEFINITIONS

a. Cholesterol: A fat-related compound. It is a normal constituent of bile and a principal constituent of gallstones. In body metabolism cholesterol is important as a precursor of various steroid hormones such as sex hormones and adrenal corticoids. Cholesterol is synthesized by the liver. It is widely distributed in nature, especially in animal tissue such as glandular meats and egg yolk.

b. Triglyceride (TG): A compound of three fatty acids esterified to glycerol. A neutral fat, synthesized from carbohydrate, stored in adipose tissue. It releases free fatty acids into the blood on being hydrolyzed by enzymes.


(1) Chylomicron: Particle of fat - lipoproteins - appearing in the lymph and blood after a meal rich in fat. These particles are composed largely of triglycerides with lesser amounts of phospholipids, cholesterol, esters, and protein. About 2 to 3 hours after a fat meal, the chylomicrons cause lactescence (milkiness) in the blood plasma; this is termed alimentary lipemia.
(2) **Very low-density Lipoprotein (VLDL):** Still carries a large lipid (TG) content but includes about 10% to 15% cholesterol; formed in the liver from endogenous fat sources.

(3) **Intermediate-density Lipoprotein (IDL):** Continues the delivery of endogenous TG to cells and carries about 30% cholesterol.

(4) **Low-density Lipoprotein (LDL):** Carries in addition to other lipids about two thirds or more of the total plasma cholesterol; formed in the serum from catabolism of VLDL. Because LDL carries cholesterol to the cells for deposit in the tissues, it is considered the main agent of concern in elevated serum cholesterol levels.

(5) **High-density Lipoprotein (HDL):** Carries less total lipid and more protein; it is also formed in the liver from endogenous fat sources. Because HDL carries cholesterol from the tissues to the liver for catabolism and excretion, higher serum levels are considered protective against cardiovascular disease.

**3-14. RISK FACTORS**

Although high cholesterol levels are a risk factor for the development of atherosclerosis, it is not the only risk factor. How aggressively the health care provider decides to treat hyperlipidemia depends on the patient’s overall risk for developing atherosclerosis (heart disease). In addition to hyperlipidemia, the following are significant risk factors:

- **a. Uncontrollable Risk Factors.** These include age (greater than 45 for males and greater than 55 for females), sex (male), and family history of premature coronary heart disease (MI, stroke, or sudden death before age 55 in a male parent or sibling, 65 in a female parent or sibling).

- **b. Controllable Risk Factors.** These include active tobacco smoking, hypertension (treated or untreated), diabetes, severe obesity (>30% overweight), physical inactivity, and Type A personality traits.

**NOTE:** A high HDL (>60 mg/dl) is actually considered a negative risk factor. This means one positive risk factor may be subtracted in overall risk assessment. When determining treatment, two or more risk factors are considered significant.

**3-15. TREATMENT**

The treatment of hyperlipidemia depends on two factors: 1) whether that patient has existing atherosclerosis and 2) the patient’s other risk factors for atherosclerosis. The treatment goal is usually expressed at the Low-density Lipoprotein (LDL) goal as this is the major carrier of cholesterol in the blood.
### Treatment goals:

<table>
<thead>
<tr>
<th>Category</th>
<th>LDL-Cholesterol Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>No atherosclerosis &amp; &lt; 2 risk factors</td>
<td>&lt;160 mg/dl</td>
</tr>
<tr>
<td>No atherosclerosis &amp; 2 or more risk factors</td>
<td>&lt;130 mg/dl</td>
</tr>
<tr>
<td>Existing atherosclerosis</td>
<td>&lt;100 mg/dl</td>
</tr>
</tbody>
</table>

**a. Diet and Exercise.** Diet and exercise are considered lifestyle modifications which may lower cholesterol levels to goal. Diet changes reduce intake of cholesterol and fat, especially saturated fat. Exercise may involve aerobic exercise for at least 20-30 minutes, 3-5 times weekly. Whether a patient is on medication to lower their cholesterol or not, diet and exercise should always be a part of the treatment regimen.

**b. Drug therapy** - Medications are often prescribed for hyperlipidemia when diet and exercise fail to normalize LDL levels. Agents may prevent cholesterol synthesis or promote the breakdown of internal cholesterol.

1. **Statins** - also called HMG CoA (hydro-methylglutaryl Coenzyme A) Reductase Inhibitors. HMG CoA is needed to produce mevalonic acid in the body, which is used to produce many products, among them cholesterol. As cholesterol synthesis is inhibited, LDL receptor site production is increased to draw cholesterol from serum. All of the statins work the same but may differ in potency (degree to which they decrease cholesterol levels). The more potent statins may significantly reduce triglycerides as well as LDL; some agents may increase HDL (this is good!). Because our liver makes most of our cholesterol at night, these agents work best when administered at bedtime. The most common side effects include muscle aches and weakness, diarrhea, constipation, and headache. Generalized muscle aches (over the entire body) must be reported immediately as this may indicate a more serious condition. Common statins include cerivastatin (Baycol®), simvastatin (Zocor®), atorvastatin (Lipitor®), and pravastatin (Pravachol®).

2. **Resins.** Resins, also known as bile acid sequestrants, bind to bile acids in the GI tract and cause us to break down our internally produced cholesterol and thus lowering our cholesterol levels. Resins may increase triglyceride levels so must be used with caution in patients that have high triglycerides. Resins are very effective, however patients express poor compliance with these agents due to the side effects of heartburn, nausea, flatulence, constipation; dosing regimens; and significant drug-drug interactions. Resins are positively charged and many medications that carry a negative charge will bind with them. Medications such as digoxin, thiazide diuretics, beta blockers, warfarin, thyroxine, and fat soluble vitamins (A, D, K, and folic acid) should not be taken after these agents. If a patient is prescribed a resin, he/she should take other medications 2 hours before or 4 hours after the resin. These agents are in
the form of a powder (must be mixed with juice) or very large tablet. Commonly prescribed resins include colestipol (Colestid®) and cholestyramine (Questran®).

(3) Fibrates. Fibrates are used primarily to treat high triglyceride levels. They also increase HDL significantly and their effect on LDL varies. Side effects include nausea, flatulence, abdominal pain, and diarrhea. While on this medication there is 2% to 4% increase in the risk of developing gallstones. This medication should not be taken with HMG CoA Enzyme Inhibitors as there is the potential for development of severe muscle aches and weakness (myopathy). Fibrates include gemfibrozil (Lopid®) and fenofibrate (Tricor®).

(4) Nicotinic Acid Derivatives (Niacin, vitamin B3). Nicotinic acid derivatives are used for reducing high LDLs and triglycerides. They are also useful for treating low HDL levels. As with fibrates, HMG CoA Reductase Inhibitors should be avoided as the combination will lead to a serum increase of HMG CoA and myopathy. The classic side effect of niacin is facial redness and flushing. Often aspirin is administered 30 minutes prior to the niacin dose or niacin is initiated at low doses and gradually increased to reduce this side effect. Other side effects include headache, gastrointestinal upset, and dizziness. Only about 50-60% of patients can tolerate niacin because of its side effects. Some other side effects other than those listed are itching, rashes, hepatotoxicity, elevated glucose levels, and gout. Niacin is relatively contraindicated in diabetics, patients with gout, and patients with peptic ulcer disease.

Continue with Exercises
EXERCISES, LESSON 3

REQUIREMENT: The exercises that follow require you to read a question and select the response that best answers that question.

After you have answered all the questions, turn to “Solutions to Exercises,” at the end of the lesson, and check your answers with the solutions.

1. From the statements below, select the statement that best describes congestive heart failure (CHF).
   a. Congestive heart failure is nonefficient pumping of the heart that leads to an increase in the heart size and heart rate.
   b. Congestive heart failure is a condition in which there is a build-up of edema in the extremities because of too forceful contractions of the myocardium.
   c. Congestive heart failure is a condition in which the heart fills with fluid after each contraction.
   d. Congestive heart failure is a state in which the heart valves open and close at inappropriate times resulting in backflow into the lungs.

2. Which of the following statements best describes the term digitalizing dose?
   a. The dose of digitalis required on a daily basis to prevent the patient from having the signs and symptoms of congestive heart failure.
   b. The large dose of digitalis which is first given to the patient in order to prevent cardiac arrhythmias.
   c. The digitalizing dose is the large initial dose of the drug that is given to the patient in order to relieve the symptoms of congestive heart failure.
   d. The large doses of digitalis that are frequently administered to patients who have acute cases of congestive heart failure.
3. The primary difference between the digitalizing dose and the maintenance dose of digitalis is ________________

   a. The digitalizing dose is the first and largest dose given to the patient, while the maintenance dose is the amount of drug given to the patient on a daily basis.

   b. The digitalizing dose is always smaller than the daily maintenance dose that is given to the patient.

   c. The digitalizing dose is the amount of digitalis given to the patient during the first three weeks of therapy, while the maintenance dose is given thereafter.

   d. The digitalizing dose is given to patients, who have acute CHF, while the maintenance dose is given to only those patients who must continue to take digitalis for the rest of their lives.

4. Phenytoin can be administered intravenously (IV) to treat ________________.

   a. Congestive heart failure.

   b. Digitalis induced arrhythmias.

   c. Cinchonism.

   d. Anorexia.

5. Inderal® is an agent used in the treatment of hypertension, angina pectoris, and ________________

   a. Cinchonism.

   b. Cardiac arrhythmias.

   c. Urine retention.

   d. Diarrhea.
6. Amiodarone is used in the treatment of _________________
   a. Cinchonism.
   b. Anorexia.
   c. Ventricular arrhythmias.
   d. Hypertension.

7. A side effect associated with the use of Zestril® is ____________
   a. Edema of the left ventricle.
   b. Localized analgesia.
   c. Dry cough.
   d. Postural hypotension.

8. One of the side effects associated with large initial doses of beta blocking agents is ___________
   a. Anemia.
   b. Hypertension.
   c. Ventricular arrhythmias.
   d. Congestive heart failure.

9. Flutter is best described as _________________________
   a. A rapid heart beat with no rhythm.
   b. A rapid heart rate of at least 200 to 400 beats per minute.
   c. A type of cardiac arrest characterized by pain in the right shoulder.
   d. A very rapid heart beat with rhythm present.
10. Hyperlipidemia is best described as_____________________________
   a. Elevated levels of cholesterol, triglycerides, and/or lipoproteins in the blood.
   b. Reduced levels of cholesterol in the blood.
   c. Reduced levels of triglycerides in the blood.
   d. Elevated levels of triglycerides in the blood.

11. The following are acceptable treatments for hyperlipidemia:
   a. Diet and exercise
   b. Drug therapy
   c. Surgical intervention.
   d. All of the above.

12. Match the generic in Column A with its corresponding trade name in Column B.

   Column A              Column B
   _____Digoxin.         a.  Coreg®
   _____Enalapril.       b.  Xylocaine®
   _____Diltiazem.      c.  Lanoxin®
   _____Carvedilol.     d.  Cardizem®
   _____Metoprolol.     e.  Vasotec®
   _____Lidocaine.      f.  Lopressor®
   _____Simvastatin .   g.  Lopid®
   _____Gemfibrozil.    h.  Zocor®

Check Your Answers on Next Page
1. a Congestive heart failure is nonefficient pumping of the heart that leads to an increase in the heart size and heart rate.  

2. c The digitalizing dose is the large initial dose of the drug that is given to the patient in order to relieve the symptoms of congestive heart failure.  

3. a The digitalizing dose is the first and largest dose given to the patient, while the maintenance dose is the amount of drug given to the patient on a daily basis.  

4. b Digitalis-induced arrhythmias.  

5. b Cardiac arrhythmias.  

6. c Ventricular arrhythmias.  

7. c Dry cough.  

8. d Congestive heart failure.  

9. d A very rapid heart beat with rhythm present.  

10. a Elevated levels of cholesterol, triglycerides, and/or lipoproteins in the blood.  

11. d All of the above  

   (para 3-2)  
   (para 3-6a)  
   (para 3-6)  
   (para 3-11d)  
   (para 3-11c)  
   (para 3-11f)  
   (para 3-4b)  
   (para 3-11c)  
   (para 3-9a)  
   (para 3-12)  
   (para 3-12, 3-15(a))
## 12.

<table>
<thead>
<tr>
<th>Column A</th>
<th>Column B</th>
</tr>
</thead>
<tbody>
<tr>
<td>__<strong>c</strong> Digoxin. (para 3-7a)</td>
<td>a. Coreg®</td>
</tr>
<tr>
<td>__<strong>e</strong> Enalapril. (para 3-4c)</td>
<td>b. Xylocaine®</td>
</tr>
<tr>
<td>__<strong>d</strong> Diltiazem. (para 3-11g)</td>
<td>c. Lanoxin®</td>
</tr>
<tr>
<td>__<strong>a</strong> Carvedilol. (para 3-8a)</td>
<td>d. Cardizem®</td>
</tr>
<tr>
<td>__<strong>f</strong> Metoprolol. (para 3-11c)</td>
<td>e. Vasotec®</td>
</tr>
<tr>
<td>__<strong>b</strong> Lidocaine. (para 3-11e)</td>
<td>f. Lopressor®</td>
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<tr>
<td>__<strong>h</strong> Simvastatin. (para 3-15b(1))</td>
<td>g. Lopid®</td>
</tr>
<tr>
<td>__<strong>g</strong> Gemfibrozil. (para 3-15b(3))</td>
<td>h. Zocor®</td>
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</table>

*End of Lesson 3*
LESSON ASSIGNMENT

LESSON 4
Vasodilator Drugs.

LESSON ASSIGNMENT
Paragraphs 4-1–4-5.

TASKS
081-824-0001, Perform Initial Screening of a Prescription.

081-824-0026, Evaluate a Prescription.

081-824-0027, Evaluate a Completed Prescription.

081-824-0028, Issue Outpatient Medications. After

LESSON OBJECTIVES
completing this lesson you will be able to:

4-1. Given one of the following terms: vasodilator, orthostatic hypotension, angina pectoris, arteriosclerosis, antherosclerosis, or peripheral vascular disease and a group of statements, select the statement that best defines the given term.

4-2. Given the trade or generic name of a vasodilator and a list of trade and/or generic names of drugs, select the trade or generic name that corresponds to the given trade or generic name.

4-3. Given the trade or generic name of a vasodilator and a list of indications, uses, side effects, patient precautionary statements, or dispensing statements, select the indication(s), use(s), side effect(s), patient precautionary statement(s), or dispensing statement for the given drug name.

SUGGESTION
After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 4

VASODILATOR DRUGS

Section I. DEFINITIONS

4-1. INTRODUCTION

Visualize a man walking down a hallway. He pauses at the foot of a stairway. From his pocket, he takes a small bottle containing some very small white tablets and he places one of these tablets under his tongue. After waiting a few seconds, he proceeds up the stairs. What was this scene? It was a man preparing his body--especially his heart--for the extra work required for walking up the stairs. This man, suffering from a condition called angina pectoris, used one of the vasodilators that will be discussed in this subcourse lesson. Without this drug, he would be unable to perform many of the energy expending tasks required for everyday life. In this lesson, you will be given the opportunity to broaden your background in some cardiovascular diseases as well as learn more about various vasodilators.

4-2. IMPORTANT TERMS AND THEIR DEFINITIONS

You have already been introduced to some of the terms below in another lesson in this subcourse. Some of the terms below might be new to you. In any event, each term applies to vasodilator agents.

a. **Vasodilator.** A vasodilator is a drug that dilates blood vessels with a resultant increase in blood flow.

b. **Orthostatic Hypotension.** Orthostatic hypotension is a condition characterized by fainting or dizziness because of inadequate blood supply to the brain because the blood has been pooled elsewhere in the body. Vasodilator agents may cause this condition. You may have experienced this condition before. Have you ever arisen quickly from a lying position to find that you are light-headed and dizzy? This is orthostatic hypotension.

c. **Angina Pectoris.** Angina pectoris is a condition manifested by excruciating chest pain sometimes radiating down the left arm. The pain probably arises from ischemia (lack of oxygen) in the heart caused by the increased demand for or decreased supply of oxygen.

d. **Arteriosclerosis.** Arteriosclerosis is characterized by thickening, hardening, and loss of elasticity of the walls of blood vessels.
e. **Atherosclerosis.** Atherosclerosis is a form of arteriosclerosis characterized by localized accumulation of lipids (fats), leading to a narrowing of the arteries and possible occlusion (blockage) of the vessels.

f. **Peripheral Vascular Disease.** Peripheral vascular disease (PVD) is a condition characterized by a narrowing or occlusion of peripheral arterioles leading to limited circulation to the extremities such as toes, fingers, and shoulders. You have probably seen elderly patients who wear extra clothing during hot weather. The cold feeling they have, even in hot weather, is probably due to lack of adequate circulation.

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**Section II. VASODILATOR DRUGS**

4-3. **INTRODUCTION**

Now that you have some background in some cardiovascular disease, you will review some general categories of vasodilators and some of the specific agents that belong to each group.

4-4. **SMOOTH MUSCLE RELAXANT VASODILATORS**

Although the agents in this category affect almost all smooth muscle, our concern here is only with their relaxant effect upon the smooth muscle of the coronary vessels as well as peripheral (to the heart) blood vessels.

a. **Amyl Nitrite.** Amyl nitrite is a vasodilator administered only by inhalation. It is rapidly absorbed from the lungs. This product is supplied in perles (like many ammonia inhalants). When a person suffering from angina pectoris feels an attack about to occur, he will crush an amyl nitrite perle and inhale its vapors. The attack of angina pectoris is warded off or aborted in from one to two minutes. Because amyl nitrite perles may explode when stored above normal room temperature, it is very difficult for the patient to carry them in his pocket. This adverse situation normally prohibits their use in the treatment of angina pectoris. The side effects associated with amyl nitrite are usually attributed to the relaxation of all smooth muscle causing vasodilation. Headache and dizziness are very common side effects associated with amyl nitrite. Amyl nitrite does have an additional use, which is the treatment of cyanide poisoning.

b. **Glyceryl Trinitrate (Nitroglycerin).** Glyceryl trinitrate is the most common smooth muscle relaxant vasodilator used in the treatment of acute angina pectoris. This drug is the product described in the introductory remarks of this subcourse lesson when the man placed the small tablet under his tongue. Sublingual nitroglycerin tablets may be used to allow a person who has angina to do extra work or to alleviate an acute angina attack. Nitroglycerin’s sublingual onset of action is from 1 to 3 minutes with duration of action of from 9 to 11 minutes. Side effects associated with this drug include
headache, dizziness, and orthostatic hypotension. The vasodilating effect of the drug may be so sudden that circulating blood pools in vascular (vessel) beds. This may cause the patient to become unconscious because of a lack of blood to the brain. Falling to the floor in a faint allows the immediate return of that blood flow to the brain and consciousness returns. Besides the sublingual form of nitroglycerin, sustained release capsules (Nitro-Bid Plateau Caps®) with 5 to 20 milligrams of drug taken daily in divided doses, topical ointments (Nitrol®, Nitro-Bid®), and transdermal patches (Nitro-Dur®) are available. The ointment is applied using special paper every 6 hours. The transdermal system patches are applied to the chest wall each morning and removed after 12 hours. The patches offer the advantage of once daily dosing and less side effects for the patient. Each of these dosage forms is used for the prevention of angina attacks. Nitroglycerin sublingual tablets are volatile. They will lose their potency quickly when they are incorrectly stored. Therefore, the tablets must be dispensed in their original container (light-resistant container). The patient should also be instructed not to remove the tablets from the original glass container (that is, to place the tablets in a fancy pillbox). Federal law requires that all nitroglycerin products should be dispensed in their original containers (that is, glass, light resistant, and not child-resistant packaging). Another problem area with the nitroglycerin prescription is the dose. Normally physicians prescribe them in grains using 1/100 grain, 1/150 grain, or 1/200-grain tablets. We should be able to convert these to micrograms or milligrams. Intravenous nitroglycerin is used in patients that present with unstable angina (persisting chest pain) or possible myocardial infarction. The physician normally orders the nitroglycerin as a drip (mcg/min) and titrates (adjusts) the dose to pain relief.

c. **Isosorbide Dinitrate** *(Isordil®, Sorbitrate®)*. Isosorbide dinitrate is thought to be effective in the prophylactic treatment of angina pectoris, as well as the treatment of acute angina attacks. The side effects associated with this drug are headache and dizziness. Isordil® is supplied in many different dosage forms to include sublingual, chewable, compressed, and sustained action tablets and capsules (Tembids®). The sublingual tablets are used in the acute angina attacks in a dose of from 2.5 to 10 milligrams. The usual oral dose is from 15 to 80 milligrams daily in divided doses. These products should be dispensed in their original containers. Isosorbide mononitrate (Ismo®, Imdur®) is another product often prescribed.

**NOTE**: Tolerance develops to nitrate products. For the agents to maintain effectiveness, the patient must have a “nitrate-free” interval as part of the dosing regimen. Nitroglycerin patches are generally applied in the morning and removed in the evening (12-hours on/ 12-hours off); isosorbide products are administer in the morning, usually at 7am or 8 am with the second dose 7 hours later (2pm-3pm). No additional doses are administered so that the patient has a nitrate-free interval.

d. **Hydralazine (Apresoline®) and Minoxidil (Loniten®)**. Hydralazine and minoxidil are direct acting peripheral vasodilators used in the treatment of hypertension. Hydralazine may be prescribed in combination with an oral nitrate in the treatment of congestive heart failure. The addition of hydralazine further dilates peripheral vessels and decreases workload on the heart.
4-5. AUTONOMIC NERVOUS SYSTEM VASODILATORS

The agent discussed in this paragraph is thought to dilate blood vessels supplying blood to skeletal muscles.

Isoxsuprine (Vasodilan®). Isoxsuprine is sometimes used in the treatment of various conditions causing peripheral vascular disease. Dilating blood vessels to skeletal muscles allows greater blood flow to peripheral areas of the body. Such increased blood flow alleviates some of the symptoms normally associated with peripheral vascular disease (for example: numbness or tingling sensations in the toes and fingers or a feeling of never being warm enough regardless of the atmospheric temperature). The effectiveness of this agent has not been supported by objective studies. The side effects associated with isoxsuprine therapy are severe rash (with some patients), tachycardia, and nausea and vomiting. Vasodilan® is supplied as 10 milligram and 20 milligram tablets. The usual daily dosage is 30 milligrams to 80 milligrams in 4 divided doses.

Continue with Exercises
EXERCISES, LESSON 4

REQUIREMENTS: The following exercises are to be answered by marking the lettered response that best answers the question; or by completing the incomplete statement; or by writing the answer in the space provided at the end of the question.

After you have completed all the exercises, turn to “Solutions to Exercises,” at the end of the lesson, and check your answers with the solutions.

1. A vasodilator is a drug which _____________________.
   a. Dilates blood vessels with a resultant increase in blood flow.
   b. Removes deposits of fat and calcium from the inside of vessels in order to increase blood flow.
   c. Causes the heart to beat faster causing an increase in blood flow to the brain and to the peripheral areas.
   d. Counteracts inadequate blood flow to the brain and peripheral areas by causing the arteries and veins to become more elastic.

2. Orthostatic hypotension is a condition characterized by _________.
   a. Dizziness, fainting, or vertigo caused by a rupture of blood vessels of the brain.
   b. Dizziness or fainting caused by excessive flow of blood to the semicircular canals of the inner ear.
   c. Fainting or dizziness because of inadequate blood supply to the brain.
   d. Fainting or dizziness caused by lack of adequate exercise.
3. Atherosclerosis is best defined as _______________________.
   a. A condition characterized by thickening, hardening, and a loss of elasticity of the walls of the blood vessels.
   b. A condition manifested by excruciating chest pain caused by lack of oxygen in the heart.
   c. A form of arteriosclerosis characterized by localized accumulation of fats in the arteries.
   d. A form of angina pectoris in which the vessels of the heart are occluded by fats and carbohydrates.

4. Amyl nitrite is a vasodilator that is used in the treatment of _____________.
   a. Angina pectoris.
   b. Frostbite.
   c. Cyanide poisoning.
   d. a and b.
   e. a and c.

5. Isoxsuprine is used in the treatment of _____________________.
   a. Tachycardia.
   b. Various conditions causing peripheral vascular disease.
   c. Orthostatic hypotension.
   d. Irregular heartbeat and muscle tension.
6. Select the side effects associated with nitroglycerin.
   a. Irregular heartbeat and tachycardia.
   b. Orthostatic hypertension and sedation.
   c. Acute angina attacks and flushing of the face.
   d. Headache and dizziness.

7. Hydralazine is used in ____________.
   a. The treatment of hypertension and congestive heart failure.
   b. The treatment of night leg cramps and frostbite.
   c. The treatment of atherosclerosis.
   d. The prophylactic treatment of angina pectoris.

8. Which of the following best describes the concept of “nitrate-free” interval associated with the use of nitrates?
   a. Nitrates prescribed day on/day off, to reduce side effects.
   b. Nitrates prescribed 8-12 hours per day, followed by a 12-16 hours drug free interval to decrease tolerance and side effects.
   c. Nitrates prescribed every 6-8 hours and instructed to skip every other dose.
   d. Nitrates prescribed week on/week off, to reduce tolerance and side effects.
9. Match the drug name listed in Column A with its corresponding name listed in Column B.

<table>
<thead>
<tr>
<th>COLUMN A</th>
<th>COLUMN B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minoxidil.</td>
<td>a. Sorbitrate®</td>
</tr>
<tr>
<td>Isosorbide dinitrate.</td>
<td>b. Nitroglycerin</td>
</tr>
<tr>
<td>Isoxsuprine.</td>
<td>c. Loniten®</td>
</tr>
<tr>
<td>Isosorbide mononitrate.</td>
<td>d. Imdur®</td>
</tr>
<tr>
<td>Glyceryl trinitrate.</td>
<td>e. Vasodilan®</td>
</tr>
</tbody>
</table>

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 4

1. a Dilates blood vessels with a resultant increase in blood flow.  
   (para 4-2a)

2. c Fainting or dizziness because of inadequate blood supply to the brain.  
   (para 4-2b)

3. c A form of arteriosclerosis characterized by localized accumulation  
   of fats in the arteries.  (para 4-2e)

4. e a and c, (Angina pectoris and cyanide poisoning).  (para 4-4a)

5. b Various conditions causing peripheral vascular disease.  
   (para 4-5)

6. d Headache and dizziness.  (para 4-4b)

7. a The treatment of hypertension and congestive heart failure.  
   (para 4-4d)

8. b Nitrates prescribed 8-12 hours per day, followed by a 12-16 hours drug  
   free interval to decrease tolerance and side effects.  (para 4-4c)

9. **COLUMN A**  
   **COLUMN B**

   _c Minoxidil.  
   (para 4-4d)  
   _a Isosorbide dinitrate.  
   (para 4-4c)  
   _e Isoxsuprine.  
   (para 4-5)  
   _d Isosorbide mononitrate.  
   (para 4-4c)  
   _b Glyceryl trinitrate.  
   (para 4-4b)  

   a. Sorbitrate®  
   b. Nitroglycerin  
   c. Loniten®  
   d. Imdur®  
   e. Vasodilan®

*End of Lesson 4*
LESSON ASSIGNMENT

LESSON 5
Drugs Acting on the Hematopoietic System.

LESSON ASSIGNMENT
Paragraphs 5-1--5-10.

TASKS
081-824-0001, Perform Initial Screening of a Prescription.

081-824-0026, Evaluate a Prescription.

081-824-0002/3, Fill a Prescription For a Controlled/Non-Controlled Drug.

081-824-0027, Evaluate a Completed Prescription.

081-824-0028, Issue Outpatient Medications. After

LESSON OBJECTIVES
completing this lesson you will be able to:

5-1. Given a group of statements, select the statement which best describes hematopoietic drugs.

5-2. Given one of the following terms: coagulant, anticoagulant, hematinic, or growth factors, and a group of statements, select the statement that best defines the given term.

5-3. Given a list of the steps involved in the clotting of blood and a group of sequences of those steps, select the proper sequence of those steps required for clotting of the blood.

5-4. Given the trade or generic name of a drug that acts on the hematopoietic and a list of other trade and generic names, select the trade or generic name that corresponds to the given name.

5-5. Given the trade and/or generic name of a drug that acts on the hematopoietic system and a list of indications, uses, side effects, or precautionary statements, select the indication(s), use(s), side effect(s), or precautionary statement(s) for that drug.
5-6. Given a group of statements, select the statement which should be communicated to each patient to whom an anticoagulant is dispensed.

**SUGGESTION**

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 5
DRUGS ACTING ON THE HEMATOPOIETIC SYSTEM

Section I. DEFINITIONS

5-1. INTRODUCTION

The word hematopoietic means, “blood producing.” Therefore, drugs acting on the hematopoietic system would pertain to drugs that act on the blood producing system of the body. As you might expect, these drugs are potentially dangerous because they can affect blood production in the body.

5-2. DEFINITIONS

a. Coagulant. A coagulant is a drug that stimulates the clotting of the blood. Coagulants can be of great aid in an emergency in which the patient may be losing a large volume of blood.

b. Anticoagulant. An anticoagulant is a drug that prevents the clotting of the blood. Anticoagulants are used in various types of surgery as well as in everyday use in order to control blood clots.

c. Hematinic. A hematinic is a drug that stimulates the formation of red blood cells. Hematinics are used in the treatment of anemias.

d. Stimulating Factors. A stimulating factor is an agent that stimulates the formation of specific blood cells (red blood cells, white blood cells, or platelets).

Section II. COAGULANTS

5-3. REVIEW OF THE CLOTTING PROCESS (FIGURE 5-1)

The area of blood clotting was discussed in paragraphs 2-7 and 2-8 of this subcourse. The actual clotting of blood involves several steps. Each step is essential to clotting.

STEP 1: The blood platelets release a substance that is known as thromboplastin.
STEP 2: Thromboplastin reacts with calcium and another substance, prothrombin, to form thrombin. Vitamin K is necessary for the proper formation of prothrombin.

STEP 3: The thrombin formed acts as an enzyme to convert fibrinogen to fibrin threads that eventually form the blood clot.

NOTE: For a more in-depth discussion of blood clotting you should locate and read a physiology text that is appropriate to your level of understanding.

Figure 5-1. The blood clotting process.

STEP 4: Clot breakdown. Plasminogen binds to fibrin as the clot forms. In response to thrombin formation and venous stasis (clot), plasminogen activators convert plasminogen to plasmin. Plasmin digests fibrin and dissolves the clot.

5-4. COAGULANTS (PROMOTING CLOT FORMATION)

There are several drugs that affect the clotting process at different stages to promote coagulation. Vitamin K derivatives and coagulation factors work by enhancing the formation or increasing the amount of circulating clotting factors and promoting the coagulation process (steps 2 and 3 above). Drugs that inhibit plasminogen or plasmin result in coagulation by preventing the breakdown of clots (step 4 above).

a. Phytonadione (Mephyton®, Aqua-Mephyton®, Vitamin K₁). Phytonadione or vitamin K is the most commonly prescribed coagulant and antidote for warfarin overdose. As a coagulant, the usual dose is 0.5 to 1.0 milligram given intramuscularly.
(IM) to infants at birth to prevent infant hemorrhagic disease. Infants are administered this medication because at birth they lack the normal intestinal flora required to produce enough Vitamin K to play its role in blood clotting. When phytonadione is used for its anticoagulant effects, the dosage is based on the level of warfarin anticoagulation in the patient. This level of anticoagulation is determined by blood sample and expressed as the International Normalized Ratio (INR) by the laboratory. Doses may be as small as 0.5-1 mg (oral) up to 10 mg administered subcutaneously. The initial effects of vitamin K take up to 6 hours with maximum effects in 2-3 days. If a patient is actively bleeding, the coagulant of choice may be fresh frozen plasma or a blood transfusion. Side effects associated with this agent include “flushing” sensations and peculiar sensations of taste. The injectable form of this agent is used only on an inpatient basis (that, in the hospital or emergency room), and it should be remembered that it should only be administered subcutaneously--severe reactions (including death) have been reported when the product was given intravenously (IV). Phytonadione will not counteract the anticoagulant action of heparin.

b. Vitamin K₃, Menadione. Menadione is another coagulant prescribed in patients who have bleeding problems. The only side effect of real concern with menadione is hepatomegaly. Hepatomegaly is a condition in which the liver becomes enlarged because of an excess of fat soluble vitamins stored in the lipid tissue. This agent is commonly supplied in tablet form.

c. Menadiol (Synkayvite®). Menadiol (observe its similarity to menadione) is a synthetic Vitamin K₃. Menadiol is also used as a coagulant available in a tablet and injectable form.

d. Specific Clotting Factors. In patients that have an acquired or hereditary clotting factor deficiency, specific clotting factors are available. Factor VIII and Factor IX are available as concentrates often stocked within the pharmacy. The agents are available for minor procedures or surgery in select patients with these deficiencies.

e. Desmopressin Acetate (DDAVP®). Desmopresin is a synthetic analog of vasopressin, the naturally occurring human antidiuretic hormone. It has the unique activity of producing a dose-related increase in circulating Factor VIII and von Willebrand’s factor levels. Both of these factors are essential to normal human coagulation. This agent is used in individuals with Hemophilia A (lacking factor VIII) or von Willebrand’s disease. Desmopressin will maintain homeostasis in these patients during surgery and post-operatively. Desmopressin may also be prescribed for uncontrolled bleeding related to surgery in patients without a coagulation dysfunction.

f. Aminocaproic Acid (Amicar®). Aminocaproic acid is an agent that inhibits fibrinolysis (clot breakdown) by inhibiting plasminogen activators. Consequently, it stabilizes clots in excessive bleeding. Aminocaproic acid is given either intravenously or orally. Individuals with bleeding dysfunction (hemophilia) may take this product 12-24 hours prior to a dental procedure or surgery. It is often prescribed with desmopressin.
g. Tranexamic Acid (Cyklokapron®) and Aprotinin (Trasylol®). Tranexamic acid is a competitive inhibitor of plasminogen activation. Its action is similar to aminocaproic acid but approximately 10x more potent. It is used in hemophiliacs undergoing invasive procedures. Aprotinin is a natural protease inhibitor that inhibits plasmin. It is used prophylactically in patients undergoing coronary artery bypass surgery to prevent peri-operative blood loss.

**NOTE:** The administration of blood products (whole blood, fresh frozen plasma, or cryoprecipitate) may be used in place of any or all of the above agents to correct excess bleeding. They are often the fastest means of correcting excess anticoagulation. Although each of the drugs discussed above has side effects, the risk/benefit of a transfusion must be weighed in each patient.

**Section III. ANTICOAGULANTS**

**5-5. INTRODUCTION**

Just as there are conditions of excess bleeding (anticoagulation), so are there conditions in which excess clotting (coagulation) may be detrimental to the patient. The major components that promote excess clot formation are: 1) **venous stasis** (altered or decreased blood flow to the deep veins of the lower extremities) which occurs with impaired mobility (traumatic injury, obesity); 2) **vascular injury** which occurs as the result of mechanical or chemical trauma causing an inflammation of the vessel; and 3) **hypercoagulability** which results from a deficiency of natural anticoagulants (antithrombin III, protein C, protein S) or a specific disease state (cancer).

Anticoagulants are essential to correcting the propensity to clot. However, they are a potentially dangerous class of drugs. One reason for their dangerous status is that anticoagulants interact with a variety of medications (over the counter and legend). Second, there is always a risk of uncontrolled bleeding when you inhibit a process that promotes clotting. One of the most important interactions to remember is the combination of anticoagulants with other drugs—especially salicylates (aspirin) or non-steroidal antiinflammatory drugs (ibuprofen, naproxen). These products can potentiate the effects of the anticoagulants by inhibiting platelet aggregation which is the first line of defense to stop bleeding.

**5-6. IMPORTANT WARNING ASSOCIATED WITH THE ANTICOAGULANTS**

There is one warning common to all anticoagulants. When you dispense an anticoagulant to a patient you should tell the person that they should not take any other medication—over the counter or legend—without first consulting the physician who prescribed the anticoagulant. Emphasize that over-the-counter products such as aspirin and ibuprofen are also classified as medications.
5-7. ANTICOAGULANT AGENTS

a. Anti-platelet agents. Anti-platelet agents are used to prevent a clot from forming (step I) or prevent the clot from getting larger and occluding the entire vessel. All patients must be warned of the increased risk of bleeding when taking these drugs.

   (1) Aspirin. Aspirin is the most widely used anti-platelet drug. It inhibits platelet aggregation for the life of the platelet (7-10 days). Because of this effect, aspirin is prescribed in the setting of acute myocardial infarction and prophylactically to prevent reinfarction. Always ask the patient if he/she has an allergy to aspirin.

   (2) Clopidogrel (Plavix®) and Ticlopidine (Ticlid®). Clopidogrel and ticlopidine work by inhibiting platelet aggregation. They are often prescribed for patients that have an aspirin allergy or are intolerant of aspirin (usually stomach upset). Both agents may be used in patients with atherosclerotic disease to prevent heart attacks, prevent strokes, and prevent coronary artery closure in patient undergoing angioplasty. Ticlopidine is administered twice daily and is associated with a risk of decreased white blood cells (neutropenia). Clopidogrel is administered once daily and has a much lower risk of neutropenia. Both agents can cause a rash.

   (3) Dipyridomole (Persantine®). Dipyridomole works by inhibiting platelets from adhering to the injured cell wall. Although not used extensively, it may be prescribed in combination with other anticoagulants. The combination product of dipyridomole and aspirin is called Aggrenox®.

   (4) Abciximab (ReoPro®), Tirofiban (Aggrastat®), and Eptifibatide (Integrelin®). The following agents are known as glycoprotein Ilb/IIIa inhibitors. The GP Ilb/IIIa receptor is the major receptor on the platelet responsible for platelets adhering to each other and forming the initial clot. These drugs are administered intravenously in patients with acute coronary syndromes (unstable angina) or in patients undergoing angioplasty with or without stent placement in the cardiac catheterization lab. The agents prevent clots from forming in the coronary arteries of the heart. The agents are not interchangeable and differ in their respective half-lives and infusion schedules. The major side effect is thrombocytopenia (low platelet count) occasionally requiring a platelet transfusion.

b. Heparin products. Heparin is used to prevent the clotting of blood in the patient and in laboratory samples by inhibiting certain clotting factors (Thrombin/Factor IIa and Factor Xa). Like anti-platelet drugs, heparin will not dissolve a clot but prevents it from getting larger. The dosage of this agent is based upon the needs of the patient (prophylactic vs. treatment doses). It may be administered subcutaneously or intravenous (IV Push or IV continuous infusion). The major side effect associated with heparin is possible hemorrhage. Protamine sulfate is used to treat heparin overdose. Although protamine sulfate is also an anticoagulant, it counteracts the effects of heparin by binding with the heparin. The net result is removing the effects of the heparin. The
primary side effects associated with protamine sulfate are temporary hypotension, bradycardia, and dyspnea.

(1) Heparin Sodium, Heparin Calcium. Commerical heparin (unfractionated heparin) comes from beef lung or pork intestinal mucosa. It is dosed in “units” and measured in the lab by the partial thromboplastin time (PTT). Although some heparin is administered in a “fixed dose” for prophylaxis against clots, it is more often administered in a “wt-based” fashion for prophylaxis and treatment of clots. Therapeutic dose goals are 1.2-1.5x the PTT control. Doses, especially for continuous infusion are adjusted to meet this goal. Heparin may be administered in a very small fixed dose (10-100 units) to clear intravenous ports in patients with long term IV lines. This dose is called a “heparin flush”. The absorption of subcutaneous heparin is unpredictable.

(2) Enoxaparin (Lovenox®), Dalteparin (Fragmin®). Enoxaparin and dalteparin are two of several "low molecular weight heparins (LMWH)” (fractionated heparin). They differ from unfractionated heparin by having more predictable subcutaneous absorption, a longer duration of action, and primarily inhibit only one clotting factor (Factor Xa). Either agent may be administered once or twice daily (SC) usually for 7-10 days. The primary use for these agents is in the prevention and treatment of deep vein thrombosis (leg clots) and pulmonary embolus (lung clots). The sides effects are the same as with unfractionated heparin however they offer distinct advantages in that the patient can self-administer these agents (discharged from the hospital sooner), they do not require monitoring of the PTT, and are just as effective as standard heparin. The major disadvantages are pain at the injection site and high cost.

c. Coumarin products. Coumarin products inhibit coagulation by interfering with the incorporation of vitamin K into vitamin-K dependent clotting factors (Factors II, VII, IX, and X). Their initial and maximum effect is based on the half-lives of each of these factors. For example, Factor VII has a half-life of 6 hours so the effect of coumarin on this factor will increase the bleeding to a certain degree within 6 hours, however Factor II and X exhibit half-lives of 48-72 hours, so the maximum effect of coumarin is not seen until 3 days after initiation or dose change. It does not matter whether the drug is given orally or intravenously, it takes the same amount of time to reach the maximum effect (essentially you cannot load a patient on coumarin agents). Coumarin products do not dissolve clots but prevent clots from forming (prophylaxis) and getting larger. The degree of anticoagulation is measured by a blood sample and expressed as the prothrombin time (PT) or the International Normalized Ratio (INR). The INR is the international standard. The therapeutic INR is generally between 2-3.5 which correlates with a 30-50% inhibition of vitamin K dependent clotting factors. Ideally, the patient should have his/her INR checked every 4-6 weeks while on this medication.

Warfarin sodium (Coumadin®). Warfarin sodium is one of the most commonly used anticoagulants (coumarins). It is used to prevent the extension of blood clots in phlebitis or deep vein thrombosis and as a prophylactic agent in patients that have mechanical heart valves (life-long therapy). The main side effect associated with the
use of warfarin sodium is hemorrhaging. This product is available in both oral and injectable forms. This agent has over 50 documented drug-drug interactions. You must research this drug carefully against the patient profile before dispensing.

d. “Clot Busters”. As discussed above, we can administer aspirin, heparin, or warfarin to prevent clots or stop clots from getting bigger. But none of these drugs can dissolve a clot that is already established. In many cases we cannot wait for the body to reabsorb these clots back into the lining of the vessel (4-6 months); we need to dissolve the clot immediately. This is the case for the patient having heart attacks and strokes. “Clot busters” do just that—by acting as tissue plasminogen activator and converting plasminogen to plasmin or mimicking fibrinolytic enzymes, they break down the clot. These agents are always administered intravenously and require close observation for bleeding in the patient. They are most effective when administered as close to onset of symptoms as possible (ideally within 3-6 hours).

(1) Streptokinase (Streptase®), Urokinase ((Abbokinase®). Streptokinase and urokinase were some of the first clot busters developed and act as fibrinolytic enzymes. Streptokinase comes from streptococcus species so patients with strep antibodies may have an allergic reaction to this agent. Urokinase comes from human kidney cells so the incidence of side effects is less. Both agents are administered via continuous IV infusion (12-24 hours) and are rarely used with the advent of recombinant products.

(2) Alteplase (Activase®). Alteplase, also known as tPA (tissue plasminogen activator) was the first recombinant product developed. It offers the advantage of short infusion time (1 hour) and is more effective than streptokinase. It is used for heart attacks (within 4-6 hours of symptoms) and strokes (within 3 hours of symptoms). Alteplase (2 mg) is also used to dissolve clots in IV lines. Reteplase (Retavase®) and anistreplase (Eminase®) are other clot busters.

Section IV. HEMATINICS

5-8. INTRODUCTION

Hematinics are drugs used to stimulate the formation of red blood cells. These agents are used primarily in the treatment of certain types of anemias. Some of these preparations are routinely given to women during pregnancy.

5-9. HEMATINIC AGENTS

a. Ferrous Gluconate (Fergon®) Ferrous Sulfate (Feosol®). Ferrous gluconate and ferrous sulfate are used to treat iron deficiency anemia. The usual dosage given is 1-4 times daily. Side effects associated with these agents include
gastrointestinal upset, constipation, and black stools. Warn the patient about these possible side effects.

b. **Iron Dextran (InFed®).** This drug is also used to treat iron deficiency anemia. Side effects associated with this agent include gastrointestinal upset, constipation, and black stools. Extreme caution should be observed with this product because it is administered parenterally and some patients have demonstrated an anaphylactic type reaction to the drug. This product is used on an inpatient basis and is administered by injection. Iron dextran should not be administered concurrently with oral iron preparation because the side effects mentioned above will be potentiated.

c. **Cyanocobalamin, Vitamin B₁₂ (Rubesol-1000®).** Cyanocobalamin is used in the treatment of pernicious anemia. Pernicious anemia is a condition characterized by a progressive decrease in the number and an increase in the size of red blood cells. Patients who have this condition are usually very weak and have various gastrointestinal disturbances. This condition results from a lack of Vitamin B₁₂. This occurs because of the lack of intrinsic factor, an element that is needed in the intestine in order to effectively absorb Vitamin B₁₂. Thus, cyanocobalamin is used to replace the Vitamin B₁₂ that was not absorbed. Cyanocobalamin should be protected from light. It is available in injectable or tablet form.

d. **Folic Acid (Folate®).** Folic acid is used in combination with other drugs to treat pernicious anemia because it causes an increase in the number of red blood cells. If the drug is administered alone to treat pernicious anemia, it will mask the symptoms of that condition. This is potentially dangerous because if the symptoms are masked, the condition might flourish and cause irreversible neurologic damage. Folic acid is available in both tablet and injectable dosage forms.

e. **Erythropoetin; EPO; Epoten alfa (Epogen®, Procrit®).** Erythropoetin is a protein naturally produced in the kidney that stimulates red blood cell production. It is administered in a variety of chronic anemia states (cancer, renal failure, dialysis, and HIV infection). It may also be used prophylactically to reduce the need for a blood transfusion in patients scheduled for major surgery. The major side effect of erythropoetin is hypertension, especially if the hematocrit rises above 36%. Erythropoetin is administered subcutaneously 1-3 times weekly. Single dose vials MUST be disposed of immediately after use. Multidose vials are discarded 21 days after initial entry. Erythropoetin requires refrigeration.

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**Section V. STIMULATING FACTORS**

5-10. INTRODUCTION

Stimulating factors are naturally occurring substances which promote the proliferation of blood components. Similar to the effects of erythropoetin, stimulating the
production of red blood cells, the stimulating factors discussed below affect the production of white blood cells and platelets.

a. **Granulocyte Colony Stimulating Factor; G-CSF; Filgrastim (Neupogen®)**. Filgrastim stimulates the growth of white blood cells, specifically the granulocytes (neutrophils). It is used in the treatment of neutropenia (low neutrophils) from chemotherapy or bone marrow transplant patients. The most common complaints associated with use are nausea, vomiting, and joint aches. Filgrastim is administered subcutaneously 5-10 mcg/kg/day until neutrophil counts rise to normal. Filgrastim is available as an injection without preservative; it requires refrigeration.

b. **Granulocyte Macrophage Colony Stimulating Factor; GM-CSF; Sargramostim (Leukine®)**. Sargramostim is used to stimulate the proliferation of granulocytes and macrophages in patients with leukemia and/or undergoing bone marrow transplant. This agent is administered 250 mcg/m²/day via IV infusion over 2-4 hours until neutrophil recovery. The side effects are similar to filgrastim. Sargramostim must be refrigerated.

*Continue with Exercises*
EXERCISES, LESSON 5

REQUIREMENTS: The following exercises are to be answered by marking the lettered response that best answers the question; or by completing the incomplete statement; or by writing the answer in the space provided at the end of the question.

After you have completed all the exercises, turn to “Solutions to Exercises,” at the end of the lesson, and check your answers with the solutions.

1. Which of the following statements best describes hematopoietic system drugs?
   a. Drugs that produce pernicious anemia or mask its effects on the body.
   b. Drugs that clot the blood.
   c. Drugs that act on the blood producing system of the body.
   d. Drugs that decrease the clotting capability of the blood.

2. Hematinic drugs _________________________.
   a. Stimulate the formation of red blood cells.
   b. Stimulate the clotting of the blood.
   c. Stimulate the production of hematin in the body.
   d. Stimulate the mechanism responsible for preventing the clotting of the blood.
3. Immediately below are the three steps involved in blood clotting. Select the sequence of steps that reflects the proper sequence of steps required for blood clotting.

   I. Thromboplastin reacts with calcium and prothrombin to form thrombin. Vitamin K is necessary for the proper formation of prothrombin.

   II. The thrombin formed acts as an enzyme to convert fibrinogen to fibrin threads that eventually form the blood clot.

   III. The blood platelets release a substance which is known as thromboplastin.

   a. II, I, and III.

   b. II, III, and I.

   c. III, I, and II.

4. Heparin sodium is used to _________________________.

   a. Stimulate the formation of red blood cells.

   b. Stimulate the clotting of the blood in people with clotting difficulties.

   c. Prevent Vitamin K from being formed and absorbed in the body.

   d. Prevent the clotting of blood in the patient and in laboratory examples.

5. Select the side effect(s) associated with ferrous gluconate.

   a. Pernicious anemia.

   b. Black stools.

   c. Phlebitis.

   d. Hepatomegaly.
6. Select the side effect(s) associated with enoxaparin.
   a. Black stools.
   b. Phelebitis.
   c. Pernicious anemia.
   d. Hemorrhaging.

7. All of the following classes of drugs are used for anticoagulation EXCEPT:
   a. Clot busters such as alteplase.
   b. Anti-platelets such as aspirin.
   c. Vitamin K derivatives such as phytonadione.
   d. Heparin derivatives such as dalteparin.

8. Folic acid can mask the symptoms of ____________ if it is administered alone.
   a. Pernicious anemia.
   b. Iron deficiency anemia.
   c. Hepatomegaly.
   d. Phlebitis.

9. Clot busters are agents used to____________________
   a. Prevent platelets from adhering to each other.
   b. Block certain clotting factors to prevent blood from clotting.
   c. Stimulate the production of certain blood components.
   d. Dissolve clots that have already formed.
10. Match the generic in Column A with its corresponding trade name in Column B.

<table>
<thead>
<tr>
<th>COLUMN A</th>
<th>COLUMN B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous gluconate.</td>
<td>a. Aqua-Mephyton®</td>
</tr>
<tr>
<td>Enoxaparin.</td>
<td>b. ReoPro®</td>
</tr>
<tr>
<td>Iron Dextran.</td>
<td>c. DDAVP®</td>
</tr>
<tr>
<td>Phytonadione.</td>
<td>d. Activase®</td>
</tr>
<tr>
<td>Warfarin sodium.</td>
<td>e. Fergon®</td>
</tr>
<tr>
<td>Desmopressin acetate</td>
<td>f. Neupogen®</td>
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<tr>
<td>Abciximab</td>
<td>g. InFed®</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>h. Lovenox®</td>
</tr>
<tr>
<td>Aprotinin</td>
<td>i. Procrit®</td>
</tr>
<tr>
<td>Erythropoetin</td>
<td>j. Coumadin®</td>
</tr>
<tr>
<td>Alteplase</td>
<td>k. Trasylol®</td>
</tr>
<tr>
<td>Filgrastim</td>
<td>l. Plavix®</td>
</tr>
</tbody>
</table>

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 5

1. c Drugs that act on the blood producing system of the body. (para 5-l)

2. a Stimulate the formation of red blood cells. (para 5-2c)

3. c III, I, and II. (para 5-3)

4. d Prevent the clotting of blood in the patient and in laboratory samples. (para 5-7b)

5. b Black stools. (para 5-9a)

6. d Hemorrhaging. (para 5-7b)

7. c Vitamin K derivatives such as phytonadione. (para 5-4)

8. a Pernicious anemia. (para 5-9d)

9. d Dissolve clots that have already formed. (para 5-7d)

10. | COLUMN A | COLUMN B |
    |--------|--------|
    | e     | Ferrous gluconate. (para 5-9a) | a. Aqua-Mephyton® |
    | h     | Enoxaparin. (para 5-7b(2)) | b. ReoPro® |
    | g     | Iron Dextran. (para 5-9b) | c. DDAVP® |
    | a     | Phytonadione. (para 5-4a) | d. Activase® |
    | j     | Warfarin sodium. (para 5-7c) | e. Fergon® |
    | c     | Desmopressin acetate. (para 5-4e) | f. Neupogen® |
    | b     | Abciximab. (para 5-7a(4)) | g. InFed® |
    | l     | Clopidogrel. (para 5-7a(2)) | h. Lovenox® |
    | k     | Aprotinin. (para 5-4g) | i. Procrit® |
    | i     | Erythropoetin (para 5-9e) | j. Coumadin® |
    | d     | Alteplase (para 5-7d(2)) | k. Trasylol® |
    | f     | Filgrastim (para 5-10a) | l. Plavix® |

End of Lesson 5
LESSON ASSIGNMENT

LESSON 6

The Human Urogenital Systems.

LESSON ASSIGNMENT

Paragraphs 6-1--6-20.

TASKS

081-824-0001, Perform Initial Screening of a Prescription.

081-824-0026, Evaluate a Prescription.

081-824-0002/3, Fill a Prescription For a Controlled/Non-Controlled Drug.

081-824--0027, Evaluate a Completed Prescription.

081-824-0028, Issue Outpatient Medications. After

LESSON OBJECTIVES

completing this lesson you will be able to:

6-1. Given a group of components, select the two components of the human urogenital system.

6-2. Given a group of functions, select the specialized function of the urinary system.

6-3. Given a group of components, select the major components of the human urinary system.

6-4. Given a drawing of the human urinary system and a group of names of the major components of the urinary system, match the name of each major component with its location on the drawing.

6-5. From a group of names of structures, select the name of the functional unit of the human kidney.

6-6. From a list of functions, select the functions(s) of the nephron.

6-7. Given a drawing of a nephron and a list of the names of the parts of a nephron, match the name of each part with its location on the drawing.
6-8. Given the name of one of the parts of the nephron and a group of statements, select the statement that best describes the role of the part in the production of urine.

6-9. Given the name of one of the hormones involved in the formation of urine and a group of statements, select the statement that best describes the role of that hormone in the formation of urine.

6-10. Given the name of a part of the urinary system and a group of statements, select the statement that best describes that part of the urinary system.

6-11. Given the name of a urinary tract disorder and a group of statements, select the statement that best describes the disorder.

6-12. From a list of organs, select the primary sex organ in the human female.

6-13. Given the name of a secondary sex organ in the human female and a group of statements, select the statement that best describes the secondary sex organ.

6-14. Given a list of organs, select the primary sex organ in the human male.

6-15. From a group of statements, select the function(s) of the testis.

6-16. Given the name of a secondary sex organ in the human male and a group of statements, select the statement that best describes the secondary sex organ.

**SUGGESTION**

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LES S S 6
THE HUMAN UROGENITAL SYSTEM

Section I. OVERVIEW OF THE UROGENITAL SYSTEMS

6-1. INTRODUCTION

The human urogenital systems are made up of the urinary organs, which produce the fluid called urine, and the genital or reproductive organs, organs of male and female humans, which together can produce a new human being.

6-2. DISCUSSION OF LESSON CONTENT

This lesson will focus on the human urinary and reproductive systems. The urinary system will be discussed first.

Section II. THE HUMAN URINARY SYSTEM

6-3. INTRODUCTION

The urinary system is one of the major systems of your body. When something goes wrong with this system, medical assistance must quickly be obtained. An understanding of the anatomy and physiology of the urinary system will help you as you study such drug categories as diuretics (those drugs which increase urine output).

6-4. THE HUMAN URINARY SYSTEM

a. Proteins. Proteins are one of the basic foodstuffs that humans consume. When the body uses proteins, residue or waste products can be poisonous (toxic) if allowed to accumulate in large amounts. The urinary system of the human body is specialized to remove these nitrogenous waste products from the circulating blood.

b. Major Parts. See Figure 6-1 for the major parts of the human urinary system. This system includes two kidneys, two ureters (one connecting each kidney to the urinary bladder), the urinary bladder, and the urethra.
6-5. THE KIDNEY

a. **General.**

(1) The kidneys have the same shape and color as kidney beans, but are about 8-10 cm (3”-3 1/2”) in length.

(2) Each kidney has a fibrous capsule. On the concave, medial side of each kidney, there is a notch called the **hilus**. Through the hilus, pass the ureter and the NAVL (nerve, artery, vein, and lymphatic), which service the kidney.

![Figure 6-1. The human urinary system.](image)

(3) Each kidney is attached to the posterior wall of the abdominal cavity, just above the waistline level. Each is held in place by special fascia and fat.

b. **Gross Internal Structure.** If we compare the structure of the kidney with that of a cantaloupe (muskmelon), the renal cortex would correspond to the hard rind, the renal medulla would correspond with the edible flesh of the melon, while the renal sinus would correspond to the hollow center (after the seeds have been removed). The medulla consists of pyramids with their bases at the cortex and forming peaks, papillae, which empty into the sinus.

**PAPILLA = pimple, nipple**

See Figure 6-2 for a section of the kidney showing the inner structure.
c. The Nephron. (See Figure 6-3 for an illustration of a nephron.) Nephrons are the functional units of the human kidney. Their primary function is to remove the wastes of protein usage from the blood. In addition, they serve to conserve water and other materials for continued use by the body. The result of nephron function is more or less concentrated fluid called urine. The kidneys contain great numbers of nephrons, about a million for each kidney. The main subdivisions of a nephron are the renal corpuscle and a tubular system.

(1) Renal corpuscle. The renal corpuscle has a hollow double walled sac called the renal capsule (“Bowman’s capsule”). Leading into the capsule is a very small artery called the afferent arteriole. Within the capsule, this artery becomes a mass of capillaries known as the glomerulus. An efferent arteriole drains the blood away from the capsule. The capsule and the glomerulus together are known as the renal corpuscle.

(2) Tubules. Each renal capsule is drained by a renal tubule. The first part of this tubule runs quite a distance in a coiled formation and is called the proximal convoluted tubule. A long loop, the renal loop (of Henle) extends down into the medulla with two straight parts and a sharp bend at the bottom. As the tube returns to the cortex layer, it becomes coiled once more and here is known as the distal convoluted tubule.

(3) Filtration/reabsorption. Except for the blood cells and the larger proteins, the fluid portion of the blood passes through the walls of the glomerulus into the cavity between the two layers of the renal capsule. This fluid is called the glomerular filtrate. By a process of taking back (resorption), the majority of the fluid is removed from the tubules and the concentrated fluid is called urine.
d. The Collecting Tubule. The distal convoluted tubules of several nephrons empty into a collecting tubule. The urine is then passed from the collecting tubule at the papilla of the medullary pyramid. Several collecting tubules are present in each pyramid.

e. Renal Pelvis. The renal pelvis is a hollow sac within the sinus of the kidney. Urine from the pyramids collects into the funnel-shaped renal pelvis. The ureter then drains the urine from the renal pelvis.

6-6. HORMONES INVOLVED IN THE FORMATION OF URINE

There are two main hormones involved in the formation of urine. These hormones are the antidiuretic hormone (ADH), and aldosterone.

a. Antidiuretic Hormone. The antidiuretic hormone is a hormone secreted by the pituitary gland. It acts on the distal and collecting tubules to increase water reabsorption. Since more water is reabsorbed, the urine becomes more concentrated.
b. **Aldosterone.** The aldosterone is secreted by adrenal cortex, that is situated above each kidney. Aldosterone increases sodium reabsorption in the distal tubules and collecting ducts. This leads to an increase in sodium reabsorption and of concentration of the urine.

**6-7. URETERS**

The ureters are tubes that connect the kidneys to the urinary bladder. The smooth muscle walls of the ureters produce a peristalsis (wave-like movement) that moves the urine along drop by drop.

**6-8. URINARY BLADDER**

a. The urinary bladder is a muscular organ for storing the urine. Near the inferior posterior corners of the urinary bladder are openings where the ureters empty into the bladder. Also at the inferior aspect of the urinary bladder is the exit, the beginning of the urethra. The triangular area, between the openings of the ureters and the urethra, is called the trigone, or base of the urinary bladder.

b. The urinary bladder wall is stretchable to accommodate varying volumes of urine.

c. Nerve endings called stretch receptors are found in the wall of the urinary bladder. Usually, the pressure within the urinary bladder is low. However, as the volume of the enclosed urine approaches the bladder’s capacity, stretching of the wall stimulates the stretch receptors. The cycle of events controlling urination (voiding or emptying of the urinary bladder) is known as the voiding reflex.

**6-9. URETHRA**

The urethra is a tube that conducts the urine from the urinary bladder to the outside of the body. It begins at the anterior base of the urinary bladder.

a. **Urethral Sphincters.** The urethral sphincters are circular muscle masses that control the passage of the urine through the urethra. There are two urethral sphincters: an internal urethral sphincter and an external urethral sphincter.

(1) The *internal urethral sphincter* is located in the floor of the urinary bladder. It is made of smooth muscle tissue. Nerves of the autonomic nervous system control it.

(2) The *external urethral sphincter* is inferior around the urethra in the area of the pelvic floor. It is made up of striated muscle tissue. It is controlled by the peripheral nervous system.
b. Male-Female Differences. The female urethra is short and direct. The male urethra is much longer and has two curvatures. Whereas the female urethra serves only a urinary function, the male urethra serves both the urinary and reproductive functions.

6-10. URINARY TRACT DISORDERS

Several disorders can affect the urinary system. Some of these disorders can present serious problems.

a. Uremia. Uremia, or as it is frequently called, toxemia, is a condition in which there is a build-up of toxic substances in the blood. These accumulated waste products are in the blood because of kidney failure. This condition can occur during pregnancy, since many pregnant women have fluid retention.

b. Glomerulonephritis. Glomerulonephritis is an inflammation of the nephrons--mainly centered in the glomerulus. This condition is due to toxic material produced by bacteria.

c. Pyelonephritis. Pyelonephritis is another condition caused by bacteria. Pyelonephritis is an inflammation of the kidney and pelvis area of the kidney.

d. Edema. Edema is a build-up of fluids in the tissues. It is found in a variety of conditions (that is, pregnancy, congestive heart failure, and renal disease).

e. Diabetes Insipidus. Diabetes insipidus is an increased urine output due to a low production of the antidiuretic hormone. As previously mentioned, the antidiuretic hormone increases the reabsorption of water. A lack of the antidiuretic hormone thus prevents water from being reabsorbed and leads to increased urine output.

f. Cystitis. Cystitis is an inflammation of the urinary bladder, which may spread to the kidneys.
6-11. SEXUAL DIMORPHISM

The human male and human female each has a system of organs specifically designed for the production of new humans. These systems are known as reproductive or genital systems. Since there are different systems for males and females, the genital systems are an example of sexual dimorphism.

- **MORPH** = form, shape
- **D1** = two
- **SEXUAL** = according to sex (gender)
- **SEXUAL DIMORPHISM** = having two different forms according to sex

6-12. ADVANTAGES OF DOUBLE PARENTING

The existence of two parents for each child means that genetic materials are recombined to produce a new type. This new type may be an improvement over previous generations.

6-13. MAJOR COMPONENT CATEGORIES OF THE GENTIAL SYSTEMS

Components of the genital systems may be considered in the following categories:

- **a. Primary Sex Organs (Gonads)**. Primary sex organs produce sex cells (gametes). A male gamete and a female gamete may be united to form the one-cell beginning of an embryo (the process of fertilization). Primary sex organs also produce sex hormones.

- **b. Secondary Sex Organs**. Secondary sex organs care for the product of the primary sex organ.

- **c. Secondary Sexual Characteristics**. Secondary sexual characteristics are those traits that tend to make males and females more attractive to each other. Secondary sexual characteristics help to ensure mating. These characteristics first appear during puberty (10-15 years of age).
6-14. PRIMARY SEX ORGANS (OVARIES)

The primary sex organ in the human female is the ovary. (See Figure 6-4 for an illustration of the female genital system.) The ovaries are located to the sides of the upper end of the uterus. They are anchored to the posterior surface of the broad ligaments. (The broad ligaments are sheets or folds of peritoneum inclosing the uterus and uterine tubes and extending to the sides of the pelvis.)

a. The ovary produces the egg cell or ovum (ova, plural).

b. The ovary produces female sex hormones (estrogens and progesterone).

c. The production of ova is cyclic. Usually, one ovum is released during each 28-day menstrual cycle.

Figure 6-4. The human female genital system.
6-15. SECONDARY SEX ORGANS

a. **Uterine Tubes (Fallopian Tubes, Oviducts)**. Extending to either side of the uterus are two muscular tubes, which open at the outer ends like fringed trumpets. The fringe-like appendages encircle the ovaries. At their medial ends, the uterine tubes open into the uterus. The function of the uterine tubes is to pick up the ovum when released from the ovary and hold it UNTIL one of the following happens:

1. **Fertilization**. Then it is fertilized. After fertilization, the initial stages of embryo development take place. The developing embryo is eventually moved into the uterus.

2. **Death of Ovum**. The nutrient stored within the ovum is used up, and the ovum dies. This may take 3-5 days.

b. **Uterus**. The uterus is the site where all but the first few days of embryo development takes place. After 8 weeks of embryonic development, it is known as the fetus.

1. **Main subdivisions**. The uterus is shaped like a pear, with the stem (cervix) facing downward and toward the rear. The fundus is the portion of the uterus above the openings of the uterine tubes. The main part, or body, is the portion between the cervix and the fundus. The uterus usually leans forward with the body slightly curved as it passes over the top of the urinary bladder. The cervix opens into the upper end of the vagina.

2. **Wall structure**. The inner lining of the uterus is called the endometrium. Made up of epithelium, it is well supplied with blood vessels and glands. The muscular wall of the uterus is called the myometrium. In the body of the uterus, the muscular tissue is in a double spiral arrangement. In the cervix, it is in a circular arrangement.

3. **Age differences**. The uterus of an infant female is undeveloped. During puberty the uterus develops. The uterus of an adult is fully developed. The uterus of an old woman is reduced in size and nonfunctional.

c. **Vagina**. The vagina is a tubular canal connecting the cervix of the uterus with the outside. It serves as a birth canal and as an organ of copulation. It is capable of stretching during childbirth. The low opening of the vagina may be partially closed by a thin membrane known as the hymen.

d. **External Genitalia**. Other terms for the external genitals of the human female are vulva and pudendum. Included are the:

1. **Mons pubis**. The mons pubis is a mound of fat tissue covered with skin and hair in front of the symphysis pubis (the joint of the pubic bones).
(2) Labia majora. Extending back from the mons pubis and encircling the vestibule (discussed below) are two folds known as the **labia majora**. Their construction is similar to the mons pubis, including fatty tissue and skin. The outer surfaces are covered with hair. The inner surfaces are moist and smooth. The corresponding structure in the male is the scrotum.

**LABIA** = lips  
**LABIUM**, singular

(3) Labia minora. The **labia minora** are two folds of skin lying within the labia majora and inclosing the vestibule. In front, each labium minus (minus = singular or minora) divides into two folds. The fold above the clitoris (discussed below) is called the prepuce of the clitoris. The fold below is the frenulum.

(4) Clitoris. The clitoris is a small projection of sensitive erectile tissue that corresponds to the male penis. However, the female urethra does not pass through the clitoris.

(5) Vestibule. The cleft between the labia minora and behind the clitoris is called the **vestibule**. It includes the urethral opening in front and the vaginal opening slightly to the rear.

e. **Pregnancy and Delivery.** When an embryo forms an attachment to the endometrium, a pregnancy exists. The attachment eventually forms a placenta, an organ joining mother and offspring for such purposes as nutrition of the offspring. The **fetal membranes** surround the developing individual (fetus), and are filled with the **amniotic fluid**.

(1) During the first 8 weeks, the developing organism is known as an embryo. During this time, the major systems and parts of the body develop.

(2) During the remainder of the pregnancy, the developing organism is known as the fetus. During this time, growth and refinement of the body parts occur.

(3) **Parturition** is the actual delivery of the fetus into a free-living state. The delivery of the fetus is followed by a second delivery--that of the placenta and fetal membranes.

f. **Menstruation and Menopause.** About 2 weeks after an ovum is released, if it is not fertilized, menstruation occurs. **Menstruation** involves the loss of all but the basal layer of the endometrium. This process includes bleeding. It first occurs at puberty and lasts until menopause (45-55 years of age). After menopause, pregnancy is no longer possible.
6-16. SECONDARY SEXUAL CHARACTERISTICS

The secondary sexual characteristics of females include growth of pubic hair, development of mammary glands, development of the pelvic girdle, and deposition of fat in the mons pubis and labia majora.

6-17. MAMMARY GLANDS

Secretion of milk begins after parturition. Stimulation from suckling helps to maintain the normal rate of milk secretion. At the time of menopause, breast tissue becomes less prominent.

Section V. THE HUMAN MALE GENITAL (REPRODUCTIVE) SYSTEM

6-18. PRIMARY SEX ORGANS (TESTES)

The primary sex organ of the human male is the testis. See Figure 6-5 for an illustration of the male genital system. The testes are egg-shaped.

a. Location. The paired testes lie within the scrotum. The scrotum is a sac of loose skin attached in the pubic area of the lower abdomen. The scrotum provides a site cooler than body temperature to maintain the viability of the spermatozoa (see below). However, when the air is too cold, muscles and muscular fibers draw the testes and scrotum closer to the body to maintain warmth. Otherwise, the scrotum hangs loosely. The tunica vaginalis is a serous cavity surrounding each testis.

b. Functions. The testis produces the male sex cells, called spermatozoa (spermatozoon, singular). The millions continuously produce the spermatozoa. One such cell may eventually fertilize an ovum of a human female. The testes also produce male sex hormones, called androgens.

6-19. SECONDARY SEX ORGANS

a. Epididymis. The epididymis is a coiled tube whose function is to aid in the maturation of spermatozoa. Its coiled length is only about 1 1/2 inches. Its uncoiled length is about 16 feet. When coiled, it extends downward along the posterior side of each testis. Its lining secretes a nutritive medium for spermatozoa. It receives spermatozoa from the testes in an immature state. As the spermatozoa pass through the nutrient, they mature.

b. Ductus (Vas) Deferens. The ductus deferens is a transporting tube that carries the mature sperm from the epididymis to the prostate. Each tube enters the abdomen through the inquinal canal. Each passes over a ureter to reach the back of the urinary bladder and then down to the prostate gland.
Figure 6-5. The human male genital system.
c. **Seminal Vesicles.** Lying alongside each ductus deferens as it crosses the back of the bladder is a tubular structure called the seminal vesicle. The seminal vesicle produces a fluid that becomes part of the ejaculate (see below).

d. **Ejaculatory Duct.** Each ductus deferens and its corresponding seminal vesicle converge to form a short tube called the ejaculatory duct. The ejaculatory duct opens into the urethra within the prostate gland (see below). The ejaculatory duct carries both spermatozoa and seminal vesicle fluid.

e. **Prostate Gland.** As the urethra leaves the urinary bladder, a chestnut-size gland called the prostate gland surrounds its first inch. The prostate gland provides an additional fluid to be added to the spermatozoa and seminal vesicle fluid.

f. **Penis.** As the urethra leaves the abdomen, it passes through the penis, the male organ of copulation.

   (1) Surrounding the urethra is a central cylinder of erectile tissue called the **corpus spongiosum**. This cylinder is bulb-shaped at each end. The posterior end is attached to the base of the pelvis. The sensitive anterior end is known as the **glans**.

   
   CORPUS SPONGIOSUM = spongy body

   (2) Overlying the corpus spongiosum is a pair of cylinders of erectile tissue called the **corpora cavernosa**. These two cylinders are separate in their proximal fourth and joined in their distal three-fourths. They are attached to the pubic bones. Together, the corpus spongiosum and the corpora cavernosa combine to form the shaft of the penis.

   
   CORPUS CAVERNOSUM = cavernous body

   (3) The prepuce, or foreskin, is a covering of skin for the glans. It may be removed in a surgical procedure called circumcision.

6-20. **SECONDARY SEXUAL CHARACTERISTICS**

The secondary sexual characteristics of male include growth of facial pubic, and chest hair, growth of the larynx to deepen the voice, and deposition of protein to increase muscularity and general body size.

*Continue with Exercises*
EXERCISES, LESSON 6

REQUIREMENT. The following exercises are to be answered by marking the lettered response that best answers the question; or by completing the incomplete statement; or by writing the answer in the space provided at the end of the question.

After you have completed all the exercises, turn to “Solutions to Exercises,” at the end of the lesson, and check your answers with the solutions.

1. Which of the following are components of the human urogenital system?
   a. Urinary organs.
   b. Pleural space.
   c. Reproductive organs.
   d. Pituitary gland.

2. Select the major components of the human urinary system.
   a. Urethra.
   b. Urinary bladder.
   c. Ureters.
   d. Kidneys.
   e. All the above.
3. Referring to the drawing below, match the name of each component of the urinary system with its location on the drawing.

   ____ Ureter
   ____ Urethra
   ____ Kidney
   ____ Urinary bladder

4. From the list below, select the function(s) of the nephron.
   a. Remove the wastes of protein usage from the blood.
   b. Remove the secretions of endocrine glands from the blood.
   c. Conserve water and other materials for continued use by the body.
   d. All the above.

5. Which of the following statements is true concerning the role of the renal tubule?
   a. The renal tubule drains into the renal capsule.
   b. The renal tubule decreases sodium reabsorption when acted on by aldosterone.
   c. The renal tubule selectively removes the wastes of protein usage from the glomerular filtrate.
   d. The renal tubule selectively removes blood cells and large proteins from the glomerular filtrate.
6. The antidiuretic hormone is one of the two main hormones involved in the formation of urine. What is its role in the formation of urine?

   a. The antidiuretic hormone dilutes the concentration of urine by increasing the amount of water reabsorbed in the distal and collecting tubules.

   b. The antidiuretic hormone dilutes the concentration of the urine by increasing sodium reabsorption in the distal tubules and collecting ducts.

   c. The antidiuretic hormone concentrates the urine by decreasing sodium and water absorption in the distal tubules and collecting ducts.

   d. The antidiuretic hormone increases water absorption in order to concentrate the urine.

7. The ureter can be best described as a _____________________.

   a. Tube that conducts the urine from the urinary bladder to the outside of the body.

   b. Tube that allows for reabsorption of water from the glomerular filtrate in order to concentrate the urine.

   c. Tube that connects the kidneys to the urinary bladder.

   d. Tube that collects the urine after it has passed through the distal convoluted tubule.

8. Uremia is a condition-characterized by___________________.

   a. An inflammation of the nephrons caused by toxic material produced by certain bacteria.

   b. A build-up of toxic substances in the blood because of kidney failure.

   c. Increased urine output due to a low production of the antidiuretic hormone.

   d. A burning and stinging sensation in the urinary bladder due to some type of chronic inflammation.
9. What is the primary sex organ in the human female?
   a. The ovary.
   b. The vagina.
   c. The uterus.
   d. The cervix.

10. The vagina is best described as ___________________________.
    a. A mound of fat tissue covered with skin and hair in front of the symphysis pubis.
    b. A small projection of sensitive erectile tissue which corresponds to the male penis.
    c. A tubular canal that connects the cervix of the uterus with the outside.
    d. The cleft between the labia minora and behind the clitoris.

11. The primary sex organ in the human male is the _____________.
    a. Epididymis.
    b. Penis.
    c. Seminal vesicle.
    d. Testis.
12. Select the function(s) of the testis.
   a. Production of androgens.
   b. Production of estrogens.
   c. Production of spermatozoa.
   d. Production of a fluid that retards the development of spermatozoa.
   e. All the above.
   f. b and d only.
   g. a and c only.

13. The prostate gland ____________________________.
   a. Provides an additional fluid that is added to the spermatozoa and seminal vesicle fluid.
   b. Is the gland that produces spermatozoa.
   c. Is a coiled gland that secretes a nutritive medium for spermatozoa so they mature.
   d. Is the tissue responsible for the production of the male sex hormones called androgens.

   *Check Your Answers on Next Page*
1. a Urinary organs. (para 6-1)
   c Reproductive organs. (para 6-1)

2. e All the above. (para 6-4b)

3. 

   ![Diagram](Figure 6-1)

   - b Ureter
   - a Urethra
   - c Kidney
   - d Urinary bladder

4. a Remove the wastes of protein usage from the blood. (para 6-5c)
   c Conserve water and other materials for continued use by the body. (para 6-5c)

5. c The renal tubule selectively removes the wastes of protein usage from the glomerular filtrate. (para 6-5c)

6. d The antidiuretic hormone increases water absorption in order to concentrate the urine. (para 6-6a)

7. c Tubes that connect the kidneys to the urinary bladder. (para 6-7)

8. b A build-up of toxic substances in the blood because of kidney failure. (para 6-10a)
9. a The ovary. *(para 6-14)*

10. c A tubular canal that connects the cervix of the uterus with the outside. *(para 6-15d)*

11. d Testis. *(para 6-18)*

12. g a and c only. *(para 6-18b)*

13. a Provides an additional fluid which is added to the spermatozoa and seminal vesicle fluid. *(para 6-19e)*

*End of Lesson 6*
LESSON ASSIGNMENT

LESSON 7
Antihypertensive Agents.

LESSON ASSIGNMENT
Paragraphs 7-1--7-12.

TASKS
081-824-0001, Perform Initial Screening of a Prescription.

081-824-0026, Evaluate a Prescription.

081-824-0002/3, Fill a Prescription for a Controlled/Non-Controlled Drug.

081-824-0027, Evaluate a Completed Prescription.

081-824-0028, Issue Outpatient Medications. After completing this lesson you will be able to:

7-1. From a group of statements, select the statement which best defines the term essential hypertension.

7-2. Given the name of a type of essential hypertension and a group of statements, select the statement that best describes that type.

7-3. Given a group of statements, select the statement that best describes why diuretics are used to treat hypertension.

7-4. Given a group of trade and/or generic names of antihypertensive agents match each trade name with its corresponding generic name.

7-5. Given the trade and/or generic name of an antihypertensive agent and a group of indications, side effects, or patient warnings; select the indication(s), side effect(s), or patient warning(s) associated with that agent.

SUGGESTION
After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 7

ANTIHYPERTENSIVE AGENTS

Section I. INTRODUCTION TO HYPERTENSION

7-1. INTRODUCTION

a. It is estimated that 23 million people in the United States suffer from hypertension. Of this number, it is thought that 11.5 million people have been diagnosed as having the condition and that 5.75 million of those people are being treated for it. Unfortunately, it is estimated that only 2.875 million of those persons treated for hypertension are being treated properly. Therefore, it is obvious that hypertension is a major medical problem which should be a concern of all medical personnel.

b. Hypertension (high blood pressure) is prevalent in both men and women. It frequently contributes to the death of many persons. The cause of most cases of hypertension is unknown. This type of hypertension is referred to as primary or essential hypertension. Hypertension that has a known cause (kidney disease, hyperthyroidism) is called secondary hypertension. Blood pressure is the force that the blood exerts on the vessel wall while the heart is contracting and at rest. The force against the vessel wall during contraction or systole is the systolic pressure and the force during rest or diastole is the diastolic pressure. The blood pressure is expressed in terms of millimeters of mercury (Hg). Normal blood pressure is less than 135 mm Hg (systolic) and less than 85 mm Hg (diastolic) = 135/85 mm Hg.

7-2. TREATMENT OF HYPERTENSION

There is no cure for hypertension. Most patients who have a bacterial infection are accustomed to taking a 10-day treatment regimen of an antibiotic in order to rid themselves of the infection. The same is not true with hypertension. Once a person begins taking an antihypertensive agent, it is likely that he will continue taking some type of antihypertensive agent for the rest of his life.

7-3. DEFINITION OF ESSENTIAL (PRIMARY) HYPERTENSION

Essential (primary) hypertension can be defined as a disorder of unknown origin characterized mainly by an elevated systolic or diastolic blood pressure associated with generalized arteriolar vasoconstriction (see Lesson 2). Essential hypertension may be divided into three classes according to the severity of the condition. Labile hypertension is a condition of elevated blood pressure with intervening periods of normal blood pressure.
7-4. CLASSES OF ESSENTIAL HYPERTENSION

a. Stage I Hypertension. Stage I hypertension is characterized by sustained, documented systolic pressure 140 to 159 mm Hg and or diastolic pressure measurements 90-99 mm Hg. Signs of this type include increased heart rate (tachycardia) and increased cardiac output with normal total peripheral vascular resistance, however the majority of patients cannot tell that they have hypertension.

b. Stage II Hypertension. Stage II hypertension is characterized by sustained, systolic elevation (160 to 179 mm of Hg) and or diastolic pressure (100 to 109 mm Hg). Symptoms are the same as noted in Stage I. Patients with Stage I or II DO NOT show signs of target end organ damage. The organs of most concern are the heart, kidneys, and eyes. Stage I and II hypertension may be treated nonpharmacologically with diet and exercise or pharmacologically with antihypertensive medications.

c. Stage III Hypertension. Stage III hypertension is characterized by a persistent elevation (systolic >180mm Hg; diastolic >110mm Hg) with target end organ damage. Damage to the heart may include strain or enlargement of the left ventricle. Kidney damage may appear as abnormal laboratory values that indicate inefficiency. Damage to the eyes may appear as small hemorrhages due to the sustained blood pressure in these small vessels. This stage is often treated immediately with antihypertensive medications.

d. Hypertensive urgency is a condition of persistent elevation in blood pressure without target end organ damage. However, the pressure is high enough that the patient presents for treatment because of symptoms of dizziness, chest pain, or confusion. The goal in treatment of this condition is to normalize the blood pressure as quickly as possible (usually over 1-3 days). Hypertensive crisis is a similar condition, however the patient has symptoms of target end organ damage. This may be a life-threatening condition. The goal of therapy is to normalize the blood pressure in 12-24 hours. Both conditions are usually treated with intravenous (IV) antihypertensives.

7-5. REVIEW OF IMPORTANT FACTORS RELATING TO HYPERTENSION

Essential hypertension is a process of variable course and severity. Several options are open to the physician depending upon the severity of the drug therapy. Condition weight reduction and diet control may be adequate treatment; however, drug therapy is sometimes needed. When drug therapy is required, it usually begins with a diuretic followed by the addition of the other agents based on the patient’s response. However, certain classes of drugs may be more advantageous (fewer side effects) when patients have other diseases. It is not unreasonable to see patients treated by the same provider on different drugs.
7-6. DIURETICS IN THE TREATMENT OF HYPERTENSION

The effectiveness of diuretics in the treatment of essential hypertension arises from the fact that diuretic agents decrease tubular reabsorption of sodium, which caused a reduction in blood pressure. Some of the common diuretics include hydrochlorothiazide, spironolactone (Aldactone®), furosemide (Lasix®), and triamterene (Dyrenium®). These agents will be discussed in detail in Lesson 8 of this subcourse.

7-7. COMBINATION THERAPY IN THE TREATMENT OF HYPERTENSION

When diuretics alone are ineffective in controlling hypertension, it is necessary to combine the diuretic therapy with one or more additional agents. The physician may use many combinations of agents in order to control the patient’s high blood pressure. The patient should be encouraged to discuss any questions he might have concerning the side effects (for example, drowsiness), which might be caused by an agent or agents.

Section II. DRUGS USED IN THE TREATMENT OF HYPERTENSION

NOTE: For this discussion commonly used antihypertensive agents will be classified into the following categories.

7-8. DRUGS WHICH ACT ON THE SYMPATHETIC NERVOUS SYSTEM

NOTE: For a review of the sympathetic nervous system you should refer to Subcourse MD0805, Pharmacology II.

a. Methyldopa (Aldomet®). Methyldopa is one of the drugs of this type. It is believed to produce its effects by its being metabolized to a substance which is very similar to norepinephrine--but with considerably less vasoconstricting activity than is shown by epinephrine. Thus, methyldopa competes with norepinephrine and thereby depresses the activity of the sympathetic nervous system. This medication is rarely used but is still one of the drugs of choice for pregnancy-induced hypertension. Side effects associated with this agent include bradycardia, swelling of the feet and lower legs (because sodium and water retention), drowsiness, and mental depression.

b. Clonidine (Catapres®, Catapres TTS®). Clonidine is an agent that is believed to act by decreasing sympathetic outflow from the brain and consequently inhibit vasoconstriction. It is used in mild to moderate hypertension. Side effects associated with this agent include swelling of the feet and lower legs (due to sodium and water retention) and mental depression. The patient taking this drug should be cautioned to check with his physician before suddenly discontinuing the medication because abrupt withdrawal from the drug may cause serious hypertension problems. Clonidine is also used in the treatment of symptoms associated with alcohol withdrawal.
7-9. BETA ADRENERGIC BLOCKERS

As you remember, beta adrenergic blocking agents block the effect of the sympathetic neurotransmitters by competing for receptors.

a. Propranolol (Inderal®). Propranolol is a drug used in the treatment of hypertension, angina pectoris, and cardiac arrhythmias. Side effects associated with propranolol include dizziness, mental confusion, and mental depression. It may also exacerbate congestive heart failure and mask the symptoms of hypoglycemia.

b. Metoprolol (Lopressor®, Toprol XL®). Metoprolol is prescribed for the same conditions as propranolol and is also indicated used in the treatment of myocardial infarction and treatment of congestive heart failure. Normal doses for hypertension are 25 - 100 mg twice daily. The dose for heart failure is 6.25 - 12.5 mg twice daily and adjusted upward as tolerated by the patient. This agent is available as an oral and injectable preparation.

c. Other Beta Adrenergic Blockers. Other beta blockers used in the treatment of hypertension include betaxolol (Kerlone®), bisoprolol (Zebeta®), labetolol (Trandate®, Normodyne®), nadolol (Corgard®), and carvedilol (Coreg®). Carvedilol is also indicated for congestive heart failure.

7-10. SMOOTH MUSCLE RELAXANTS

Drugs in this category treat hypertension by acting directly on vascular smooth muscle by relaxing the blood vessels. Consequently, they cause vasodilation and a decrease in peripheral resistance results in a lower blood pressure.

a. Hydralazine (Apresoline®). Hydralazine is given orally or injected in the management of hypertension. Preferably, it is used in conjunction with other antihypertensive agents. Side effects associated with this agent include chest pain (angina pectoris), a general feeling of weakness, unexplained sore throat, joint pain, and headache. The patient should to be told to avoid getting up suddenly from a lying or a sitting position.

b. Alpha adrenergic blockers. Alpha adrenergic blockers block alpha receptors in peripheral vessels, therefore causing vasodilation. Agents in the class include prazosin (Minipress®), doxazosin (Cardura®), and terazosin (Hytrin®). Doxazosin and terazosin offer the advantage of once daily dosing and the added benefit of relieving the symptoms of benign prostatic hyperplasia (enlarged prostate gland). Dizziness, drowsiness, and headache are common side effects associated with these agents, especially with the first dose. Patients must be counseled on these side effects and instructed to take the first dose in the evening at home. Some patients who have taken this drug have also experienced syncope (unconsciousness due to decreased oxygen supply to the brain).
c. **Calcium Channel Blockers.** Calcium channel blockers are potent peripheral vasodilators used in the treatment of hypertension. Similar to beta blockers that can slow the heart rate, calcium channel blockers are also used in the treatment of atrial fibrillation to control the heart rate. Many of the products are available in oral and injectable form and may be administered once daily. Side effects include dizziness, headache, heartburn, edema, and constipation. Agents include diltiazem (Cardizem®, Tiazac®, Dilacor®), verapamil (Calan®, Isoptin®, Covera®, Verelan®), amlodipine (Norvasc®), felodipine (Plendil®), and nifedipine (Procardia XL®, Adalat CC®).

d. **Angiotensin Converting Enzyme Inhibitors (ACE Inhibitors).** ACE inhibitors work by inhibiting the enzyme which converts angiotensin I to angiotensin II. Angiotensin II is one of the most potent vasoconstrictors known to man. By inhibiting the enzyme, these agents produce vasodilation and are used in the treatment of hypertension and heart failure. Most products are administered 1-2 times daily. The most common side effects are rash, dry cough, and hyperkalemia. These agents are contraindicated in pregnancy. Selected agents include benazepril (Lotensin®), captopril (Capoten®), enalapril (Vasotec®), lisinopril (Prinivil®, Zestril®), and ramipril (Altace®). Enalapril is available in an injectable form.

e. **Angiotensin II receptor blockers (ARBs).** ARBs work by directly blocking the angiotensin II receptor to cause vasodilation and lower blood pressure. They appear to have less side effects than ACE inhibitors, especially the dry cough. Selected agents include irbesartan (Avapro®), losartan (Cozaar®), and valsartan (Diovan®).

7-11. COMBINATION PRODUCTS

It should be apparent that in order to control hypertension the patient may be required to take extremely large amounts of medication. In an attempt to develop a more convenient method of controlling hypertension, researchers have combined diuretic and antihypertensive agents in order to maximize the best attributes of each. These combination products are very convenient for the patient to use if the dosage of the product is exactly what the patient needs to control his hypertension. Since these combination products tend to be rather expensive, military pharmacies frequently have a limited selection of these items in stock. Two examples of combination products are listed below.

a. **Aldactazide® (Spironolactone and Hydrochlorothiazide).** Spironolactone and hydrochlorothiazide are both diuretics. This particular drug is used in the treatment of hypertension, congestive heart failure and cirrhosis of the liver. The patient taking this medication should be told to take the preparation with or after meals to minimize stomach upset.

b. **Dyazide® (Triamterene and Hydrochlorothiazide).** Triamterene and hydrochlorothiazide are both diuretics. This product is used as a diuretic and as an antihypertensive agent.
7-12. THE TREATMENT OF A HYPERTENSIVE CRISIS OR EMERGENCY

Patients presenting with extreme elevations of blood pressure and symptoms of impending stroke, pulmonary edema, kidney failure, or heart attack must be promptly treated. The following agents are used to treat hypertensive crisis:

a. **Diazoxide (Hyperstat® I.V.)** This agent is administered by rapid intravenous (I.V.) injection (150 to 300 milligrams immediately, repeated in 30 minutes and every four hours if needed). When administered, this agent produces a fall in blood pressure in from one to five minutes. Hyperglycemia and sodium retention are side effects associated with this agent.

b. **Nitroprusside (Nipride®).** Nitroprusside is administered by continuous intravenous infusion at a rate of 0.5 to 0.8 micrograms per kilogram of patient weight per minute. The patient must be closely observed, when he is receiving this drug since overdosage of nitroprusside results in cyanide poisoning. Nitroprusside is not intended for direct injection. Instead, the drug must be used as an infusion with sterile 5 percent dextrose in water. The intravenous infusion must be used within four hours once it is prepared. Furthermore, the prepared intravenous infusion must be protected from light (for example: the bottle must be wrapped with foil). Nausea, vomiting, and headache are side effects commonly associated with this agent.

*Continue with Exercises*
EXERCISES, LESSON 7

**REQUIREMENT:** The following exercises are to be answered by marking the lettered response that best answers the question; or by completing the incomplete statement; or by writing the answer in the space provided at the end of the question.

After you have completed all the exercises, turn to “Solutions to Exercises,” at the end of the lesson, and check your answers with the solutions.

1. Match the drug name in **Column A** with its corresponding name listed in **Column B**.

<table>
<thead>
<tr>
<th>COLUMN A</th>
<th>COLUMN B</th>
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</thead>
<tbody>
<tr>
<td>_____ Lisinopril.</td>
<td>a. Cardura®</td>
</tr>
<tr>
<td>_____ Spironolactone and</td>
<td>b. Catapres®</td>
</tr>
<tr>
<td>hydrochlorothiazide</td>
<td>c. Adalat CC®</td>
</tr>
<tr>
<td>combination.</td>
<td></td>
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<tr>
<td>_____ Doxazosin.</td>
<td>d. Inderal®</td>
</tr>
<tr>
<td>_____ Diltiazem.</td>
<td>e. Calan®</td>
</tr>
<tr>
<td>_____ Metoprolol.</td>
<td>f. Cardizem®</td>
</tr>
<tr>
<td>_____ Propranolol.</td>
<td>g. Zestril®</td>
</tr>
<tr>
<td>_____ Clonidine.</td>
<td>h. Lopressor®</td>
</tr>
<tr>
<td>_____ Verapamil.</td>
<td>i. Aldactazide®</td>
</tr>
<tr>
<td>_____ Nifedipine.</td>
<td></td>
</tr>
</tbody>
</table>
2. Which of the following statements best defines the term essential hypertension?

a. A disorder of unknown origin characterized mainly by an elevated systolic or diastolic pressure associated with generalized arteriolar vasoconstriction.

b. A disorder caused by too many fats in the diet and by an excess of sodium in the intracellular fluid.

c. A disorder produced by unknown causes which results in a diastolic pressure which is higher than the systolic pressure.

d. A disorder of unknown origin that can be cured by a 10-day treatment regimen of diuretics and antihypertensives.

3. Which of the following statements best describes Stage I primary hypertension?

a. A type of essential hypertension characterized by documented pressure measurements greater than 159 mm Hg (systolic) and/or greater than 99 mm Hg (diastolic).

b. A type of essential hypertension characterized by a persistent elevation in diastolic pressure with minor target organ (heart and kidney damage).

c. A type of essential hypertension characterized by marked elevated blood pressure with definite target organ (heart and kidney) damage.

d. A type of essential hypertension characterized by a mild, but sustained, elevation in diastolic pressure without target organ (heart and kidney) damage.
4. Stage III primary hypertension is best described as a type of essential hypertension characterized by _______________________.

   a. Persistent elevated diastolic pressure with minor damage to the heart and/or kidneys.
   
   b. Documented diastolic pressure associated with generalized arteriolar vasoconstriction.
   
   c. A mild, but sustained, elevation in diastolic pressure without damage to the heart and/or kidneys.
   
   d. Marked elevated blood pressure with definite damage to the heart and/or kidneys.

5. The indication for nitroprusside (Nipride®) is ________________.

   a. Treatment of essential hypertension.
   
   b. Treatment of a hypertensive crisis.
   
   c. Treatment of labile primary hypertension.
   
   d. Treatment of moderate primary hypertension.

6. Select the side effect associated with beta blockers.

   a. Swelling of the feet and lower legs.
   
   b. Tachycardia.
   
   c. Restlessness.
   
   d. Mask symptoms of hypoglycemia.
7. What should the patient taking terazosin be told?
   a. To be aware that many patients taking the drug experience impotence or decreased sexual interest.
   b. To take the medication one hour before meals in order to increase the absorption of the drug.
   c. To arise slowly from a lying or sitting position because of the possibility of orthostatic hypotension and syncope.
   d. To avoid taking the medication with fats because absorption of the drug is affected.

8. The patient taking nitroprusside should be closely monitored because ____________________.
   a. Hyperglycemia and sodium retention occur so abruptly with this agent that death can result if the drug is not withdrawn after their onset.
   b. Overdosage of nitroprusside results in cyanide poisoning.
   c. Abrupt withdrawal of this agent can result in an extreme hypertensive crisis.
   d. Too rapid administration of this product can result in a cerebrovascular accident.

9. Which of the following is a side effect associated with the use of enalapril?
   a. Hypokalemia (low potassium).
   b. Dry cough.
   c. Syncope.
   d. Chest pain.
10. What is/are the indications for Coreg®?
   a. Antihypertensive.
   b. Congestive Heart Failure.
   c. Antianginal agent (treatment of angina pectoris).
   d. a and b only.
   e. a, b, and c.

*Check Your Answers on Next Page*
### SOLUTIONS TO EXERCISES, LESSON 7

<table>
<thead>
<tr>
<th>COLUMN A</th>
<th>COLUMN B</th>
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<tbody>
<tr>
<td>1. g</td>
<td>Lisinopril (para 7-10d).</td>
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<tr>
<td>i</td>
<td>Spironolactone and hydrochlorothiazide combination. (para 7-11a)</td>
</tr>
<tr>
<td>a</td>
<td>Cardura®</td>
</tr>
<tr>
<td>b</td>
<td>Catapres®</td>
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<tr>
<td>c</td>
<td>Adalat CC®</td>
</tr>
<tr>
<td>a</td>
<td>Doxazosin (para 7-10b).</td>
</tr>
<tr>
<td>f</td>
<td>Diltiazem (para 7-10c).</td>
</tr>
<tr>
<td>h</td>
<td>Metoprolol (para 7-9b).</td>
</tr>
<tr>
<td>d</td>
<td>Propranolol (para 7-9a).</td>
</tr>
<tr>
<td>b</td>
<td>Clonidine (para 7-8b).</td>
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<tr>
<td>e</td>
<td>Verapamil (para 7-10c).</td>
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<tr>
<td>c</td>
<td>Nifedipine (para 7-10c).</td>
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<td>h</td>
<td>Lopressor®</td>
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<tr>
<td>i</td>
<td>Aldactazide®</td>
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</tbody>
</table>

2. a  A disorder of unknown origin characterized mainly by an elevated systolic or diastolic pressure associated with generalized arteriolar vasoconstriction. (para 7-3)

3. a. A type of essential hypertension characterized by documented pressure measurements greater than 159 mm Hg (systolic) and/or greater than 99 mm Hg (diastolic). (para 7-4a)

4. d  Marked elevated blood pressure with definite damage to the heart and/or kidneys. (para 7-4c)

5. b  Treatment of a hypertensive crisis. (para 7-12b)

6. d  Mask symptoms of hypoglycemia. (para 7-9a)

7. c  To arise slowly from a lying or sitting position because of the possibility of orthostatic hypotension. (para 7-10b)

8. b  Overdosage of nitroprusside results in cyanide poisoning. (para 7-12b)

MD0806 7-13
9. b Syncope. (para 7-10d)

10. d a and b only. (para 7-9c)

End of Lesson 7
LESSON ASSIGNMENT

LESSON 8
Diuretic and Antidiuretic Agents.

LESSON ASSIGNMENT
Paragraphs 8-1–8-7.

TASKS
081-824-0001, Perform Initial Screening of a Prescription.

081-824-0026, Evaluate a Prescription.

081-824--0002/3, Fill a Prescription For a Controlled/Non-Controlled Drug.

081-824-0027, Evaluate a Completed Prescription.

081-824-0028, Issue Outpatient Medications.

LESSON OBJECTIVES
After you finish this lesson you should be able to:

8-1. Given a group of statements, select the statement that best defines the term diuretic.

8-2. Given a list of conditions, select the condition(s) that are treated with diuretic therapy.

8-3. Given the name of a type of diuretic and a group of statements describing the mechanisms of action of different types of diuretics, select the mechanism of action for that type of diuretic.

8-4. Given the trade and/or generic name of a diuretic agent or antidiuretic agent and a list of indications, uses, side effects, or precautionary statements, select the indication(s), use(s), side effect(s), or precautionary statements(s) for that particular agent.

8-5. Given a group of trade and/or generic names of various diuretic or antidiuretic agents match each trade or generic name with its corresponding trade or generic name.
8-6. Given the trade or generic name of a diuretic agent and a list of types of diuretic agents select the type of diuretic to which that agent belongs.

**SUGGESTION**

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 8
DIURETIC AND ANTIDIURETIC AGENTS

Section I. DIURETIC AGENTS

8-1. INTRODUCTION

In Lesson 3 of this subcourse, congestive heart failure was described as a condition characterized by sodium retention that results in expanded extracellular fluid volume or edema. This same process of increased tubular reabsorption of sodium—resulting in an accumulation of fluid—may accompany cirrhosis of the liver, renal disease, toxemia of pregnancy, the side effects of drugs, and other states of fluid retention. In all of these conditions, treatment of sodium retention is what is desired. REMEMBER: WHERE SODIUM GOES, WATER GOES! Therefore, the treatment as sodium retention by sodium excretion—not just the increase in urine volume—is the desired goal. 

Diuretic agents increase the amount of sodium excreted from the body.

8-2. DEFINITION OF DIURETIC

A diuretic is any agent that produces diuresis (an increase in the volume of urine output that results in the mobilization of edema fluid). You have heard the term edema before. Edema is the presence of abnormally large amounts of fluid in the body. Many diuretics reduce edema by increasing the amount of sodium removed from the body. Remember, where sodium goes, water goes. Thus, when sodium is removed from the body, there is a corresponding increase in the volume of urine produced.

8-3. USES OF DIURETICS

The general uses of diuretics include the treatment of congestive heart failure, hypertension, glaucoma, ascites, toxemia of pregnancy, and diabetes insipidus. Congestive heart failure has been discussed in Lesson 3 of this subcourse, hypertension has been discussed in Lesson 7 of this subcourse, and glaucoma has been discussed in MD0805, Pharmacology II. Review these materials if you have a need. The other conditions will be explained in this paragraph. Ascites is the accumulation of fluid in the abdominal cavity. Toxemia of pregnancy is a group of pathologic conditions—essentially metabolic disturbances—which sometimes occurs in pregnant women. Toxemia of pregnancy is manifested by preeclampsia (a toxemia of late pregnancy characterized by hypertension, albuminuria, and edema) and fully developed eclampsia (this condition includes convulsions and coma, which might occur in a pregnant woman or in a woman who has just delivered). Hypertension, edema, and/or proteinuria characterize eclampsia. Diabetes insipidus is a metabolic disorder caused by a lack of production of antidiuretic hormone (ADH), which is marked by great thirst and the passage of a large amount of dilute urine with no excess of sugar.
8-4. TYPES OF DIURETICS

There are several types of diuretics. The categories are defined based upon their mechanism of action.

a. Osmotic Diuretics. Osmotic diuretics produce a diuresis of water rather than a diuresis of sodium. The body does not metabolize osmotic diuretics. Instead, the drug molecules are not reabsorbed in the kidney tubules. This greatly affects the tonicity of every part of the kidney tubules through which the glomerular filtrates pass. By the process of osmosis, the drug molecules draw an increased amount of water from the interstitial fluid compartment. The result is that a great volume of urine is produced (water diuresis). It just so happens that sodium is contained in that urine and is subsequently removed from the body. Thus, the osmotic diuretics indirectly produce a removal of sodium from the body. Following is one example of an osmotic diuretic:

Mannitol. Mannitol is used to prevent acute renal (kidney) failure, evaluate kidney functioning, treat glaucoma (by the reduction of intraocular pressure), promote the urinary excretion of toxic substances (diuresis in certain drug intoxications) and reduce intracranial pressure (pressure in the head). The usual dosage of mannitol is from 50 to 200 grams in a 24-hour period by intravenous infusion. Side effects associated with the use of mannitol include pulmonary congestion, fluid and electrolyte imbalance, acidosis, electrolyte loss, and dryness of mouth and dehydration. Since mannitol may crystallize on exposure to low temperatures, you should observe mannitol vials and premixed bags for such crystals. When you observe these crystals, you should warm the vials or bags in a 500° C water bath in order to dissolve the crystals. The product should be cooled to body temperature before the mannitol solution is administered. Mannitol is available in a 5, 10, 15, 20, and 25 percent injection.

b. Thiazide Diuretics. Thiazide diuretics work by the inhibition of sodium reabsorption in the first portion of the distal tubule. The passive diffusion of the accompanying water and chloride is correspondingly reduced. Thus, the result is an increased excretion of sodium, water, and chloride from the body. When the thiazide acts on the proximal tubule, the carbonic anhydrase activity in the distal tubule is also decreased. This causes increased secretion of potassium. Consequently, the water lost contains sodium, potassium, and chloride. This loss of potassium can present problems to the patient.

(1) Hydrochlorothiazide (Hydrodiuril®). Hydrochlorothiazide is used in the treatment of essential hypertension and edema found in congestive heart failure. The usual dose of this drug is from 12.5 to 100 milligrams per day. Side effects commonly associated with hydrochlorothiazide include hypokalemia, hyperglycemia, and hyperuricemia. This drug should be used in caution in patients suffering from diabetes or gout and in patients who take digitalis.
(2) Chlorothiazide (Diuril®). This drug is used as a diuretic and as an antihypertensive. It is available in both parenteral and oral dosage forms. For side effects, refer to hydrochlorothiazide.

(3) Chlorthalidone (Hygroton®). Although chlorthalidone is not the same chemically as the thiazide diuretics, it has the same effects as these agents. For indications and side effects, you should refer to hydrochlorothiazide.

c. Potassium-Sparing Diuretics. This type of diuretic is used when there is a need to maintain normal levels of potassium in the patient along with the diuresis. The specific mechanisms of actions of selected drugs in this category.

(1) Spironolactone (Aldactone®). Spironolactone causes sodium diuresis and potassium retention by acting as an aldosterone competitive antagonist. That is, this drug acts on the distal tubule to block the sodium-potassium exchange mechanism. The net result is sodium loss and potassium retention. Consequently, by antagonizing aldosterone, sodium as well as water diuresis and potassium retention are affected. Spironolactone is used for primary hyperaldosteronism, edema associated with congestive heart failure, cirrhosis of the liver or ascites, essential hypertension, and in hypokalemia when other means are considered inappropriate or inadequate. The usual dose of this drug is from 25 to 400 milligrams per day depending upon the condition of the patient. Although spironolactone is a mild diuretic, it can hasten major side effects such as gastrointestinal symptoms (for example: cramping and diarrhea), lethargy, hyperkalemia, and hyponatremia. Hyperkalemia is a major side effect that occurs in patients who have impaired renal function. Hyperkalemia can cause irregularities that may be fatal. Spirolactone also causes estrogen-like side effects because of its hormone-like structure.

(2) Triamterene (Dyrenium®). While triamterene produces effects similar to those of spironolactone, the effects produced by triamterene are not dependent on the presence of aldosterone. This agent acts directly on the distal tubule where it prevents the passage of sodium across the membrane of the tubule. Thus, by blocking sodium reabsorption, potassium loss is reduced. Triamterene is used for edema associated with congestive heart failure and cirrhosis of the liver. The usual dosage of this drug is from 25 to 200 milligrams per day. The daily dose should not exceed 300 milligrams. Side effects associated with this agent include electrolyte imbalances, hyperkalemia, weakness, and dry mouth. Like spironolactone, hyperkalemia is a major side effect which can occur in patients who have impaired renal function or when the drug is administered alone.

d. Carbonic Anhydrase Inhibitor Diuretics. Carbonic anhydrase inhibitors produce diuresis by inhibiting carbonic anhydrase in the renal tubules. Carbonic anhydrase is an enzyme that catalyzes the following reaction:

\[
\begin{align*}
\text{CO}_2 + \text{H}_2 & \quad \xrightarrow{\text{carbonic anhydrase}} \quad \text{H}_2\text{CO}_3 \\
\text{H}_2\text{CO}_3 & \quad \xrightarrow{\text{H}^+} \quad \text{H}^+ + \text{HCO}_3^-
\end{align*}
\]
From the reaction above, it can be deduced that removal of or blocking the enzyme carbonic anhydrase would result in a much slower reaction. Consequently, there would be a greatly reduced production of hydrogen ions and bicarbonate ions. This interferes with the ion exchange mechanism at the distal tubule, where the sodium ion that accompanies the bicarbonate ion is reabsorbed only by exchange for hydrogen or potassium ions secreted into the tubule. Normally the bicarbonate ion that accompanies the sodium ion (provided by the glomerular filtrate) is reabsorbed almost complete at the distal tubule. With reduced production of hydrogen ion due to inhibition of the carbonic anhydrase, the bicarbonate ion, together with the sodium ion will not be reabsorbed. Thus, the sodium will be excreted in an unusually large amount—with a corresponding loss of water (remember, where sodium goes, water goes).

**Acetazolamide (Diamox®).** Acetazolamide is one example of a carbonic anhydrase inhibitor. Although rarely used today, it may be used in the treatment of edema because of congestive heart failure; drug-induced edema; petit mal and unlocalized seizures; and open-angle and secondary glaucoma. The usual dosage of this drug ranges from 250 milligrams to 2 grams—depending on the type of condition being treated. Actually, the dosage recommendations for glaucoma and epilepsy differ considerably from those of congestive heart failure, since the first two conditions are not dependent on carbonic anhydrase inhibition in the kidney which requires intermittent dosage if it is to recover from the inhibitory effect of the therapeutic agent. The side effects of this agent include loss of appetite, transient myopia (nearsightedness), drowsiness, and acidosis. Acetazolamide is available in the injectable form.

e. **Inhibition of Sodium Transport in the Ascending Limb of the Loop of Henle, the Distal Tubule, and the Proximal Sites Diuretics.** Diuretics of this type are extremely potent and rapidly acting. In fact, they are used only after less potent—but safer—diuretics have failed. As the category type states, this type of diuretic acts by inhibiting sodium transport in the ascending limb of the loop of Henle, the distal tubule, and in the proximal sites. Thus, a greater fraction of filtered sodium can escape reabsorption. Thereby, increased sodium and water excretions occur. Diuretics of this type are called “loop diuretics”.

(1) **Furosemide (Lasix®).** Furosemide is used in the treatment of edema associated with congestive heart failure, cirrhosis of the liver and renal disease, pulmonary edema, and hypertension. It is particularly useful when an agent with a greater diuretic potential than that of those commonly used is desired. This agent is also a rapidly acting diuretic. When administered orally it acts within one hour. When administered by injection it acts within 5-10 minutes. However, the agent does produce massive changes in electrolyte and water balance in the body. The usual dosage of furosemide is 20 to 80 milligrams given in a single dose—preferably in the morning. Depending on the patient's response, this dose can be repeated, maintained, or reduced. There are numerous adverse effects associated with the use of furosemide. These adverse effects include hypokalemia, hyponatremia, hyperglycemia, electrolyte depletion, and hypovolemia. Reservsible and irreversible hearing impairment and loss may occur with any of the loop diuretics. It is often associated with rapid infusion and
the use of extremely high doses. The injectable form of the drug must be stored at controlled room temperature and should not be used if the solution is yellow. The oral solution and tablet preparations should be dispensed in light-resistant containers.

(2) Other loop diuretics include bumetanide (Bumex®), ethacrynic acid (Edecrin®), and torsemide (Demadex®).

f. Inhibition of Sodium and Chloride Reabsorption Diuretics. The mechanism of action of this type is very similar to the thiazide diuretics. That is, drugs of this category inhibit sodium and chloride reabsorption that results in the increased excretion of sodium, chloride, and water.

Chlorthalidone (Hygroton®). This agent differs from the thiazide diuretics only in chemical structure. Chlorthalidone’s pharmacological action is indistinguishable from the thiazide diuretics. Chlorthalidone is used in the management of hypertension—either as the sole therapeutic agent or to enhance the effect of other antihypertensive drugs in patients who have the more severe forms of hypertension. It is also used as adjunctive therapy in the treatment of edema associated with congestive heart failure, hepatic cirrhosis, and various forms of renal dysfunctions. Refer to the information on hydrochlorothiazide for side effect information.

g. Combination Diuretics (Potassium-Sparing and Thiazide Diuretic Combination). The potassium-sparing and thiazide diuretics have different but complementary mechanisms and sites of action. Therefore, when given together they produce additive diuretic and antihypertensive effects. The thiazide component blocks the reabsorption of sodium and chloride ions and thus increases the quantity of sodium traversing the distal tubule and the volume of water excreted in the urine. This characteristically induces potassium loss. The potassium-sparing component inhibits the reabsorption of sodium in exchange for potassium and hydrogen ions at the distal tubule, so that sodium excretion is greatly favored and the excess loss of potassium, as well as hydrogen and chloride ions induced by the thiazide, is reduced.

(1) Aldactazide® (combination of spironolactone and hydrochlorothiazide). This drug is used for the treatment of edema associated with congestive heart failure, cirrhosis of the liver and ascites and for essential hypertension.

(2) Dyazide® (combination of triamterene and hydrochlorothiazide). This agent is used in the treatment of edema associated with congestive heart failure, cirrhosis of the liver, and hypertension. The usual dosage of this product from 1 to 2 capsules taken twice daily after meals. The patient should take no more than four capsules per day. The side effects associated with this agent include hyperglycemia, hyperuricemia, and gastrointestinal disturbances. Each Dyazide® capsule contains 37.5 milligrams of triamterene and 25 milligrams of hydrochlorothiazide. There are other combinations of these diuretics available as generics or as Maxide® (75/50; 50/25). One must be very careful and doublecheck the active ingredients to ensure that the correct product is dispensed.
Section II. ANTIDIURETIC AGENTS

8-5. INTRODUCTION

The antidiuretic hormone has been discussed in Lesson 6 of this subcourse. As you will remember, it is a hormone secreted by the pituitary gland. The antidiuretic hormone (ADH) acts on the distal tubule and collecting ducts to increase water reabsorption (and thus to decrease urine output). The agents discussed below are those that work in a manner opposite the diuretics. This process is called antidiuresis. Antidiuresis is the suppression of urinary secretion. Consequently, an antidiuretic is an agent that suppresses urine formation as well as the rate of urine formation.

8-6. MECHANISM OF ACTION OF ANTIDIURETICS

Antidiuretics work by increasing the reabsorption of water at the distal tubule and collecting ducts without significantly modifying the rate of glomerular filtration.

8-7. EXAMPLES OF ANTIDIURETIC AGENTS

Two examples of antidiuretic agents are presented below.

a. **Vasopressin (Pitressin®)**. This agent is used for the control or prevention of the symptoms and complications of diabetes insipidus. For vasopressin injection, the dose is 5 to 10 units (0.25 to 0.5 milliliters) by intramuscular or subcutaneous injection as required (usually every 2 to 3 hours as needed). The side effects associated with this product include abdominal cramps, fluid retention, and increased blood pressure. It is dispensed for hospital use only and should never be administered intravenously. This drug is available as a solution containing 20 pressor units per milliliter.

b. **Lypressin (Diapid®)**. This agent is also used for the control or prevention of the symptoms and complications of diabetes insipidus. The usual dosage of this drug is 1 to 2 sprays applied to each nostril four times daily. The side effects associated with lypressin are abdominal cramps, nasal congestion, fluid retention, and increased bowel movements. Lypressin is useful in patients suffering from diabetes insipidus who have become unresponsive to other therapy or who experience allergic or other undesirable reactions to antidiuretic hormone of animal origin. The product has to be kept refrigerated. This product has an expiration date of 36 months. It is available as a nasal spray, 0.185 milligrams of lypressin per milliliter of solution (equivalent to 50 units per milliliter).

*Continue with Exercises*
EXERCISES, LESSON 8

REQUIREMENTS: The following exercises are to be answered by marking the lettered response that best answers the question; or by completing the incomplete statement; or by writing the answer in the space provided at the end of the question.

After you have completed all the exercises, turn to “Solutions to Exercises,” at the end of the lesson, and check your answers with the solutions.

1. Which of these conditions is/are treated with diuretics?
   a. Asthma.
   b. Congestive heart failure.
   c. Diabetes mellitus.
   d. Gallstones.

2. Select the statement that best describes the mechanism of action for the thiazide diuretics.
   a. Thiazide diuretics cause sodium diuresis and potassium retention by acting as an aldosterone competitive antagonist.
   b. Thiazide diuretics produce a diuresis of water by drawing water from the cells in the body and thus by increasing the glomerular filtrate.
   c. Thiazide diuretics work by the inhibition of sodium reabsorption in the first portion of the distal tubule.
   d. Thiazide diuretics inhibit sodium transport--and thus sodium excretion--in the ascending limb of the Loop of Henle, the distal tubule, and in the proximal tubule.

3. Mannitol is used to __________________________.
   a. Prevent or treat acute liver failure.
   b. Treat dehydration and electrolyte imbalance.
   c. Promote the excretion of toxic substances in the urine.
   d. Treat epilepsy.
4. Hydrochlorothiazide is used to treat _________________.
   a. Essential hypertension.
   b. Diabetes mellitus.
   c. Hyperglycemia.
   d. Cramping and diarrhea.

5. Vasopressin is used _________________.
   a. For the control or prevention of the symptoms and complications of diabetes insipidus.
   b. To treat hypovolemia.
   c. To treat nasal congestion.
   d. To prevent hyperkalemia.

6. Which of the following is/are side effect(s) associated with Dyazide®?
   a. Hypouricemia.
   b. Hyperglycemia.
   c. Hypernatremia.
   d. Fluid retention.

7. Select the use(s) of Diamox®.
   a. The treatment of edema because of congestive heart failure.
   b. The treatment of drug-induced edema.
   c. The treatments of open–angle glaucoma and secondary edema.
   d. All the above.
8. Match the drug name in Column A with its corresponding trade or generic name listed in Column B.

<table>
<thead>
<tr>
<th>Column A</th>
<th>Column B</th>
</tr>
</thead>
<tbody>
<tr>
<td>_____Aldactazide®</td>
<td>a. Chlorothiazide.</td>
</tr>
<tr>
<td>_____Spironolactone.</td>
<td>b. Aldactone.</td>
</tr>
<tr>
<td>_____Furosemide.</td>
<td>c. Combination of spironolactone and hydrochlorothiazide.</td>
</tr>
<tr>
<td>_____Diapid®</td>
<td>d. Lypressin.</td>
</tr>
<tr>
<td>_____Diuril®</td>
<td>e. Lasix®.</td>
</tr>
<tr>
<td>_____Dyrenium®</td>
<td>f. Triamterene.</td>
</tr>
</tbody>
</table>

*Check Your Answers on Next Page*
**SOLUTIONS TO EXERCISES, LESSON 8**

1. b Congestive heart failure.  *(para 8-3)*  

2. c Thiazide diuretics work by the inhibition of sodium reabsorption in the first portion of the distal tubule.  *(para 8-4b)*  

3. c Promote the excretion of toxic substances in the urine.  *(para 8-4a)*  

4. a Essential hypertension.  *(para 8-4b(1))*  

5. a For the control or prevention of the symptoms and complications of diabetes insipidus.  *(para 8-7a)*  

6. b Hyperglycemia.  *(para 8-4g(2))*  

7. d All the above.  *(para 8-4d)*  

8. **Column A**  
   c  Aldactazide®.  *(para 8-4g(1))*  
   b  Spironolactone.  *(para 8-4c(1))*  
   e  Furosemide.  *(para 8-4e(1))*  
   d  Diapid®.  *(para 8-7b)*  
   a  Diuril®.  *(para 8-4b(2))*  
   f  Dyrenium®.  *(para 8-4c(2))*  

   **Column B**  
   a  Chlorothiazide.  
   b  Aldactone.  
   c  Combination of spironolactone and hydrochlorothiazide.  
   d  Lypressin.  
   e  Lasix®.  
   f  Triamterene

*End of Lesson 8*
LESSON ASSIGNMENT

LESSON 9  Toxicology and Poison Control.


TASKS  081-824-0001, Perform Initial Screening of a Prescription.

081-824-0026, Evaluate a Prescription.

081-824-0002/3, Fill a Prescription For a Controlled/Non-Controlled Drug.

081-824-0027, Evaluate a Completed Prescription.

081-824-0028, Issue Outpatient Medications.

LESSON OBJECTIVES  After completing this lesson you will be able to:

9-1. Given a list of numbers, select the number of deaths per year which are caused by accidental poisonings.

9-2. Given a list of statements and one of the following terms: poison and toxicology, select the definition of the given term.


9-4. From a group of statements, select the requirement(s) of the Poison Prevention Packaging Act of 1970.

9-5. Given a prescription and a list of types of prescription containers, select the type of container that should be used to contain the medication when it is dispensed to the patient.

9-6. Given a group of statements, select the statement(s) that best explain(s) the exceptions to the Poison Prevention Packaging Act of 1970.

9-8. Given a situation involving an accidental poisoning and a list of references, select the reference that would provide the information required by the description of the situation.

**SUGGESTION**

After completing the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 9
TOXICOLOGY AND POISON CONTROL

Section I. INTRODUCTION

9-1. GENERAL

It is estimated that accidental poisonings result in about 4,000 deaths per year, while suicides by chemical agents result in about 6,000 deaths per year in the United States. Each year there are some 500,000 children involved in accidental poisonings. Approximately 90 percent of these poisonings occur in children who are too young to attend school. You have probably read and heard about many cases of accidental poisonings. As a pharmacy technician you may be asked to provide information to professional personnel or to the public in an emergency situation. It is therefore imperative that you be familiar with some general treatment procedures and information sources pertinent to poisoning. Just as important, you can provide guidance which can help persons avoid the tragedy associated with an accidental poisoning.

9-2. DEFINITIONS

a. Poison. A poison is any substance which when ingested, inhaled, absorbed, applied, injected, or even manufactured by the organism itself may cause damage to the structure of that organism or destruction to the normal functioning of that organism.

b. Toxicology. Toxicology is the scientific study of poisons--their actions, detection, and the treatment of the conditions they produce.

9-3. CAUSES OF POISONING

a. Intentional. Individuals for a variety of reasons can intentionally ingest poisons. Some of these reasons are:

   (1) To commit suicide.

   (2) To gain personal attention.

   (3) To commit child abuse.

b. Accidental. Accidental poisonings usually affect children. In the years from 1972 through 1976, there were from one to two million cases of accidental poisoning per year in the United States. Since 1976, this number of accidental poisonings has dropped to approximately 500,000 cases per year. This decrease is attributed to the Poison Prevention Packaging Act and to poison prevention publicity. The most common sources of accidental poisoning were plants, various types of cleaners (soaps,
detergents, and cleaners), vitamins and minerals, and aspirin. It is interesting to note that aspirin is no longer the most common cause of accidental poisoning (this is probably due to child resistant packaging).

Section II. THE PHARMACY AND POISON PREVENTION

9-4. THE POISON PREVENTION PACKAGING ACT OF 1970

The purpose of the Poison Prevention Packaging Act of 1970 is to reduce poisonings among small children. The Act provides that certain household products (such as aspirin and certain other drugs, including oral prescription drugs; furniture polish; oil of wintergreen, antifreeze; some cleaners for drains and ovens; turpentine; and cigarette lighter fluid), which are found to be hazardous or potentially hazardous must be sold in safety packaging. This safety packaging must be designed so that most children under five years of age cannot open the packages.

9-5. THE REQUIREMENTS OF THE POISON PREVENTION PACKAGING ACT OF 1970

a. The Act requires the previously mentioned products to be packaged in containers which are sufficiently difficult to open in order to prevent 80 percent of children under five years of age from opening them. However, the containers must allow access to at least 90 percent of adults who will be able to open and properly close the packaging conveniently.

b. The Act requires that the prescription filled in the pharmacy--with the exceptions noted in paragraph 9-6 below--be dispensed in child-resistant containers. The requirements below are especially important:

   (1) Prescriptions which are not to be refilled. For a prescription that is not to be refilled, the medication must be dispensed in either a glass or a plastic container with a child-resistant top.

   (2) Prescriptions which are to be refilled. For a prescription that is to be refilled, the medication must be dispensed in either a glass or a plastic container which has a child-resistant top. If the medication is dispensed in a glass container, a new child-resistant top must be placed on the container whenever the prescription is refilled. If the medication is dispensed in a plastic container, upon refilling, the medication must be placed in a new plastic container with a new child-resistant top. That means that a new label must be prepared for the refill when the medication is placed in a plastic container.
9-6. EXCEPTIONS TO THE ACT

Some patients (that is, those who have arthritis) may find child-resistant packaging too difficult to open. Furthermore, some patients (for example: those with certain types of heart conditions) may wish to obtain their medications from the container in a short period of time when they need them. For these types of patients, alternatives to child--resistant packaging are available.

a. Nitroglycerin Must NOT be Dispensed in Child--Resistant Packaging. This drug is for patients who have certain types of heart conditions. These patients must be able to obtain their nitroglycerin quickly in the event they need it.

b. Alternative Packaging. The manufacturer can market one size of a product in conventional (not child-resistant) packaging--if the same product is also available in child-resistant packaging. However, the conventional packaging must have a label which clearly states:

This packaging for household without young children or if the package is small:

Package not child-resistant

c. Patient or Physician Request. The patient or prescribing physician may request that prescription medicines be put into ordinary packaging without safety features. Although some pharmacists may ask for a written statement from a patient before providing a conventional closure, this is not a requirement of the Federal law.

9-7. CONSIDERATIONS FOR THE OUTPATIENT PHARMACY

Child--resistant packaging has been in use for quite some time. It has, without a doubt, decreased the number of cases of accidental poisonings. If you have purchased items or received prescriptions packaged in child-resistant containers, you are aware of the advantages and disadvantages of this means of preventing accidental poisonings. In your position in the pharmacy, you may hear comments about the packaging. Some patients are quick to complain about the packaging. Here are some considerations about the act that are pertinent to you:

a. You should be very familiar with your pharmacy's policies regarding childresistant packaging. For example, if a patient requests conventional packaging for a prescription item, does your pharmacy require the patient to sign or initial the prescription or a special form? You should carefully read and study your local Standing Operating Procedures (SOP) to insure you do what is required.

b. Some patients may request conventional packaging. Suppose a retired individual asks you to package his prescription in a conventional container. Does this person have grandchildren who frequently come to the home? Remember, many
poisonings occur when a small child visits grandparents and goes through the medicine cabinet or grandmother’s purse.

c. Some pharmacies sponsor poison prevention campaigns. These campaigns focus on the basics of poison prevention. Frequently overlooked basics include keeping materials (cleaners, drugs, insecticides, and so forth) in their original containers and disposing of unused medications. Many persons repackage substances (like insecticides in soft drink bottles) only to tragically discover that a young child has ingested the poison thinking it was something else. Above all, these publicity campaigns seek to make people aware of dangerous practices which could result in tragedy.

Section III. THE TREATMENT OF POISONING

9-8. INTRODUCTION

Suppose a poisoning has occurred. What should be done to treat the patient? Because of your position in the pharmacy you probably will not be called upon to treat persons who are victims of intended or accidental poisoning. You should know the essentials of first aid and you should know to immediately take the victim to medical professionals who have been trained to treat poisoning victims. The information given below is not intended to serve as a strict procedure for the treatment of poisonings. Instead, it is intended to give general guidelines. Remember, the treatment given depends, to a great extent, on the poison ingested, absorbed, or inhaled.

9-9. TREATMENT GUIDELINES FOR POISONING VICTIMS

a. **Screen the Patient.** In the screening process it is important to identify the specific poison affecting the person and how the person was exposed to it. That is, if a child is suffering from poisoning from a particular insecticide (for example, malathion) was the insecticide swallowed or was it absorbed through the skin?

b. **Minimize Absorption.** There are two ways in which the amount of poison absorbed into the patient’s system may be decreased.

   (1) **Remove the poison.** The poison, if swallowed, can sometimes be removed by emesis (having the patient to vomit). Depending upon the type of poison ingested, the physician may or may not have the patient to vomit. Syrup of Ipecac and apomorphine are recognized as effective emetics. Emetic agents should not be administered to all patients. Specifically, emetic agents should not be administered to patients who are unconscious or convulsing, to persons who have ingested caustic or corrosive agents, or to patients who have ingested volatile petroleum products. One should not administer sodium bicarbonate (NaHCO₃) to a patient who has ingested a substance containing a corrosive agent such as hydrochloric acid (HCl), because the
two chemicals might react to form carbon dioxide gas ($\text{HCl} + \text{NaHCO}_3 \rightleftharpoons \text{NaCl} + \text{CO}_2(↑) + \text{H}_2\text{O}$) that could distend or even perforate the stomach.

(2) **Administer gastric lavage.**

(3) **Administer cathartics.**

c. **Retard Absorption.** There are two methods by which the absorption of toxins can be retarded.

(1) **Dilute the poison.** Water, milk, flour or cornstarch suspension can be used to dilute (lower the concentration of) the poison. When the concentration of the poison is lowered, the amount of poison absorbed in a given period of time is usually lower.

(2) **Administer activated charcoal.** The activated charcoal adsorbs the poison and thereby reduces the amount of the poison which is available for adsorption. It should be noted that if both syrups of ipecac and activated charcoal are to be used, the activated charcoal must not be given until after the ipecac-induced emesis has occurred since the charcoal will render the ipecac ineffective.

c. **Administer Systemic Antidotes (when possible).** As you know, antidotes are substances which counteract the effects of other substances. Unfortunately, not every substance which is a toxin has an antidote which will serve to render its effects harmless. When the physician sees the poisoning victim, he must know what the identity of the ingested poison is before he considers giving an antidote. Furthermore, even after the identity of the poison is known, there must be an antidote in existence for that particular poison. Some examples of antidotes are naloxone (Narcan®), for narcotic poisonings— atropine, for the treatment of certain insecticide poisonings—BAL in Oil, for arsenic, gold, and mercury poisoning—Edetate Calcium Disodium, for lead poisoning— and flumazenil (Romazicon®) for benzodiazepine overdose.

d. **Speed the Elimination of the Poison.** As you might expect the effects of a toxin can be reduced in many instances if that substance is quickly eliminated from the body. Methods such as forced diuresis, through the administration of hypertonic solutions and through adjustment of urine pH; peritoneal dialysis, and hemodialysis (hematodialysis) can be used to speed the elimination of certain poisons from the body.

e. **Support the Patient.** In all poisonings the patient must be supported. That is, the physician must carefully monitor the patient—through observation and by laboratory tests. When required, the physician may administer drugs for pain, replace fluids and electrolytes, regulate body temperature, maintain respiration, and maintain the nutrition of the patient.
9-10. INTRODUCTION

As with many types of emergencies, the poisoning emergency happens without notice. It is important that information sources pertaining to poisoning be maintained in the pharmacy and at certain other locations (that is, hospital emergency rooms and poison control centers). These sources of information must be up to date. Furthermore, the personnel who work in the area must be trained in the rapid use of these references.

9-11. POISON INFORMATION/CONTROL CENTERS

Poison control/information centers provide ready sources of information concerning poisons and chemical substances. These centers are usually staffed on a 24-hour basis. The Physicians' Desk Reference contains a section entitled “Directory of Poison Control Centers” which states the location and telephone number of poison control centers located in the United States. Regardless of the size of the medical treatment facility or the pharmacy, the number of the closest Poison Control Center should be posted on the wall or telephone where everyone can see the number.

9-12. SUGGESTED REFERENCES TO BE MAINTAINED IN THE PHARMACY IN RELATION TO POISONING INFORMATION

Lesson 1 of MD0804, Pharmacology I, discussed journals and texts pertinent to the practice of pharmacy. In addition to the references listed in that lesson, the pharmacy should maintain, at a minimum, the following references.

a. Physician’s Desk Reference. This reference contains product information (that is, the ingredients in a particular product). It is indexed so that the information can be found if the manufacturer, trade name, or chemical composition of the product is known. The Product Identification Section of the Physicians’ Desk Reference is very helpful in that if a tablet or capsule of the medication is on hand, this section can be used to rapidly identify it in most instances. Also helpful is the “Guide to Management of Drug Overdose” found on the back inside cover.

b. American Drug Index. In this text the trade and generic names of the medications are cross-indexed. No specific information on toxicity’s is included in this text.

c. Merck Index. In this text the trade and generic names of the products are cross--indexed. Foreign as well as American products are included in this text.
d. **Handbook of Poisoning.** This text is organized according to the type of setting in which poisoning might occur (that is, agricultural, industrial, household, plant, insect, and so forth.). The text also presents an excellent discussion of such pertinent topics as poison prevention, emergency treatment, and poisoning diagnosis.

e. **Handbook of Nonprescription Drugs.** This reference identifies the ingredients of over-the-counter products.

f. **Clinical Toxicology of Commercial Products.** This comprehensive text contains information on over 17,000 products and ingredients. It discusses the signs, symptoms, and treatment of various types of poisonings. One caution: It is rather a complex book to use. Therefore, you should acquaint yourself with this text before you have to use it in an emergency situation.

g. **Poisindex®.** Poisindex®, as part of the subscription to Micromedex is available as a quick, thorough reference. Most drug information centers and emergency departments will have Poisindex® set up as an icon on their desktop computers for quick reference.

9-13. **CONCLUDING COMMENTS**

The references just described contain essential information on topics related to poisoning. The quick use of these references to learn of poisoning signs, symptoms, and treatment have saved many a patient’s life. Just think, many accidental poisonings can be prevented. The best therapy is that of prevention. You are in a unique position to help the patient realize that they should safeguard their medications in order to prevent any type of accidental poisoning. It is much easier to prevent most poisonings than it is to treat those poisonings. Some pharmacies emphasize poisoning prevention through such programs as the collection of unused medication. You can have your own poisoning prevention program in your own home.

*Continue with Exercises*
EXERCISES, LESSON 9

REQUIREMENT. The following exercises are to be answered by marking the lettered response that best answers the question; or by completing the incomplete statement; or by writing the answer in the space provided at the end of the question.

After you have completed all the exercises, turn to “Solutions to Exercises,” at the end of the lesson, and check your answers with the solutions.

1. Select the number of deaths per year caused by accidental poisonings.
   a. 2,000.
   b. 4,000.
   c. 6,000.
   d. 500,000.

2. The term poison is best defined as _____________________.
   a. A chemical which will cause death if it is ingested.
   b. Any substance which will cause destruction of living cells.
   c. Any substance which when ingested, inhaled, absorbed, applied, injected, or even manufactured by the organism itself will cause damage to the organism or will interfere with its normal functioning.
   d. Any substance or chemical which when ingested, inhaled, or in any other way taken into the body, will cause death to the cells of the organism.

3. What is the purpose of the Poison Prevention Packaging Act of 1970?
   a. To reduce poisonings among small children.
   b. To reduce the number of intentional poisonings among children and adults.
   c. To reduce the number of accidental deaths caused by aspirin.
   d. To require packaging which could be opened only by children over the age of 13.
4. You are to fill the prescription below. Select the type of container which must be used to dispense the drug to the patient.

a. A glass container without a child-resistant top.
b. A plastic container without a child-resistant top.
c. A plastic or glass container without a child-resistant top.
d. A glass or plastic container with a child-resistant top.
5. Which of the following statements best explains an exception to the Poison Prevention Packaging Act of 1970?

a. Aspirin (ASA) must not be dispensed in child-resistant packaging for the convenience of those patients who have arthritis.

b. Nitroglycerin must not be dispensed in child-resistant packaging.

c. Federal law requires that patients who desire their medications be dispensed in conventional packaging must sign a disclaimer statement on the back of the prescription form.

d. Only persons who suffer from heart disease or arthritis may request their medications be dispensed in conventional packaging.

6. You suspect that your two-year-old child has just ingested some poisonous substance. Select the first thing you should do.

a. Make the child ingest some syrup of ipecac.

b. Identify the substance to which the child was exposed and how he was exposed to it.

c. Make the child drink a 5 percent solution of sodium bicarbonate (NaHCO3).

d. Administer a hypertonic solution intravenously to the child.

7. The Chief, Pharmacy Service, has asked you to prepare a brief report on poison prevention. Which of the following references would you use to prepare the report?

a. Handbook of Nonprescription Drugs.

b. Physicians’ Desk Reference.

c. Merck Index.

d. Handbook of Poisoning.
8. You are asked to find some information on an insecticide not used in the United States. Which of the references below would you use to locate some information on this product?

a. Clinical Toxicology of Commercial Products.

b. Handbook of Nonprescription Drugs.

c. Handbook of Poisoning.

d. Merck Index.

*Check Your Answers on Next Page*
SOLUTIONS TO EXERCISES, LESSON 9

1. b 4,000. (para 9-1)

2. c Any substance which when ingested, inhaled, absorbed, applied, injected, or even manufactured by the organism itself will cause damage to the organism or will interfere with its normal functioning. (para 9-2b)

3. a To reduce poisonings among small children. (para 9-4)

4. d A glass or plastic container with a child-resistant top. (para 9-5b(1))

5. b Nitroglycerin must not be dispensed in child-resistant packaging. (para 9-6a)

6. b Identify the substance to which the child was exposed and how he was exposed to it. (para 9-9a)

7. d Handbook of Poisoning. (para 9-12d)

8. d Merck Index. (para 9-12c)

End of Lesson 9
ANNEX

DRUG PRONUNCIATION GUIDE

This Drug Pronunciation Guide was developed to help you to learn how the trade and
generic names of commonly prescribed medications are frequently pronounced. Not all
the drugs in the guide are discussed in this subcourse. Remember, it is not enough to be
able to know the uses, indications, cautions and warnings, and contraindications for a
drug—you must also know how to pronounce that drug’s name.

<table>
<thead>
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<th>Trade Name</th>
<th>Generic Name</th>
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<tr>
<td>Actifed (Ak’-ti-fed)</td>
<td>Triprolidine (Tri-pro’-li-deen) and Pseudoephedrine (Soo-do-e-fed’-rin)</td>
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<td>Adapin (Ad’-a-pin)</td>
<td>Doxepin (Dok’-se-pin)</td>
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<td>Sinequan (Sin’a-kwan)</td>
<td>&quot;</td>
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<td>Afrin (Af’-rin)</td>
<td>Oxymetazoline (Ok-see-met-az’-o-leen)</td>
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<td>Aldactazide (Al-dak’-ta-zide)</td>
<td>Spironolactone (Spi-ro-no-lak’tone) and Hydrochlorothiazide (Hy-dro-klor-thi’a-zide)</td>
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<td>Piperazine (Pi-per’-ah-zeen)</td>
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<td>Sulfipyrazone (Sul-fin-pie’-ra-zone)</td>
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<td>Anusol (An’-u-sol)</td>
<td>Pramoxine (Pram-ok’-seen)</td>
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<td>Phenylbutazone (Fen-il-bute’-a-zone)</td>
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<td>Ergotamine (Er-got’-a-meen), Phenobarbital (Feen-o-bar’-bi-tal) and Belladonna (Bel-la-don’-na) Alkaloids</td>
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<td>Primaquine (Pri'-mah-kwin)</td>
<td>Same</td>
</tr>
<tr>
<td>Probanthine (Pro-ban'-theen)</td>
<td>Same</td>
</tr>
<tr>
<td>Pronestyl (Pro-nes'-til)</td>
<td>Same</td>
</tr>
<tr>
<td>Prophylthiouracil (Pro-pil-thi-o-u'-rah-sil)</td>
<td>Same</td>
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<tr>
<td>Prostaphlin (Pro-staff'-lin)</td>
<td>Oxacillin (Oks'-ah-sil-in)</td>
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<tr>
<td>Provera (Pro-ver'-ah)</td>
<td>Medroxyprogesterone (Med-rok-see-pro-jes'-ter-one)</td>
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<tr>
<td>Pyridium (Pie-rid'-ee-um)</td>
<td>Phenazopyridine (Fen-ahs-o-per'-i-deen)</td>
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<tr>
<td>Quinidine (Kwin'-i-deen)</td>
<td>Same</td>
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<tr>
<td>Quinine (Kwie'-nine)</td>
<td>Same</td>
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<tr>
<td>Reserpine (Ree-ser'-peen)</td>
<td>Same</td>
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<tr>
<td>Retin A (Reh'-tin A)</td>
<td>Tretinoin (Tret'-i-noin)</td>
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<tr>
<td>Rifadin (Rie-fad'-in)</td>
<td>Rifampin (Rie-fam'-pin)</td>
</tr>
<tr>
<td>Riopan (Rie'-o-pan)</td>
<td>Magaidrate (Mag'-al-drate)</td>
</tr>
<tr>
<td>Trade Name</td>
<td>Generic Name</td>
</tr>
<tr>
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<tr>
<td>Rimactane (Rim-act’-ane)</td>
<td>Rifampin (Rie-fam’-pin)</td>
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<tr>
<td>Ritalin (Rit’-a-lin)</td>
<td>Methylphenidate (Meth-il-fen’-i-date)</td>
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<td>Robaxin (Ro-bak’-sin)</td>
<td>Methocarbamol (Meth-o-ka-r’-ba-mol)</td>
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<td>Robitussin (Row-i-tus’-sin)</td>
<td>Guaiifenesin (Gwie-fen’-eh-sin)</td>
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<td>Robitussin DM</td>
<td>Guaiifenesin and Dextromethorphan               (Dek-tro-meh-or’-fan)</td>
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<td>Sansert (San’-sert)</td>
<td>Methysergide (Meth-ee-ser’-jide)</td>
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<tr>
<td>Seconal (Sek’-o-nal)</td>
<td>Secobarbital (Sek-o-bar’-bi-tal)</td>
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<td>Selsun (Sel’-sun)</td>
<td>Selenium (Se-lee’-nee-um)</td>
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<td>Septra (Sep’-tra)</td>
<td>Sulfaethoxazole</td>
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<tr>
<td>Serax (See’-raks)</td>
<td>Oxazepam (Oks-az’-eh-pam)</td>
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<td>Silvadene (Sil’-va-deen)</td>
<td>Silver Sulfadiazine (Sul-fa-die’-a-zeen)</td>
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<td>Sinemet (Si’-ne-met)</td>
<td>Levodopa (Le-vo-do’-pa)</td>
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<td>Sinequan (Sin’-a-kwan)</td>
<td>Doxepin (Dok’-seh-pin)</td>
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<td>Sorbitrate (Sor’-bi-trate)</td>
<td>Isosorbide (I-so-sor’-bide)</td>
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<td>Stelazine (Stel’-a-zeen)</td>
<td>Trifluoperazine (Tri-flo-o-per’-a-zeen)</td>
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<td>Sudafed (Soo’-da-fed)</td>
<td>Pseudophedrine (Soo-do-eh-feh’-drin)</td>
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<td>Sulamyd (Sul’-a-mid)</td>
<td>Sulfaetamide (Sul-fa-set’-a-mide)</td>
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<td>Sulfamylon (Sul-fa-mie’-lon)</td>
<td>Mafenide (Maf’-eh-nide)</td>
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<td>Sultrin (Sul’-trin)</td>
<td>Sulfathiazole (Sul-fa-thi’-ah-zeole)</td>
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<td>Surfak (Sur’-fak)</td>
<td>Dioctyl (Di-ok’-til) Calcium (Kal’-see-um)</td>
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<td>Synalar (Sine’-a-lar)</td>
<td>Sulfosuccinate (Sul-fos-suk’-si-nate)</td>
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<td>Synthroid (Sin’-throid)</td>
<td>Fluocinolone (Flo-o-sin’-o-lone)</td>
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<td>Tace (Tace)</td>
<td>Levothyroxine (Lee-vo-thi-rok’-sin)</td>
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<td>Tagamet (Tag’-a-met)</td>
<td>Chlorotrianisene (Klor-o-tri-an’-i-seen)</td>
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<td>Talwin (Tal’-win)</td>
<td>Cimetidine (Si-met’-i-deen)</td>
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<td>Tandearil (Tan’-da-ril)</td>
<td>Pentazocine (Pen-taz’-o-seen)</td>
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<td>Tegretol (Teg’-reh-tol)</td>
<td>Oxyphenbutazone (Ok-see-fen-bute’-a-zone)</td>
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<td>Tessalon (Tess’-a-lon)</td>
<td>Carbamazepine (Kar-ba-maz’-eh-pee)</td>
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<td>Tetracycline (Tet-ra-si’-kleen)</td>
<td>Benzonatate (Benz-on’-a-tate)</td>
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<td>Thorazine (Thor’-a-zeen)</td>
<td>Chlorpromazine (Klor-pro’-ma-zeen)</td>
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<td>Thyroid (Thy’-roid)</td>
<td>Same</td>
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<td>Tigan (Tie’-gan)</td>
<td>Trimethobenzamide (Tri-meth-o-benz’-a-mide)</td>
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<td>Timoptic (Tim-op’-tic)</td>
<td>Timilol (Tim’-o-lol)</td>
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<td>Trade Name</td>
<td>Generic Name</td>
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<td>Tinactin (Tin-act’-in)</td>
<td>Tolnaftate (Tol-naf’-tate)</td>
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<td>Titralac (Ti’-tra-lak)</td>
<td>Calcium (Kal-see-um) Carbonate (Kar’-bon-ate) and Glycine (Gly’-seen)</td>
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<td>Tofranil (Toe’-fra-nil)</td>
<td>Imipramine (I-mip’-rah-meen)</td>
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<td>Tolectin (Tow-lek’-tin)</td>
<td>Tolmetin (Tol-met’-in)</td>
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<td>Triavil (Tri’-a-vil)</td>
<td>Perphenazine (Per-fen’-a-zeen) and Amitriptyline (Am-i-trip’-ti-lean)</td>
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<td>Trilafon (Try’-la-fon)</td>
<td>Perphenazine (Per-fen-a-zeen)</td>
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<td>Tylenol (Tie’-leh-nol)</td>
<td>Acetaminophen (As-et-am’-ino-fen)</td>
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<td>Tylenol #3</td>
<td>Acetaminophen and Codeine (Ko’-deen)</td>
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<td>Unipen (U’-ni-pen)</td>
<td>Nafcillin (Naf-sil-lin)</td>
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<td>Urecholine (Ur-eh-ko’-leen)</td>
<td>Bethanecol (Beth-an’-eh-kol)</td>
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<td>Valisone (Val’-i-sone)</td>
<td>Betamethasone (Beh-tah-meth’-a-sone)</td>
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<td>Valium (Val’-ee-um)</td>
<td>Diazepam (Die-ze-eh-pam)</td>
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<td>Vermox (Ver’-moks)</td>
<td>Mebendazole (Meh-ben’-dah-zole)</td>
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<td>Vibramycin (Vie-bram’-y-sin)</td>
<td>Doxycycline (Doks-see-si’-kleen)</td>
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<td>Xylocaine (Zie’-low-kain)</td>
<td>Lidocaine (Lie-do-kain)</td>
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<td>Zarontin (Zar-on’-tin)</td>
<td>Ethosuximide (Eh-tho-suks’-a-mide)</td>
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<td>Zyloprim (Zie’-low-prim)</td>
<td>Allopurinol (Al-lo-pure’-in-ol)</td>
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