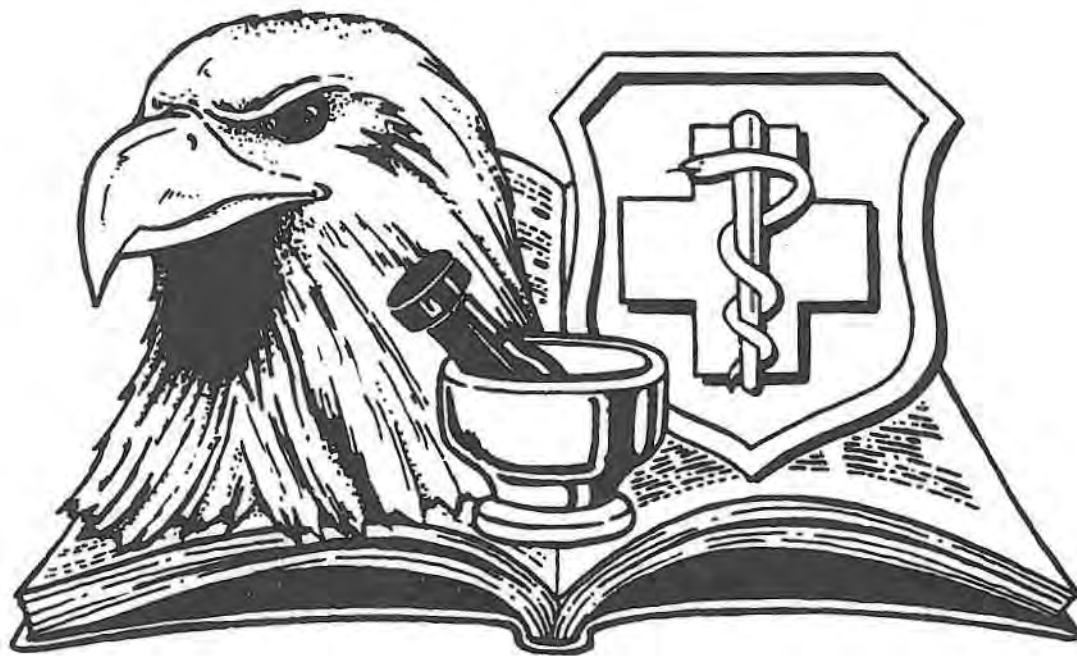


CDC 4P051B

Pharmacy Journeyman

Volume 4. Anatomy, Physiology, and Pharmacology Part 3



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This volume continues with the body systems. Unit 1 discusses the nervous system. The anatomy and physiology covered differentiates between the two major divisions—the nervous system, and the central and peripheral nervous systems. We then cover a number of disorders that you will be exposed to in your medical career and the medications used to treat those disorders.

Unit 2 covers the respiratory system. A detailed explanation of exactly how we breathe and transfer air from the atmosphere to our bloodstream is given. Respiratory disorders including asthma, COPD, and tuberculosis are covered. There are some common and interesting drugs in this section that you will be very familiar with in your daily duties.

Unit 3 touches on the sensory system—the eyes, ears, and other special organs of sense. Again, the disorders that affect these organs and the medications that are found in the DOD Core Formulary which are used to fight them are covered.

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This volume is valued at 15 hours and 5 points.

Acknowledgment

COVER artwork for this volume, "Air Force Pharmacy, A Proud Heritage," was originally designed by SrA Shirley Mack, 55th MDSS, Offutt AFB, Nebraska.

Intense editing by Major Thomas Bacon and Captain Rodney Jorstad, made sure that I covered everything that you need to know. Without the guidance of these two pharmacists my work would have been much harder.

NOTE:

In this volume, the subject matter is divided into self-contained units. A unit menu begins each unit, identifying the lesson headings and numbers. After reading the unit menu page and unit introduction, study the section, answer the self-test questions, and compare your answers with those given at the end of the unit. Then do the unit review exercises.

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NONE of our body's systems are capable of functioning on its own. They all are interdependent and work simultaneously as one unit so that normal conditions (homeostasis) within our bodies may prevail. The nervous system acts as the chief coordinating agency for our bodies. This unit discusses the anatomy and physiology of the nervous system, conditions associated with the nervous system, and the drugs used to treat those conditions.

1-1. Anatomy and Physiology of the Nervous System

Conditions within and outside our bodies are constantly changing. One purpose of the nervous system is to respond to these internal and external changes (stimuli). Consequently the nervous system will cause the body to adapt itself to new conditions. A person's internal harmony and balance between themselves and the environment are maintained by the instructions and directions sent to the various organs via the nervous system. You might compare the nervous system to a telephone switching center. Our nerve trunks act as cables for carrying messages to and from these centers.

600. Parts of the nervous system

The different parts of the nervous system may be grouped together according to their structure and function. Anatomically, the nervous system is divided into two main areas:

1. The *central nervous system*—includes the brain and spinal cord.
2. The *peripheral nervous system*—made up of *cranial* and *spinal* nerves.

The nerves that carry impulses to and from the brain are known as cranial nerves. Those that carry messages to and from the spinal cord are known as spinal nerves.

From a structural standpoint, the central and peripheral nervous systems combined contain most of the nerve tissue within our bodies. However, some peripheral nerves have a special function, and consequently those are grouped together under the label *autonomic nervous system*. This separation is because the autonomic nervous system, for the most part, has to do with activities that go on more or less automatically. The autonomic nervous system carries impulses from the central nervous system to the glands, the involuntary muscles located in the walls of tubes and hollow organs, and the heart.

Certain nerves that carry autonomic nervous system impulses are cranial and others are spinal. The autonomic nervous system is subdivided into two systems:

1. Sympathetic nervous system.
2. Parasympathetic nervous system.

We'll be discussing these two systems later in this lesson.

Nerves

Nerve cells are neurons. Each neuron is composed of a *cell body*, which contains the nucleus and *nerve fibers*, which are thread-like projections of the cytoplasm.

The white fibers (covered or myelinated fibers) are found in the white matter of the brain and spinal cord, along with the nerve trunks in all parts of the body. The fibers (and cell bodies) of the gray matter of the brain are not covered with myelin. Nerve fibers in the nerves of the peripheral nervous system are also covered with myelin. They are also covered by a thin, cellular sheath known as the *neurilemma*. The neurilemma assists in the repair of damaged nerve fibers.

There are two types of nerve fibers:

1. *Dendrites*—conduct impulses *to* the cell body.
2. *Axons*—conduct impulses *away from* the cell body.

The dendrites of sensory neurons differ greatly from those of other neurons. Dendrites of the sensory neurons are usually single. They may be very long (up to 3 foot in length) or they can be short. Either way, they *do not* have the treelike appearance so typical of other dendrites. Each sensory nerve fiber (dendrite) has a special structure known as the *receptor*, or *end organ*. This is where the stimulus is received and the sensory impulse begins.

There is no anatomical unity between neurons, and each neuron is a separate unit. Logically, we should be asking how is it possible for neurons to be in contact with one another? Or how the axon of one neuron can be in functional contact with the dendrite of another neuron? The answer is *synapse*, from the Greek word meaning "to clasp." Synapses, therefore, are the points of junction for transmission of nerve impulses. Specific chemicals, known as *neurotransmitters* or *transmitter substances*, are released from the nerve fiber endings; enabling the impulse to leap the synaptic junction. With assistance from chemical transmitters, impulses can be conducted between neurons and from a neuron or group of neurons to another type of cell. Similar to switches that open an electrical current to allow the passage of electricity, the synapses, with the assistance of the neurotransmitters, allow the conduction of nerve impulses.

A *nerve* is a bundle of nerve fibers, located *outside* the central nervous system, that directs impulses from one place to another. *Tracts* are bundles of nerve fibers *within* the central nervous system. They are located within the spinal cord and direct impulses to and from the brain. You can compare a nerve or tract with an electric cable made up of many wires. In nerves, the "wires" or nerve fibers, are bound together with connective tissue.

Afferent (sensory) nerves

Afferent nerves are nerve fibers that are connected with receptors, for receiving stimuli. They conduct impulses *to* the brain and spinal cord.

Efferent nerves

Efferent nerves are the nerve fibers that carry impulses *from* the centers out to the muscles and glands. The nerve fibers of motor neurons carrying impulses leading to the contraction of skeletal muscles, are classified as efferent neurons.

Mixed nerves

Some nerves contain a mixture of afferent and efferent nerve fibers and are often called mixed nerves.

601. Central nervous system

If you'll remember from an earlier lesson the central nervous system includes the brain and spinal cord. This lesson discusses the main parts of the brain, the structure of the cerebral hemisphere, the diencephalon (interbrain), the division and functions of the brainstem and cerebellum, ventricles of the brain, and brain studies. The spinal cord topics to be covered are the location, structure, and functions of the spinal cord, and the lumbar puncture. We'll also discuss the coverings of the brain and spinal cord, and cerebrospinal fluid. Sounds like a lot of information, doesn't it? Well, it is; so let's get started.

Main parts of the brain

The brain, occupying the cranial cavity, is covered by bony tissue called the *skull*. The *cerebrum*, the largest part of the brain, is divided into the right and left *cerebral hemispheres*. Another division of the brain is the *brainstem*, which connects the cerebrum with the spinal cord. The upper portion of the brainstem is known as the *midbrain*. The *pons* and *medulla oblongata* are located below the brainstem and are clearly visible from the underview of the brain. The pons connect the midbrain with the medulla, and the medulla connects the brain with the spinal cord through a large opening in the base of the skull. The third main part of the brain is the *cerebellum*. The word "cerebellum" means "little brain." The cerebellum is located immediately below the back part of the cerebral hemispheres. It is connected with the cerebrum, brainstem, and spinal cord by way of the pons.

Cerebral hemisphere's structure

The *cerebral cortex* is the outer nerve tissue of the cerebral hemispheres (gray matter). This gray cortex is arranged in folds that form elevated portions called *convolutions*. These convolutions are separated by depressions or grooves known as *fissures* or *sulci*. The internal portion of the cerebral hemispheres are made mostly of white matter and a few islands of gray matter. Two spaces, extending in a slightly irregular manner, lie inside the hemispheres. These are called the *lateral ventricles*. They are filled with a watery fluid, common to both the brain and spinal cord. This fluid is called *cerebrospinal fluid*. We'll be discussing this fluid later in this section.

There are many fissures, a few of which are especially important landmarks.

1. *Longitudinal fissure*—This fissure is a deep groove that separates the cerebral hemispheres from each other.
2. *Central fissure*—This fissure lies between the frontal and parietal lobes of each hemisphere, at a right angle to the longitudinal fissure.
3. *Lateral fissure*—This fissure curves slightly along the side of each hemisphere. It separates the temporal lobe from the frontal and parietal lobes.

Next, let's take a look at the cerebral cortex. The cerebral cortex is the layer of gray matter forming the surface of each cerebral hemisphere. Impulses are received and analyzed within the cerebral cortex. These impulses form the basis of knowledge—with the brain "storing" information, the majority of which may be recalled on demand, by way of the miracle we commonly call "memory." Within the cerebral cortex, the thought process (for example, association, judgment, and discrimination) takes place. Additionally, it is from the cerebral cortex that the orders originating from conscious thought originate. In other words, voluntary actions are directed here.

Division and functions of the cerebral cortex

The cerebral cortex of each hemisphere is divided into four *lobes*. These areas are named from their overlying cranial bones. Coordination among the numerous areas of the brain occurs to produce human behavior, and certain portions influence particular categories of function. Some of the characteristic of the four lobes, and their functions are listed here:

1. *Frontal lobe*. This lobe is larger in human beings than in any other organism. It lies in front of the central fissure. The frontal lobe contains the motor cortex, which directs action. The

left side of the brain governs the right side of the body and the right side of the brain governs the left side of the body. In addition, this lobe contains two areas that are important to speech.

2. *Parietal lobe.* This lobe occupies the upper part of each hemisphere and lies just behind the central fissure. The *sensory* area is in this lobe. This is where impulses from the skin, such as touch, pain, or temperature are interpreted. In addition, interpretations of the determination of distances, sizes, and shapes take place here.
3. *Temporal lobe.* This lobe is located below the lateral fissure. It folds under the hemisphere on each side. The *auditory area* for receiving and interpreting impulses from the ear is located here. The *olfactory area*, is also located in the temporal lobe. The olfactory area is concerned with the sense of smell and is located in the medial part of the temporal area. It is stimulated by impulses arising from receptors in the nose.
4. *Occipital lobe.* This lobe lies behind the parietal lobe. It extends over the cerebella. The *visual area* for interpreting impulses arising from the retina of the eye is located in this lobe.

Below the gray matter of the cerebral cortex lies the white matter. The white matter, consists of nerve fibers that connect the cortical areas with each other and also with other parts of the nervous system. The *corpus callosum*, a very important band of white matter, acts as a bridge between the right and left hemispheres. It allows impulses to cross from one side of the brain to the other. The *internal capsule* is another group of nerve fibers. The internal capsule is a crowded strip of white matter consisting of many fibers (forming tracts). There are masses of gray matter located deep within each cerebral hemisphere known as *basal ganglia*. These neuron groups aid in the regulation of body movement and facial expression communicated from the cerebral cortex. The neurons of the basal ganglia secrete a transmitter substance known as *dopamine*.

Areas of communication

An example of the way in which areas of the cerebral cortex interrelate is demonstrated by our ability to communicate by written and verbal means. The development and use of these areas are closely associated with the process of learning.

Auditory areas

These areas are found in the temporal lobe. In one of these areas *sound impulses*, from the environment, are detected. In the surrounding area, known as the *auditory speech center*, the sounds are interpreted and understood. The beginnings of language are learned by auditory means. Therefore, the auditory area for understanding sounds is very close to the auditory receiving area of the cortex. Oftentimes, babies seem to understand what is being said long before they do any talking themselves. Normally, it is several years before children learn to read or write words.

Motor areas

These areas are for communication (talking and writing) and are found in the front of the lowest part of the motor cortex of the frontal lobe. Because the lower part of the motor cortex controls the muscles of the head and neck, it is logical to think of the motor speech center as an extension forward in this area. Control of the muscles of speech (the tongue, soft palate, and larynx) is conducted here. Correspondingly, the written speech center is located in front of the cortical area, controlling the muscles of the arm and hand. Usually, the ability to write is one of the last phases in the development of learning words and their meaning.

Visual areas

The visual areas of the cortex are involved in communication through the receipt of visual impulses in the occipital lobe. The interpretation of these images into words takes place in the visual area lying in front of the receiving location. This area is where the ability to read and understand is developed. For example, you may *see* writing of another language, but this involves only the visual receiving area in the occipital lobe, unless you were able to *read* the words.

There is definitely a functional relationship among areas of the brain. In order for a person to receive, interpret, and respond to verbal and written messages, as well as to touch (tactile) and other sensory stimuli, numerous neurons must be working together.

Diencephalon

The interbrain, or diencephalon, may only be viewed by cutting into the central section of the brain. The diencephalon contains the *thalamus* and the *hypothalamus*. The majority of sensory impulses travel through the masses of gray matter forming the thalamus. The thalamus' action is to sort out the impulses and direct them to particular areas of the cerebral cortex. The hypothalamus, located in the midline area below the thalamus, contains cells that aid in controlling body temperature, water balance, sleep, appetite, and some emotions (e.g., fear and pleasure). Both the sympathetic and parasympathetic divisions of the autonomic nervous system are under the control of the hypothalamus. Therefore, it influences the heart beat, the contraction and relaxation of the walls of blood vessels, and other vital body functions.

The brainstem and cerebellum's divisions and functions

The midbrain, the pons, and the medulla oblongata are located in the brainstem and connect the cerebrum with the spinal cord.

Midbrain

The midbrain, located just below the center of the cerebrum, forms the forward part of the brainstem. The upper part of the midbrain is formed by four rounded masses of gray matter that are hidden by the cerebral hemispheres. These four masses act as relay centers for certain eye and ear reflexes. The white matter located at the front of the midbrain conducts impulses between the higher centers of the cerebrum and the lower centers of the pons, medulla, cerebellum, and spinal cord. Cranial nerves III and IV originate from the midbrain.

Pons

The pons is located between the midbrain and the medulla, in front of the cerebellum. The majority of the pons is made of myelinated nerve fibers that serve to connect the two halves of the cerebellum with the brainstem, and also with the cerebrum above and the spinal cord below. The pons is an important connecting link between the cerebellum and the rest of the nervous system. It also contains nerve fibers carrying impulses to and from the centers located above and below it. Some reflex (involuntary) actions are integrated in the pons—for example, some of those occurring in respiration. Cranial nerves V and VIII originated from the pons.

Medulla oblongata

The brain's medulla oblongata is located between the pons and the spinal cord. The medulla oblongata looks white externally because, like the pons, it contains many myelinated nerve fibers. Internally, it houses a collection of cell bodies (gray matter) called *centers* or *nuclei*. These vital centers are among those housed within the medulla oblongata:

- *Respiratory center*—controls the muscles of respiration in response to chemical and other stimuli.
- *Cardiac center*—helps to regulate the rate and force of the heart beat.
- *Vasomotor center*—regulates the contraction of smooth muscle in the blood vessel walls and therefore helps to determine blood pressure.

The last four pairs of cranial nerves are connected with the medulla. Also, the nerve fibers carrying messages through the spinal cord up to the brain continue through the medulla, as do similar descending or *motor fibers*. These groups of nerve fibers form tracts (bundles) and are grouped together according to function. The motor fiber from the motor cortex of the cerebral hemispheres extend down through the medulla, and the majority of them cross from one side to the other

(decussate) while going through this part of the brain. Within the medulla, shifting of nerve fibers occurs, causing the right cerebral hemisphere to control muscles in the left side of the body, and the upper portion of the cortex to control muscles in the lower portions of the person. The medulla is an important reflex center. Certain neurons end and impulses are relayed to other neurons here. Cranial nerves IX through XII arise from the medulla.

Cerebellum

There are three parts of the cerebellum: the middle portion and two lateral hemispheres. Similar to the cerebral hemispheres, the cerebellum has an outer area of gray matter, and an inner portion that is mostly white matter. The cerebellum's functions are to:

1. Aid in the *coordination of voluntary muscles* so that they'll function smoothly and in an orderly fashion. Disease of the cerebellum causes muscular jerkiness and tremors.
2. Help *maintain balance* in standing, walking, sitting, and during more strenuous activities. Messages from the internal ear and from the tendon and muscle sensory end organs assist the cerebellum.
3. Aid in *maintaining muscle tone* so that all muscle fibers are slightly tensed and ready to produce necessary changes in position as quickly as may be necessary.

The brain's ventricles

There are four fluid-filled spaces within the brain. They are called *ventricles*. The ventricles extend into various parts of the brain in a somewhat irregular manner. If you will recall, we've already discussed the largest ventricles, the lateral ventricles in the two cerebral hemispheres. The lateral ventricles' extensions into the lobes of the cerebrum are known as *horns*. These paired ventricles communicate with a midline space, the third ventricle, by way of openings called *foramina*. The third ventricle is bounded on each side by the two parts of the thalamus, while the floor is occupied by the hypothalamus. There is a small canal continuing down from the third ventricle, called the *cerebral aqueduct*. It extends through the midbrain into the fourth ventricle. The fourth ventricle is connected with the neural, or central, canal of the spinal cord. There are three openings in the roof of the fourth ventricle, allowing the escape of fluid to the area that surrounds the brain and spinal cord. This fluid is called *cerebrospinal fluid*.

Studies of the brain

Diagnostic tests are performed to examine the brain and its related structures. One such test involves the removal of some of the cerebrospinal fluid. Air and other substances may be injected, and radiologic (x-ray) films known as *encephalograms* or *ventriculograms* may be taken.

Another type of x-ray study is the computerized axial tomography (CAT or CT). This study provides multiple x-ray pictures taken from different angles simultaneously. The information is organized by means of a computer and displayed as a photograph of the bone, soft tissue, and cavities of the brain. Anatomic lesions (such as tumors or scar tissue accumulation) may be readily viewed.

Electric currents may be measured in the brain due to the many interactions of its billions of nerve cells. These currents are recorded by an instrument known as an *electroencephalograph*. The recorded tracings or brain waves produce an *electroencephalogram*, or *EEG*.

The spinal cord

In an embryo, the spinal cord takes up the entire spinal canal and extends down into the tail portion of the vertebral column. However, the column of one grows much faster than the nerve tissue of the cord, so that the end of the cord no longer reaches the lower portion of the spinal canal. This unevenness in growth increases so that in the adult, the cord ends in the region just below the area to which the last rib attaches (between the first and second lumbar vertebrae).

Spinal cord structure

Spinal cord examination reveals that it has a small, irregularly shaped internal section. This internal section consists of nerve cell bodies, and a larger area consisting of nerve fibers. A cross section of the spinal cord shows that the gray matter is arranged so that a column of cells extends up and down dorsally (one on each side). Another column is found in the ventral region, while a third, less conspicuous part is situated on each side. These three pairs of columns of nerves give the cross section an H-shaped appearance. There are thousands of nerve fibers in this section. These nerve fibers are arranged in three areas external to the nerve cell bodies on each side.

Spinal cord functions

Spinal cord functions may be divided into three aspects:

1. *Reflex activities*—involves the transfer and integration of messages that enter the spinal cord, so that a sensory (afferent) impulse entering the center will become a motor (efferent) message leaving the cord.
2. *Pathway for conducting sensory impulses*—from afferent nerves upward through ascending tracts to the brain.
3. *Pathway for conducting motor (efferent) impulses*—from the brain down through descending tracts to the nerves that supply muscles and glands.

Usually, the reflex pathway through the spinal cord involves three or more neurons:

1. *Sensory neuron*—has its beginning in a receptor and its nerve fiber in a nerve that leads to the spinal cord.
2. *Central neurons*—(one or more) are entirely within the spinal cord.
3. *Motor neuron*—receives the impulse from a central neuron and then carries it by way of its long axon through a nerve to a muscle or a gland.

An example of a spinal reflex would be a knee jerk. The impulse pathway that makes this reflex possible includes a sensory neuron that has its receptor in the tendon just below the knee. Its sensory nerve fiber is located in the nerves that extend to the spinal cord. Its central neurons are located inside the lower part of the spinal cord. Its motor neurons send processes through the nerves from the cord to the effectors in the quadriceps femoris (the thighs kicking muscle).

Lumbar puncture

The spinal cord is approximately 18 inches long and ends some distance above the level of the hip line. A *lumbar puncture* (spinal tap) is usually done between the third and fourth lumbar vertebrae, at about the level of the top of the hip bone. During a lumbar puncture, a small amount of cerebrospinal fluid may be removed from the space below the spinal cord. This fluid may then be studied in the laboratory for evidence of disease or injury.

Medications or anesthetics are, at times, injected into the space below the spinal cord. Anesthetic agents will temporarily block all sensation from the lower part of the body. This method of anesthesia administration has an advantage for certain procedures or surgeries. The patient is awake, but feels nothing in the lower body.

The *meninges* are three layers of connective tissue surrounding the brain and spinal cord, forming a complete enclosure. The *dura mater* is the outermost of these membranes and is the thickest and toughest of the meninges. Within the skull, the dura mater splits in certain places to provide venous channels for the blood coming from the brain tissue. The *arachnoid membrane* is the second layer around the brain and spinal cord. This membrane is loosely attached to the deepest of the meninges by a web-like fiber, allowing a space for the movement of cerebrospinal fluid between the arachnoid and the innermost membrane. The *pia mater* is the third layer around the brain. It is attached to the nerve tissue of the brain and spinal cord, and dips into all the depressions. The pia mater is made of a

delicate connective tissue in which there are many blood vessels. The blood supply to the brain is carried, to a large extent, by the pia mater.

Cerebrospinal fluid (CSF)

CSF is a clear liquid formed inside the ventricles of the brain, particularly by structures called the *choroid plexuses*. Some may be formed by filtration from the capillaries. The CSF's function is to cushion shocks that would otherwise injure the delicate structures of the CNS. CSF also carries nutrients to the cells and transports waste products from the cells. This fluid normally flows freely from ventricle to ventricle and finally out into the subarachnoid space surrounding the brain and spinal cord. The majority of CSF is returned to the blood in the venous sinuses through projections called the *arachnoid villi*.

602. Peripheral nervous system

The peripheral nervous system is all of the nervous system that is not the brain, or spinal cord. In other words, it is all of the nerves that branch off of the spinal cord. There are thirty-one pairs of nerves that branch off of the spinal cord. Each nerve then branches off into millions of nerves that affect a specific muscle, organ, or gland.

There are two kinds of movements that are caused by nerve impulses. There is a voluntary action and an involuntary action. A voluntary action is caused by one thinking about wanting to do something, and then doing it of his or her own free will. The thinking portion (frontal lobe) of the brain tells the signal to go through the nerves to the target organ.

Some voluntary actions include picking up a piece of steak, tying a shoe, or writing a paper. A person has to tell his or her body to do these things. The involuntary action is not caused by the frontal lobe. Instead, it is caused by the medulla. This time the signal is sent by the medulla, down through the nerves to the target organ.

There are two kinds of involuntary actions, constant actions, such as the heart beat or digestion, and a reflex. Someone would not tell his or her body to beat its heart or to digest food. Neither does the person tell his or her hand to go away from a hot pot after he touches it. Instead, a reflex occurs and he automatically withdraws his hand without thinking about it.

In addition to the nerves that go to target organs in the body, the nerves in the brain called the cranial nerves, are part of the peripheral nervous system. There are twelve nerves in all and they all have different functions.

1. Olfactory: smell—sends sensory information from smell to the brain.
2. Optic: vision—sends sensory information from the eyes to the brain.
3. Oculomotor: movement—causes eye muscles to contract and relax.
4. Trochlear: movement—controls the muscles in the upper, inner part of the eye.
5. Trigeminal: both sensory and movement—controls chewing and feelings in face.
6. Abducens: movement—moves eye laterally.
7. Facial: movement—facial expressions and facial movements.
8. Vestibulocochlear: movement—balance and hearing.
9. Glossopharyngeal: both sensory and movement—taste, tastebuds, swallowing.
10. Vagus: both sensory and movement—internal organs.
11. Accessory: movement—swallowing, speaking
12. Hypoglossal Nerves: movement—tongue movement

The peripheral nervous system is divided into two nervous systems. The first division of the peripheral system is the somatic nervous system. The somatic system is in charge of voluntary

actions, or the actions that you consciously control, such as the movement of the arm, leg, or other external and internal parts of the body.

The autonomic nervous system is the second division. It coordinates the involuntary movements of the body. Involuntary movements are the movements that you consciously have no control over, such as breathing, the beating of the heart, the circulation of blood, the digestion of food, the urinary system, the reproductive system, and it plays a key role in the body's stress reaction.

We'll take a quick look at each of these division of the peripheral nervous system.

Somatic nervous system

The twelve pairs of cranial nerves and the 31 pairs of spinal nerves which were mentioned earlier make up the somatic nervous system. All of the spinal nerves and most of the cranial nerves are mixed, that is, they contain both sensory and motor neurons. All of our conscious awareness of the external environment and all of our motor activity to deal with that environment operate through the somatic division of the peripheral nervous system.

Autonomic nervous system

Our internal organs, such as the heart, lungs, and stomach, contain nerve endings and nerve fibers for conducting sensory messages to the brain and spinal cord. But most of these impulses do not reach the conscious level. These *afferent* impulses from the viscera are translated into reflex responses without ever reaching the higher centers of the brain. The organ's sensory neurons are grouped with those that come from the skin and voluntary muscles. Conversely, the *efferent* neurons supplying the glands and the involuntary muscles are arranged very differently from those supplying the voluntary muscles. This variation in their location and arrangement of *visceral efferent* neurons has led to their classification as part of a separate division called the autonomic nervous system.

Parts of the autonomic nervous system

There are many ganglia found in the autonomic nervous system. They serve as "relay stations." Within these ganglia, each message is transferred at a synapse from the first neuron to a second one, which in-turn carries the impulse to the muscle or gland cell. In voluntary muscles, each nerve fiber extends all the way from the spinal cord to the muscle with no intervening relay station. Let's take a look (roughly) at the location of the parts of the autonomic nervous system.

Sympathetic pathway

The sympathetic pathway starts in the spinal cord with the cell bodies of the *thoracolumbar* area. This area serves various organs located in the head region through those in the lower extremities.

The sympathetic nerve fibers arise from the spinal cord level of the first thoracic nerve down to the level of the second lumbar spinal nerve. From this part of the spinal cord, nerve fibers extend to the ganglia of one of the sympathetic trunks. These trunks are like two cordlike strands extending up and down on either side of the spinal column from the lower neck to the upper abdominal region. There are bead-like enlargements on this trunk known as *lateral ganglia*. The lateral ganglia contain the cell bodies of the second set of neurons whose fibers extend to the glands and involuntary muscle tissues.

Parasympathetic pathway

The parasympathetic pathway originates in the *craniosacral* areas. Fibers arise from cell bodies of the midbrain, medulla, and lower (sacral) portion of the spinal cord. From these centers, the first set of fibers extends to autonomic ganglia, which are normally located near or within the walls of the organs. The pathway then goes on along a second set of neurons, stimulating the visceral tissues.

Autonomic system functions

The autonomic nervous system regulates the action of glands, smooth muscles of hollow organs, and the heart. All these actions are carried on automatically, and whenever changes occur that call for regulatory adjustment, it is done without our being conscious of it. The sympathetic portion of the

autonomic nervous system tends to act mostly as an accelerator, especially under conditions of stress. Take a moment and think of what happens to a person who is frightened or angry. You can easily remember the effects of impulses from the sympathetic nervous system. They are as follows:

- Adrenal gland stimulation produces hormones, to include *epinephrine*, preparing the body to meet emergency situations in many ways. The sympathetic nerves and hormones from the adrenal gland reinforce one another. We'll study these hormones in a different volume.
- Dilation of the pupil and decreased focusing ability (for near objects).
- Increase in the rate and forcefulness of heart contractions.
- Increase in blood pressure, this partly due to the more effective heartbeat and partly to constriction of small arteries in the skin and internal organs.
- Bronchial tube dilation, in order to allow for more oxygen to enter.
- Peristalsis and secretory activity inhibition, so that digestion is slowed.

Have you ever tried to eat while you are angry? You may have noticed that your saliva was thicker, and so small in amount that it was hard to swallow your food. Then when you finally do swallow the food, it seems to remain there longer than usual.

Once the crisis has passed, the parasympathetic portion of the autonomic nervous system will normally act as a balance for the sympathetic system. The parasympathetic system causes:

- Constriction of the pupil.
- Slowing of the heart rate.
- Constriction of the bronchial tubes.
- Stimulation of peristolic and secretory activities.

Autonomic nervous system disorders

Injury caused by wounds from penetrating objects, tumors, hemorrhage, or spinal column dislocation or fracture, may cause damage to the sympathetic trunk. Additionally, there are a number of conditions where symptoms such as heart palpitations, increased blood pressure, and stomach aches indicate autonomic malfunction. But, the method of operation is not quite so well understood. These disorders are related to the part that psychologically play in the function of the viscera. This is owed to the close interrelationship between the brain, brain stem, and spinal cord, and the autonomic nervous system.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

600. Parts of the nervous system

1. What are the two anatomical divisions of the nervous system?
2. What are cranial nerves?
3. What are spinal nerves?

4. Where does the autonomic nervous system carry impulses to and from?
5. What are the two subdivisions of the autonomic nervous system?
6. What are neurons composed of?
7. What are the two types of nerve fibers and what do they do?
8. Define nerve.
9. What are afferent nerves?
10. What are efferent nerves?

601. Central nervous system

1. What is the largest part of the brain?
2. What division of the brain connects the cerebrum with the spinal cord?
3. What is the cerebral cortex?
4. List the four lobes of the cerebral cortex of each hemisphere of the brain.
5. Where are the auditory areas of the brain located?
6. Where are the motor areas of the brain located?
7. Where are the midbrain, pons, and medulla oblongata located?

8. What is the function of the respiratory center of the medulla oblongata?
9. What are the three parts of the cerebellum?
10. How many fluid-filled spaces are there within the brain, and what are they called?
11. Describe Computerized Axial Tomography (CAT)?
12. Describe reflex activities of the spinal cord.
13. What is the meninges?
14. What is the function of cerebrospinal fluid (CSF)?

602. Peripheral nervous system

1. What is the function of the olfactory nerve?
2. Where does the sympathetic pathway of the autonomic nervous system begin?
3. Where does the parasympathetic pathway begin?
4. What actions does the autonomic nervous system regulate?

1-2. Conditions Associated with the Nervous System

There are a multitude of conditions associated with the nervous system. For simplicity sake, this unit breaks these conditions down into four separate categories: brain disorders; spinal cord disorders; disorders of the coverings of the brain, spinal cord, and cerebrospinal fluid; and disorders of the cranial and spinal nerves.

603. Brain and spinal cord disorders

Due to the lack of space, we will not be discussing all the disorders of the brain and spinal cord. The following brain disorders have been chosen for discussion: encephalitis, stroke, cerebral palsy, epilepsy, tumors, and aphasia. The following spinal cord disorders have been chosen for discussion: poliomyelitis, paraplegia, tumors, multiple sclerosis, and amyotrophic lateral sclerosis.

Now let's look at the following brain disorders:

Encephalitis

The scientific name for the brain is *encephalon*. Therefore, inflammation of the brain is known as *encephalitis*. There are various causes of encephalitis, but the two main pathogens are:

1. *Viruses*. Viruses cause some of the epidemic types of sleeping sickness sometimes found in the United States and in other parts of the world.
2. *Protozoa*. A certain protozoa known as *trypanosoma* causes the commonly called African sleeping sickness. A type of fly known as the *tsetse* carries this protozoa which is capable of invading the cerebrospinal fluid, infecting the surrounding tissue.

Stroke (cerebrovascular accident, CVA)

By far, the most common brain disorder is the stroke. Blood vessels rupturing (with a consequent *cerebral hemorrhage*), thrombosis, or embolism may cause destruction of brain tissue. These disorders are more frequent in the presence of artery wall disease, and therefore are more common after the age of 40. A stroke's effect depends on the location of the artery and the extent of the involvement. Hemorrhage into the white matter of the internal capsule in the lower part of the cerebrum may cause extensive paralysis to the opposite side of the affected area. This type of paralysis is known as *hemiplegia*, and the paralyzed person is known as a *hemiplegic*.

Cerebral palsy

This disorder is caused by brain damage occurring before or during the birth process. Cerebral palsy is characterized by an assorted number of disorders of the muscles. These disorders vary in degree of disturbance from weakness to complete paralysis, and in extent from a slight disorder of the lower extremity muscles to paralysis of all four extremities and the speech muscles. Children affected with the disorder may be helped by muscle and speech training, and other therapeutic approaches.

Epilepsy

This is a chronic disorder where there is an abnormality of the electrical activity of the brain. This may be with or without apparent changes in the nerve tissues. Seizure activity is one manifestation of epilepsy, this may be so mild as to be hardly noticeable, or so severe as to result in a loss of consciousness. The cause in most cases remains unknown. EEGs usually show some type of abnormality and is a very helpful tool in both the diagnosis and treatment of epilepsy. Many persons with epilepsy lead normal active lives if they use appropriate medication(s) as prescribed by their healthcare provider. Modern techniques with laser surgery may prove beneficial in controlling seizure activity.

Tumors

Brain tumors may develop at any age, but are slightly more common in young and middle-aged adults. A large number of brain tumors originate from the neuroglia and are called *gliomas*. The symptoms produced by a brain tumor depend largely on the location of the growth, its destructiveness, and the degree to which it compresses the brain tissue. In cases where the frontal portion of the cerebrum is involved, patients often experience mental symptoms (such as changes in personality and in levels of consciousness). Early surgery, chemotherapy, and radiation therapy offer a hope of cure in some cases.

Aphasia

This term refers to the loss of the ability to speak or write, or the loss of the understanding of written or spoken language. There are different types of aphasia, depending on what portion of the brain is affected. These lesions causing aphasia are most likely to be found in the left cerebral hemisphere, in right handed persons. A lot may be done for these patients through the use of patient retraining and much understanding. The brain's resources are tremendous, and it is an organ that has a remarkable capacity for adapting itself to different conditions. In some instances, even though speech areas of the brain are damaged, some means of communication may be possible.

Now let's look at the following spinal cord disorders:

Poliomyelitis

Poliomyelitis (polio) is an acute viral disease affecting both the spinal cord and brain, and occurring mostly in children. The virus enters the body through the nose and the throat. It multiplies in the GI tract and then travels to the CNS, possibly by way of the blood. Motor nerve cells in the spinal cord may be destroyed, in which case paralysis of one or more limbs is the result. The virus may also attack some of the cells of the brain and cause death. The oral polio vaccine is a means of prevention of poliomyelitis and is one of many significant advances in preventive medicine.

Paraplegia

Spinal cord injuries occur in instances in which the bones of the spinal column are broken or dislocated. For example, in swimming or diving accidents. The spinal cord may be damaged to varying degrees by gunshot or shrapnel wounds. Because the nerve tissue of the brain and spinal cord cannot repair itself, severing the cord causes paralysis of the muscles supplied by nerves, below the level of the injury. Loss of sensation and motion in the lower portion of the body is known as *paraplegia*.

Tumors

Other disorders of the spinal cord include tumors that grow from within the cord or that compress the cord from the outside.

Multiple sclerosis

The term "sclerosis" means hardening. Multiple sclerosis involves the entire spinal cord, in addition to the brain. In this disease, the myelin (fat-like substance that forms a sheath around certain nerve fibers) disappears and the nerve axons themselves degenerate. Multiple sclerosis is an extremely disabling disease. However, it usually progresses slowly, so the patient may have many years of relatively comfortable life remaining.

Amyotrophic lateral sclerosis

This is a disorder of the nervous system in which motor neurons are destroyed. Muscle atrophy and loss of motor control are the result of the progressive destruction of this disorder. This destruction continues until finally the person is unable to swallow or talk.

604. Miscellaneous nervous system disorders.

There are other nervous system disorders that we should know about, but don't fit into the above category and are not large enough to be a category of their own. In this section, we'll look at disorders involving the covering of the brain and spinal cord and cerebrospinal fluid as well as the nerves themselves.

Inflammation of the meninges

An inflammation of the brain and spinal cord coverings caused by pathogenic bacteria, notably a diplococcus called the *meningococcus*, is called *meningitis*. In cases where this organism only attacks the membranes around the spinal cord, the condition is called *spinal meningitis*. If it attacks the entire

membranous enclosure, it is known as *cerebrospinal meningitis*. In some cases, other bacteria or viruses cause inflammation of the meninges. At times, the inflammatory processes may be so severe as to cause permanent brain damage or even death. Squeezing a pimple or a boil in the area of the nose or forehead may result in the spread of staphylococci or streptococci through associated veins to the meninges, causing a serious meningitis.

Trauma to the meninges

Bleeding between the skull and brain may be caused by trauma to the head. Arterial bleeding outside the dura mater causes *epidural hematomas* with rapidly progressing symptoms (such as coma and dilated pupils). *Subdural hematomas* are caused by tears in the dural walls of the venous sinuses. This type of hematoma is a slow leak and has less dramatic symptoms. Frequent observations of a patient's consciousness level, pupil response, and extremity reflexes are very important procedures for patients with head injuries.

Hydrocephalus

Hydrocephalus may be caused by any obstruction to the flow of cerebrospinal fluid (CSF)—for example, an injury to the membranes around the three exit openings. As CSF accumulates, the mounting pressure can squeeze the brain against the skull and destroy brain tissue.

This condition is more common in infants than in adults. In addition, if the fontanels of the infant's skull have not closed, the cranium itself can become greatly enlarged. Because cranial enlargement cannot occur in the adult, a slight increase in CSF results in symptoms of increased pressure within the skull as brain tissue is damaged. To treat hydrocephalus, a shunt is created to drain excess CSF from the brain.

Cranial nerve disorders

Destruction of optic nerve (II) fibers may be caused by increased pressure of the eye fluid on the nerves, as occurs in glaucoma, the influence of poisons, and certain infections. Certain medications when used in high doses for a long period of time, can damage the branch of the vestibulocochlear nerve responsible for hearing. Injury to a nerve containing motor fibers causes paralysis of the muscles supplied by these fibers.

The oculomotor nerve (III) may be damaged by certain infections or various poisonous substances. Because this nerve supplies so many muscles connected with the eye, including the levator, which raises the eyelid, injury to this nerve causes a paralysis that usually interferes with eye function.

Bell's palsy is a facial paralysis due to damage to the facial (VII) nerve usually on one side of the face. This injury results in distortion of the face because of one-sided paralysis of the muscles of facial expression.

Neuralgia means "nerve pain." Particularly, it refers to a severe spasmodic pain affecting the fifth cranial nerve. It goes by several names, to include the following:

- Trigeminal neuralgia
- Trifacial neuralgia
- Tic douloureux

Initially, the pain comes in relatively long intervals, but as time goes by, it is likely to appear at shorter intervals with the attacks of pain becoming longer in duration. New treatments include microsurgery and high frequency current.

Spinal nerve disorders

We discuss three disorders in this area: neuritis, sciatica, and herpes zoster.

Neuritis

Inflammation of a nerve is called *neuritis*, this term is also used to describe degenerative and other disorders involving the nerves. Neuritis may affect a single nerve, or many nerves throughout the body. It may be the result of blows, bone fractures, or other mechanical injuries. Additional causative agents include: nutritional deficiency; various poisons such as alcohol; carbon monoxide; and barbitals.

This is a common disorder in chronic alcoholic persons. Its frequency in alcoholics is thought to be the result of the severe malnourished state these people display. Vitamin B deficiencies, especially thiamine, are related to both malnourishment and alcoholism. Actually, neuritis is a symptom—not a disease. Therefore, thorough physical and laboratory studies are usually necessary to discover the cause.

Sciatica

This is a type of neuritis, usually characterized by severe pain along the sciatic nerve and its branches. There are a multitude of causes for this disorder. Probably, the most common being a ruptured disk(s) between the lower lumbar vertebrae and arthritis of the lower portion of the spinal cord.

Herpes zoster

Herpes zoster is commonly known as “shingles.” It is characterized by numerous blisters along the course of certain nerves. Most often the intercostal nerves are affected. These are branches of the thoracic spinal nerves in the waist area. Herpes zoster is caused by the chicken pox virus. It attacks the sensory cell bodies inside the spinal ganglia. Normally, recovery occurs within a few days, but the neuralgic pains may last for years, and be very distressing. There are times when this infection may involve the first branch of the fifth cranial nerve. In this case it would cause pain in the eyeball and surrounding tissues.

605. Psychosis and anxiety disorders

Psychosis is a term formerly applied to any mental disorder, but now is generally restricted to those disturbances of such magnitude that there is a personality disintegration and loss of contact with reality. The disturbances are without clear physical cause or structural change in the brain. Psychotic disorders affect the central nervous system and may be caused by an imbalance, overabundance or deficiency of the chemical neurotransmitters. This lesson focuses on bipolar disorder. After that is discussed, we'll look at anxiety.

Bipolar disorder

Bipolar disorder is also known as manic-depressive illness and the names are used interchangeably. This is a mental illness involving episodes of serious mania and depression. The person's mood usually swings from overly high and irritable to sad and hopeless and then back again, with periods of normal mood in between. At least 2 million Americans suffer from bipolar disorder. It tends to run in families and is believed to be inherited in many cases. There have been vigorous research efforts, but a specific genetic defect associated with the disease has not yet been detected.

As stated above, bipolar disorder involves cycles of mania and depression. Signs and symptoms of the mania include:

- Extreme irritability and distractibility.
- Excessive high or euphoric feelings.
- Increased energy, activity, restlessness, racing thoughts, and rapid talking.
- Decreased need for sleep.
- Unrealistic belief in one's abilities and power.
- Uncharacteristically poor judgement.

- Obnoxious behavior.
- Denial that anything is wrong.

Signs and symptoms of the depression include:

- Persistent sad, anxious, or empty mood.
- Feelings of hopelessness or pessimism.
- Feelings of guilt, worthlessness, or helplessness.
- Loss of interest or pleasure in ordinary activities.
- Decreased energy, fatigue, being "slowed down."
- Sleep disturbances.
- Loss of appetite and weight, or weight gain.
- Thoughts of death or suicide, suicide attempts.

Almost all people with bipolar disorder, even the most severe forms, can obtain substantial stabilization of their mood swings. Treatment with medications including lithium, anti-convulsants, and anti-depressants can be helpful. Electroconvulsive therapy is often helpful in severe cases when the patient does not respond to medications. As an adjunct to medications, psychotherapy is often helpful in providing support, education, and guidance to the patient and his family.

Anxiety

We all get a little jittery when something important comes up. Maybe if it's your turn to do the in-service briefing and you have to stand up in front of your co-workers and brief them on your topic, your heartbeat feels heavy, you shake a little, and you can't stand still. Well, when that happens to someone without cause, they may be suffering from an anxiety disorder. Anxiety is different from psychotic disorders, but often the two occur together. A person who suffers from generalized anxiety tends to worry about big and little issues and feels uncomfortable physical symptoms throughout most of the day. The table below lists the possible physical symptoms during anxiety.

Body System	Symptom
Cardiovascular	Tachycardia, palpitations, headaches, cold fingers
Musculoskeletal	Muscles tense, involuntary trembling, aches and pains
Central nervous	Apprehensive, aroused, insomnia, fatigue, poor concentration
Genitourinary	Need for frequent urination
Gastrointestinal	Dry mouth, difficulty swallowing, "butterflies" in the stomach, gurgling sounds of gas in the intestines, colon spasms, diarrhea or constipation
Respiratory	Hyperventilation symptoms

It needs to be pointed out that a number of general medical conditions may cause anxiety symptoms, including endocrine conditions, cardiovascular conditions, respiratory conditions, metabolic conditions, and neurological conditions.

606. Parkinson's disease and attention deficit/hyperactivity disorder

We've added these two disorders to the previously covered ones because you'll see a good number of prescriptions for medications to treat them. These two disorders of the brain affect opposite ends of the spectrum. Parkinson's disease affects older people while attention deficit/hyperactivity disorder is found in children. We'll start off with Parkinson's disease.

Parkinson's disease

Parkinson's disease was first described in England in 1817 by James Parkinson. The disease affects approximately 2 out of 1,000 people, and most often develops after age 50. It affects both men and women and is one of the most common neurologic disorders of the elderly. The term "parkinsonism" refers to any condition that involves a combination of the types of changes in movement seen in Parkinson's disease, which happens to be the most common condition causing this group of symptoms. Parkinsonism may be caused by other disorders or by external factors (secondary parkinsonism).

Parkinson's disease is caused by progressive deterioration of the nerve cells of the part of the brain that controls muscle movement (the basal ganglia and the extrapyramidal area). Dopamine, which is one of the substances used by cells to transmit impulses (transmitters), is normally produced in this area. Deterioration of this area of the brain reduces the amount of dopamine available to the body. Insufficient dopamine disturbs the balance between dopamine and other transmitters, such as acetylcholine. Without dopamine, the nerve cells cannot properly transmit messages, and this results in the loss of muscle function. The exact reason that the cells of the brain deteriorate is unknown. The disorder may affect one or both sides of the body, with varying degrees of loss of function.

In addition to the loss of muscle control, some people with Parkinson's disease become severely depressed. Although early loss of mental capacities is uncommon, with severe Parkinson's the person may exhibit overall mental deterioration (including dementia, hallucinations, and so on). Dementia can also be a side effect of some of the medications used to treat the disorder.

Parkinson's disease is rare in children. When present, it appears to be due to decreased sensitivity of the nerves (post-synaptic) to dopamine rather than deterioration of the area of the brain that produces dopamine.

Symptoms of Parkinson's disease

There are many symptoms of Parkinson's disease mainly affecting the muscles, here is a list of some of the more prevalent symptoms:

Muscular symptoms			
Muscle rigidity	Stiffness	Difficulty bending arms or legs	Unstable, stooped, or slumped-over posture
Loss of balance	Gait (walking pattern) changes	Shuffling walk	Slow movements
Difficulty beginning to walk	Difficulty initiating any voluntary movement	Small steps followed by the need to run to maintain balance	Freezing of movement when the movement is stopped, inability to resume – movement
Muscle aches and pains (myalgia)	Shaking, (varying degrees, may not be present)	Tremors characteristically occur at rest, may occur at any time	May become severe enough to interfere with activities
May be worse when tired, excited, or stressed	Finger-thumb rubbing (pill-rolling tremor) may be present	Changes in facial expression	Reduced ability to show facial expressions
"Mask" appearance to face	Staring	May be unable to close mouth	Reduced rate of blinking
Voice/speech changes			
Slow speech	Low-volume voice	Monotone	Difficulty speaking

NOTE: Initial symptoms may be mild and nonspecific (mild tremor, slight feeling that one leg/foot is stiff and dragging, and so on).

Prevention

Selegiline, begun early in the disorder, can slow progression of the disease. There is evidence that "antioxidants" such as vitamin E and selenium may be of some benefit. Currently, research is being done on a test that may detect Parkinson's disease in its early stages, before it affects speech and movement.

Attention deficit hyperactivity disorder (ADHD)

The National Institute of Mental Health has recently agreed that attention-deficit hyperactivity disorder (ADHD) is indeed a legitimate psychologic condition but its definition has not been fully pinned down. ADHD is a syndrome generally characterized by inattention, distractibility, impulsivity, and hyperactivity. It is further categorized into three subtypes: behavior marked by hyperactivity and impulsivity but not inattentiveness; behavior that is marked by the reverse characteristics; and a mixed type. Some experts are concerned that these refinements may increase the diagnosis in children who may simply be aggressive. No laboratory or imaging tests have yet detected specific abnormalities that might make a diagnosis of ADHD clearer. In addition, although, according to the criteria, ADHD is not diagnosed in people whose symptoms appear after age seven, some studies show that the disorder, particularly the subtype marked by inattentiveness, can first show up in older children and adolescents. Defining ADHD is made more difficult because it is often accompanied by learning disabilities and other neurologic or emotional problems. It is likely that, eventually, the term attention deficit hyperactivity disorder will give way to subgroups of problems that include some of these general symptoms.

Advanced imaging techniques have detected differences in the brains of ADHD children compared to those of non-ADHD children. In some studies, brain scans reveal that the right side of the brain is smaller in ADHD children than in non-ADHD children (ordinarily they are the same size). The right side contains three important areas: the prefrontal cortex; the caudate nucleus; and globus pallidus. The prefrontal cortex, which is located in the front of the brain, is thought to be the brain's command center and regulates the ability to inhibit responses. The caudate nucleus and globus pallidus, located near the center of the brain, speed up or stop orders coming from the prefrontal cortex. Abnormalities in these areas may impair a person's ability to brake actions, resulting in the impulsivity typical of ADHD people. Also located here are important neurotransmitters—chemical messages in the brain—including norepinephrine, dopamine, and serotonin, which affect mental and emotional functioning. Dopamine is under particularly scrutiny. One recent study, for example, reported that adults with ADHD had abnormally low levels of DOPA decarboxylase, the enzyme that produces dopamine.

Both psychostimulant drugs and behavioral therapy are available and proving to be effective for treating many children with ADHD. At this time, there are five steps in the management of a child with ADHD:

1. Diagnosis.
2. Appropriate treatment.
3. Vigilant monitoring.
4. Communication between physicians, caretakers, and schools
5. An on-going exchange of information.

Behavioral techniques should usually be tried first before resorting to medications. If the symptoms are severe or do not respond, then medication is advisable. In general, a combination of drugs and behavioral methods are usually recommended. Family therapy may help ADHD children and their parents and siblings cope with the emotional conflicts that nearly always arise in the lifelong process of managing the condition. Separate psychological therapies for specific family members might be needed, particularly in light of the high incidence of psychiatric and other emotional problems in families with ADHD children.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

603. Brain and spinal cord disorders

1. What does the term encephalitis mean?
2. What are the two main pathogens that cause encephalitis?
3. What is the most common brain disorder?
4. What causes cerebral palsy?
5. Although brain tumors may develop at any age, when are they most common?
6. Define aphasia.
7. How does the poliomyelitis virus enter the body?
8. Define paraplegia.
9. Describe the disease "multiple sclerosis."
10. What is amyotrophic lateral sclerosis?

604. Miscellaneous nervous system disorders

1. Define meningitis.
2. What causes subdural hematomas?

3. How is hydrocephalus treated?
4. List the cause of optic nerve (II) fiber destruction.
5. What is the result of injury to a nerve fiber that contains motor fibers?
6. What is Bell's palsy?
7. Define neuralgia.
8. Define neuritis.
9. What is the most common cause of sciatica?
10. What is the common term for herpes zoster?

605. Psychosis and anxiety disorder

1. What is bipolar disorder?
2. List the signs and symptoms of depression in bipolar disorder.
3. Define anxiety.

606. Parkinson's disease and attention deficit/hyperactivity disorder

1. What causes Parkinson's disease?
2. List 4 symptoms of Parkinson's disease.

3. What symptoms generally characterize ADHD?
4. What neurotransmitter is under scrutiny in ADHD studies?
5. What are the five steps in managing a child with ADHD?

1-3. Drugs Used to Treat Conditions Associated with the Nervous System

There are a variety of drugs used to treat conditions associated with the nervous system. We'll discuss antianxiety agents, antidepressants, hypnotics, anticonvulsants, antipsychotics, antiemetics and antivertigo drugs, and drugs to treat ADD/ADHD. As you can see, we have a lot of material to cover, so let's get started.

607. Antianxiety agents

Antianxiety agents have now surpassed antibiotics in sales and are the most widely prescribed drugs in the United States. These drugs are pharmacologically sedative-hypnotic in type. Antianxiety agents have the ability to induce various levels of sedation. All antianxiety agents produce mild sedation in doses unlikely to adversely affect the clarity of consciousness and the quality of psychomotor performance. Furthermore, many of these drugs produce other pharmacological properties, such as hypnotic, muscle relaxant, and anticonvulsant actions. We'll be discussing several drugs in this category, which includes the benzodiazepines along with buspirone, and hydroxyzine.

Benzodiazepines

Benzodiazepines work in the brain. They focus on, or bind to, specific receptor sites associated with the neurotransmitter gamma-aminobutyrate (GABA). Benzodiazepines are involved in the treatment of many disorders: muscle relaxation, anti-convulsant, ataxia, as well as emotional behavior. Of course, we'll only talk about the drugs in this section that are used for their antianxiety properties. The antianxiety properties of benzodiazepines are separate from their effects of sedation and motor impairment. The three benzodiazepines that fall into our antianxiety area are lorazepam, alprazolam, and diazepam.

Indications and dosing

These benzodiazepines are indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. All these drugs are controlled substances in schedule IV.

Drug	Dose (oral)	Available oral dosage forms
Alprazolam	0.25 to 0.5 mg TID maximum 4 mg/day	0.25, 0.5, 1, and 2 mg tablets 0.5/5ml and 1 mg/ml solution
Diazepam	2 to 10 mg 2 – 4 times daily	2,5, and 10 mg tablets, 15 mg SR capsule, 5mg/5ml solution
Lorazepam	2 to 3 mg/day divided into 2 or 3 doses	0.5, 1, and 2 mg tablet, 2 mg/ml solution

Contraindications

Benzodiazepines are contraindicated in patients with hypersensitivity to benzodiazepines, psychosis, and acute narrow-angle glaucoma.

Warnings

The effectiveness and usefulness of these drugs has not been established in use longer than 4 months. There have been withdrawal symptoms noticed after as little as 4 to 6 weeks of treatment.

Pregnancy – Benzodiazepines freely cross the placenta and enter fetal circulation. This may cause congenital malformations, therefore, all of these drugs are in pregnancy category D.

Lactation – Benzodiazepines are excreted into breast milk. It is possible for toxic levels to build up in neonates. Benzodiazepines should not be given to nursing mothers.

Drug interactions

Benzodiazepines are metabolized in the liver. The following drugs inhibit hepatic metabolism so that the effects of benzodiazepines may be increased causing excessive sedation and impaired psychomotor function:

cimetidine	contraceptives, oral	disulfiram	fluoxetine	isoniazid
ketoconazole	propoxyphene	metoprolol	propranolol	valproic acid

Patient information

The following information should be given to patients taking benzodiazepines for anxiety:

1. May cause drowsiness; avoid driving or other tasks requiring alertness.
2. Avoid alcohol or other CNS depressants.
3. May be taken with food or water if stomach upset occurs.
4. Patients on long-term or high dosage therapy may experience withdrawal symptoms on abrupt cessation of therapy; do not discontinue therapy abruptly or change dosage except on advice of physician.

Buspirone

Buspirone is not pharmacologically or chemically related to benzodiazepines. It does not exert any anticonvulsant or muscle relaxant effects. It also lacks the sedative effects that are normally associated with antianxiety drugs. Buspirone appears to act as a dopamine agonist. It also increases norepinephrine metabolism.

Indications and dosage

Buspirone is indicated for the management of anxiety disorders or short-term relief of symptoms of anxiety. The normal dose for buspirone is 5 mg given three times daily. The dosage may go higher if needed, (20 – 30 mg) but 60 mg/day should not be exceeded. Buspirone is available in 5 and 10 mg tablets.

Contraindications

Any patient who shows a sensitivity to buspirone or is in need of antipsychotic therapy should not use buspirone.

Warnings

Even though buspirone is not a controlled substance nor forms dependence, it is difficult to predict how a CNS drug could be misused. Therefore, patients with a history of misuse or dependence should be watched closely.

Pregnancy – Buspirone is in pregnancy category B. No well controlled studies have been performed in pregnant women.

Lactation – In tests, buspirone has been excreted into breast milk. Avoid using buspirone in nursing women, if possible.

Drug interactions

Haloperidol and buspirone coadministration may result in increased haloperidol concentrations.

Patient information

5. Inform physician if any chronic abnormal movements occur (e.g., motor restlessness, involuntary repetitive movements of facial or neck muscles).
6. May cause drowsiness and dizziness. Use caution while driving or performing other tasks requiring alertness. Avoid alcohol and use other CNS depressants with caution.
7. Inform physician if you are pregnant, become pregnant or are planning to become pregnant while taking buspirone or if you are breast-feeding.
8. Optimum results are generally achieved after 3 to 4 weeks of treatment. Some improvement will be seen in 7 to 10 days.

Hydroxyzine

Hydroxyzine is an anti-histamine. Along with its anti-pruritic activity, hydroxyzine has some CNS depressant properties that are useful in the management of emotional disturbances which are manifested by anxiety, tension, agitation, apprehension, or confusion. Hydroxyzine is a true, rapid-acting ataraxic (calmative) that induces its calming effect without impairing mental alertness.

Indications and dosage

Hydroxyzine is indicated for the symptomatic relief of anxiety and tension associated with psychoneurosis and as an adjunct in disease states in which anxiety is manifest. Patients treated for severe anxiety are usually started on IM therapy and maintained with oral medication. The dosing for hydroxyzine in treating anxiety is 50 to 100 mg 4 times daily. Hydroxyzine is available in 10, 25, 50, and 100 mg tablets, 10 and 25 mg/5ml oral liquid, and 25 and 50 mg/ml injection. Hydroxyzine Pamoate is also available in 50 mg capsules.

Contraindications

Patients who are sensitive to hydroxyzine or ceterizine should not use hydroxyzine. Hydroxyzine should not be used in early pregnancy or lactation.

Warnings

Injectable hydroxyzine is for deep IM administration only. Tissue necrosis may occur if given subcutaneously or intra-arterial. Hemolysis (destruction of red blood cells) may occur if given intravenously.

Pregnancy – Hydroxyzine has induced fetal abnormalities in animals and should not be used during pregnancy.

Lactation – It isn't known if hydroxyzine is excreted into breast milk, however, ceterizine, a metabolite of hydroxyzine, has been detected. Hydroxyzine should not be given to nursing mothers.

Drug interactions

Hydroxyzine potentiates the actions of other CNS depressants. When hydroxyzine is given concomitantly with CNS depressants, reduce the CNS depressant dosage by 50 percent.

Patient information

Hydroxyzine may produce drowsiness; patients should observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity. Avoid alcoholic beverages and other CNS depressants; they may intensify this effect.

608. Antidepressants

Depression is a very complex disorder. It requires a large arsenal of drugs to help treat it. Most of the medications that we'll talk about deal with the chemical serotonin. It seems that the longer that the serotonin can hang around, the less depressed people feel. This lesson covers two classes, tricyclic antidepressants and selective serotonin reuptake inhibitors; and two individual drugs, lithium and trazodone. We'll start off our discussion with the tricyclic antidepressants.

Tricyclic antidepressants (TCAs)

Tricyclic antidepressants, as their name implies, work in three different ways. First, they block the amine pump. The amine hypothesis of depression proposes a relationship between depression and levels of CNS bioamines at the postsynaptic adrenergic receptors in the brain. TCAs are characterized by their ability to inhibit the reuptake of these chemicals. Secondly, TCAs cause sedation. Lastly, TCAs provide peripheral and central anticholinergic action. The TCAs that we'll be looking at are amitriptyline, doxepin, imipramine, and nortriptyline.

Indications and dosage

All of the TCAs are indicated for relief from the symptoms of depression. Some of the agents, with significant sedative action may also be useful in depression associated with anxiety and sleep disturbances. The dosages and dosage forms are listed below.

Drug	Dose	Dosage Form
Amitriptyline	75 mg/day in divide doses, may increase to 150 mg/day	10, 25, 50, 75, 100, and 150 mg tablets; 10 mg/ml injection
Doxepin	75 mg/day up to 150 mg/day at bedtime	10, 25, 50, 75, 100, and 150 mg capsules; 10 mg/ml oral sol
Imipramine	Starting at 75 mg/day, increased to 150 mg/day once daily at bedtime	10, 25, 50, mg tablets 25 mg/2ml injection
Nortriptyline	25 mg 3 – 4 times daily up to 150 mg/day	10, 25, 50, 75 mg capsules; 10 mg/5ml oral solution

Contraindications

Patients should not use TCAs if they have had any prior sensitivity to them. TCAs are not recommended for use during the acute recovery phase following myocardial infarction.

Doxepin exhibits a higher anticholinergic action than the other TCAs and therefore should not be used in patients suffering from urinary retention or glaucoma.

Warnings

TCAs lower a person's seizure threshold. They should be used cautiously in patients with a history of seizures. TCAs may also produce arrhythmias. They should be used with extreme caution in patients with cardiovascular disorders.

Safety for use during pregnancy has not been established. Use TCAs only when clearly needed and when the potential benefits outweigh the potential hazards to the fetus.

Lactation - These agents are excreted into breast milk in low concentrations (approximate milk: plasma ratio of 0.4 to 1.5). Exercise caution when using in a nursing woman.

Drug interactions

The following table lists drug interactions involving TCAs.

Drug	Interaction
Anticholinergics	Anticholinergic effects may be enhanced by the coadministration of TCAs
Levodopa	The absorption of levodopa may be delayed and it's bioavailability decreased by TCAs

Barbiturates	Barbiturates may lower levels of TCAs while the central and respiratory effects are additive
Cimetidine	Cimetidine has increased TCA concentrations. Extreme anticholinergic symptoms have occurred
Fluoxetine	Fluoxetine may increase the pharmacologic and toxic effects of TCAs.
Oral contraceptives	OCs inhibit the metabolism of TCAs and may increase plasma levels
Clonidine	Dangerous elevation in blood pressure and hypertensive crisis have occurred in patients receiving both TCAs and clonidine.

Patient information

Before using, tell your doctor and pharmacist (1) if you have other medical conditions; (2) what other medications you are currently taking; (3) if you have ever had an unusual or allergic reaction to any tricyclic antidepressant; (4) if you are pregnant or may become pregnant, and (5) if you are breast-feeding.

Discontinue this drug therapy and get emergency help if any of the following occur: Seizures; difficult or fast breathing; fever with increased sweating; high or low blood pressure; loss of bladder control; severe muscle stiffness; unusual tiredness or weakness.

Do not discontinue therapy or take other drugs without consent of physician. Abrupt discontinuation of therapy may cause nausea, headache and malaise.

These drugs may cause drowsiness, dizziness or blurred vision; use caution when driving or performing other tasks requiring alertness, coordination or dexterity. Avoid alcohol and other CNS depressant drugs.

Avoid prolonged exposure to sunlight or sunlamps; photosensitivity may occur.

Selective Serotonin Reuptake Inhibitors (SSRIs)

Selective serotonin reuptake inhibitors (SSRIs) are oral antidepressant agents chemically unrelated to the tricyclic or other available antidepressants. The antidepressant action of the SSRIs is presumed to be linked to their inhibition of CNS neuronal uptake of serotonin. Serotonin hangs around in the brain stem. Its presence has some control over behavior, aggression, and some physiological actions.

Serotonin is reabsorbed into the presynaptic cells. If the receptors in the brain stem are inefficient, the person may feel the symptoms of depression. The SSRIs stop the presynaptic cell from reabsorbing (reuptaking) the serotonin so it remains at the receptor longer to do its work. The SSRIs that we'll be discussing are fluoxetine, paroxetine, and sertraline. One of the major differentiators in this class is the amount of time that a patient must take the drug before feeling effects. This is also known as "steady state." There are pros and cons for each side of amount of time to steady state. If a drug has a longer time to steady state, therapeutic effects won't be felt for up to six weeks, but conversely, when the therapy is ceased there is no need to taper the drug because the blood levels slowly decrease. Now that all that has been said, let's dive into the SSRIs.

Indications and dosage

All of the SSRIs are indicated for the treatment of depression and obsessive-compulsive disorder. The next chart lists the dosing and other information on each drug.

Drug	Dose	Steady State	Dosage Forms
Fluoxetine	20 – 8- mg/day in the AM or divided into AM and noon	28 – 35 days	10 and 20 mg capsules, 20 mg/5ml oral solution
Paroxetine	Depression - 20 – 50 mg/day in the AM OCD – 40 – 60 mg/day	10 days	10, 20, 30, and 40 mg tablets
Sertraline	50 mg/day in the AM, may be increased as high as 200mg	7 days	25, 50, and 100 mg tablets and capsules

Contraindications

People who have shown any sensitivity to SSRIs should not take these drugs.

Warnings

The effectiveness of these drugs for long term use has not been established. Patients need to be monitored regularly to see if the medication is still useful.

Pregnancy – Fluoxetine in category B, paroxetine and sertraline are in C. In tests, 5.5 percent of women who took fluoxetine in the first trimester of pregnancy delivered babies with major structural anomalies. Fourteen percent of the babies were premature when mothers took fluoxetine in later pregnancy. There are no tests on paroxetine or sertraline.

Lactation – SSRIs are excreted into breast milk. However, no adverse effects were noted in nursing infants.

Drug interactions

The next two tables list the interactions associated with SSRIs. The first table lists drugs that affect the SSRIs while the second table lists drugs affected by SSRIs.

Drug affecting SSRI	Description
Cimetidine	Blood concentrations of SSRIs increased by 50 percent
Dextromethorphan	May cause hallucinations
Phenobarbital	Reduced SSRI levels by 25 percent
Phenytoin	Reduced SSRI levels by 50 percent

Drugs affected by SSRIs	Description
Tricyclic antidepressants	Plasma levels of TCAs may be increased
Benzodiazepines	Clearance of benzodiazepines is decreased
Beta blockers	Levels of Beta blockers increased, possible bradycardia and hypotension
Bupropion	Effects of bupropion are decreased
Carbamazepine	Carbamazepine levels increased, possible toxicity
Diltiazem	Bradycardia has occurred with concurrent use
Digoxin	Bioavailability of digoxin is decreased by 15%
Haloperidol	Haloperidol concentrations may be increased affecting memory
Lithium	Lithium levels may be increased to possible toxic levels
Sumatriptan	Coadministration may cause weakness and incoordination
Warfarin	Increased prothrombin times have occurred
Theophylline	Reduced theophylline clearance elevating levels

Patient information

Hazardous tasks: SSRIs may cause dizziness or drowsiness. Patients should observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity.

Concomitant medication: Patients should consult their physician or pharmacist before taking concomitant over the counter or prescription drugs. Avoid alcohol or other depressant medications.

Pregnancy or lactation: Notify your physician of pregnancy, of intent to become pregnant, or if breastfeeding.

Rash: Notify your physician if rash or hives develop.

Completing course of therapy: While patients may notice improvement in therapy in 1 to 4 weeks, advise patients to continue therapy as directed.

Photosensitivity: These medications may cause photosensitivity (sensitivity to sunlight). Avoid prolonged exposure to the sun and other ultraviolet light. Use sunscreens and wear protective clothing until tolerance is determined.

Lithium

Lithium is a monovalent cation which competes at cellular sites with other cations in the body. Cations are involved in the synthesis, storage, release and reuptake of neurotransmitters. The origin and development of mania appears to be affected by neurotransmitters such as dopamine and norepinephrine. Lithium alters sodium transport in nerve and muscle cells and may reduce concentrations of catecholamine neurotransmitters. However, the specific biochemical mechanism of lithium action in the control of mania is unknown. Unlike other antimanic agents, lithium does not possess general sedative properties. Lithium is available as lithium carbonate in several regular and extended release oral dosage forms and as lithium citrate in oral syrup form.

Indications and dosage

Lithium is indicated for the treatment of manic episodes of manic-depressive illness. Maintenance therapy prevents or diminishes the frequency and intensity of subsequent manic episodes in those manic-depressive patients with a history of mania. The following chart gives lithium dosing.

Acute mania	600 mg TID or 900 mg SR BID
Maintenance therapy	300 mg 3 – 4 times daily

Contraindications

Patients with significant renal or cardiovascular disease, severe debilitation or dehydration or sodium depletion, and patients receiving diuretics should not take lithium.

Warnings

Pregnancy – Lithium is category D. Lithium crosses the placenta and concentration is equal in the mother and the fetus. Lithium may cause fetal harm when given to a pregnant woman.

Lactation – Lithium is excreted into breast milk at about 50 percent concentration. Do not nurse during lithium therapy except in rare cases where the potential benefits to the mother outweigh the possible hazards to the infant.

Drug interactions

The next two tables describe drug interactions associated with lithium. The first table describes drugs that affect lithium and the second one has drugs that lithium affects.

Drugs affecting lithium	Interaction description
Carbamazepine	Neurotoxic effects of lithium are increased
Fluoxetine	Lithium levels are increased
Haloperidol	Neurotoxic effects of lithium are increased
Loop diuretics	Lithium levels are increased
NSAIDs	Decreased renal clearance of lithium (increased lithium levels)
Theophyllines	Increased renal clearance of lithium (decreased lithium levels)
Thiazide diuretics	Decreased renal clearance of lithium (increased lithium levels)
Verapamil	Reduction in lithium levels and toxicity

Drugs affected by lithium	Description
Sympathomimetics	Activity of the sympathomimetic may be decreased
Tricyclic antidepressants	Pharmacologic effects of TCAs may be increased

Patient information

Take lithium immediately after meals or with food or milk to avoid stomach upset.

Stop lithium therapy and contact your physician if signs of overdose or toxicity occur, such as diarrhea, vomiting, unsteady walking, tremor, drowsiness or muscle weakness.

Lithium may impair mental or physical abilities; use caution while driving or performing other tasks requiring alertness.

Drink 8 to 12 glasses of water or other liquid every day while on this drug. Prolonged exposure to the sun can lead to dehydration. Maintain a regular diet (including salt). Contact your physician if fever or diarrhea develops.

Prolonged exposure to the sun can lead to dehydration.

Trazodone

The mechanism of trazodone's antidepressant action in man is not fully understood. In animals, trazodone selectively inhibits serotonin uptake by brain synaptosomes and potentiates the behavioral changes induced by the serotonin precursor, 5-hydroxytryptophan.

Indications and dosage

Trazodone is indicated in the treatment of depression. Initiate trazodone dosing at a low level and increase gradually. The instance of drowsiness may require the administration of a major portion of the daily dose at bedtime or a reduced dosage. Trazodone should be taken shortly after a meal or light snack. Symptomatic relief may be seen during the first week, with optimal effects typically evident within 2 weeks. Approximately 25 percent of those who respond to trazodone therapy require 2 to 4 weeks of drug administration. An initial dose is 150 mg/day. This may be increased by 50 mg/day every 3 to 4 days. The maximum dose for outpatients usually should not exceed 400 mg/day in divided doses. Inpatients or more severely depressed subjects may be given up to, but not in excess of, 600 mg/day in divided doses. Trazodone is available in 50, 100, 150, and 300 mg tablets.

Contraindications

Patients who have demonstrated a sensitivity to trazodone should not use it.

Warnings

Depressed patients who are recovering from myocardial infarction should not use trazodone. Trazodone may cause arrhythmia in this type of patient.

Pregnancy – Trazodone is in pregnancy category C. Trazodone has caused fetal abnormalities. Use trazodone in pregnant women only if the potential benefit justifies the risk to the fetus.

Lactation – Trazodone is excreted into breast milk. Caution should be exercised when giving trazodone to a nursing mother,

Drug interactions

- Trazodone may enhance the CNS depressant effects of alcohol, barbiturates and other CNS depressants.
- Concurrent dosing of trazodone and digoxin showed increased levels of digoxin.
- Pheytin levels were increased in patients receiving trazodone.
- The effects of warfarin may be decreased when taking trazodone.

Patient information

- Take trazodone with food.
- Trazodone may produce drowsiness or dizziness; patients should observe caution while driving or performing other tasks requiring alertness, coordination or dexterity.

- Notify your physician of dizziness, lightheadedness, fainting or blood in urine.
- This medication may cause dry mouth, irregular heartbeat, shortness of breath, nausea and vomiting; notify your physician if these become pronounced.
- Avoid alcohol and other depressant drug while taking trazodone.

609. Hypnotics

The definition of hypnotic is any drug that causes insensitivity to pain by inhibition afferent impulses or by inhibiting the receiving of sensory impressions in the cortical centers of the brain, thus causing partial or complete unconsciousness. Hypnotics include sedatives, analgesics, anesthetics, and intoxicants. They are sometimes called somnifacients and soporifics when used to induce sleep. Luckily for you, we're only going to discuss two drugs that are used to induce sleep. This lesson covers Temazepam and Zolpidem. Since they are in two different classes, we'll have to cover them separately.

Temazepam

Temazepam is a benzodiazepine that is used strictly for sleep. The benzodiazepines effect three types of receptors in the brain, those for memory, sleep mechanisms, and sensory/cognitive functions. Temazepam binds to these sites, potentiating the inhibition of gamma aminobutyric acid (GABA). This action causes sleep.

Indications and dosage

Temazepam is indicated for insomnia characterized by difficulty falling asleep, frequent nocturnal awakenings, or early morning awakening. Since insomnia is normally transient and intermittent, Temazepam is not indicated for long term use. The normal dosage for temazepam is 15 – 30 mg before bedtime. Temazepam is available in 7.5, 15, and 30 mg capsules.

Contraindications

Patients who have showed any sensitivity to benzodiazepines or are pregnant should not use temazepam. Also, patients with established or suspected sleep apnea should not use temazepam.

Warnings

Pregnancy - Temazepam is in pregnancy category X. Benzodiazepines may cause fetal damage when given during pregnancy.

Lactation – The safety of temazepam has not been established. Temazepam is excreted into breast milk. The administration of temazepam to nursing mothers is not recommended.

Drug interactions

There aren't too many interactions that you need to know. The next table lists the three most notable ones.

Drug	Interaction
Theophylline	Theophylline antagonizes the effects of benzodiazepines
Digoxin	Benzodiazepines may increase blood levels and toxicity of digoxin.
Phenytoin	Benzodiazepines may increase blood levels and toxicity of phenytoin.

Patient information

Patients taking temazepam should avoid alcohol and other CNS depressants.

Do not discontinue temazepam abruptly after prolonged therapy.

Advise patients that they may experience disturbed nocturnal sleep for the first or second night after discontinuing temazepam.

Temazepam is meant to induce sleep, observe caution while driving or performing other tasks requiring alertness.

Inform your physician if you are planning to become pregnant, if you are pregnant, or if you become pregnant while taking this medicine.

Zolpidem

Zolpidem is a non-benzodiazepine hypnotic. It modulates the GABA receptors at only the sleep site. This action allows for deeper sleep than can be obtained from benzodiazepines.

Indications and dosage

Zolpidem is indicated in the short-term treatment of insomnia. Normally 7–10 days is sufficient therapy. The normal dose for zolpidem is 10 mg immediately before bedtime. Zolpidem is available in 5 and 10 mg tablets. There are no contraindications for zolpidem.

Warnings

Following the rapid dose decrease or abrupt discontinuation of zolpidem, signs and symptoms similar to those associated with withdrawal from other CNS-depressant drugs have occurred.

Pregnancy – Zolpidem is in pregnancy category B. There are no adequate and well controlled studies in pregnant women. Use zolpidem during pregnancy only if clearly needed. Children born of mothers taking sedative/hypnotic drugs may be at some risk for withdrawal symptoms from the drug during the postnatal period.

Lactation – Zolpidem is excreted into breast milk. The effects of zolpidem on nursing infants are unknown. The use of zolpidem in nursing mothers is not recommended.

Drug interactions

Zolpidem does not interact with any other medications. However, in tests Zolpidem was given while fasting or 20 minutes after a meal. With food, the bioavailability of Zolpidem was decreased by 15 – 25 percent. So for faster sleep onset, do not administer with or immediately following a meal.

Patient information

Zolpidem is meant to induce sleep. Zolpidem should not be taken when you are required to perform dangerous tasks or those requiring alertness.

610. Anticonvulsants

Anticonvulsant drugs include a variety of agents, all possessing the ability to depress abnormal neuronal discharges in the CNS, thus inhibiting seizure activity. Because of differences in pharmacology, therapeutic use and adverse reaction potential, these agents are normally grouped into these subcategories: barbiturates, hydantoins, succinimides, oxazolidinediones, benzodiazepines, and miscellaneous anticonvulsants. Of course, we'd be here forever if we studied all of these. Thank goodness that the DOD Core Formulary has set our standard. This lesson covers barbiturates (phenobarbital and primidone), hydantoins (phenytoin), benzodiazepines (clonazepam), and two miscellaneous anticonvulsants (carbamazepine, and divalproex sodium). Even with paring down the list, it's still quite a mouthful, so let's get started.

Primidone and phenobarbital

Primidone and phenobarbital are discussed as one agent since phenobarbital is a metabolite of primidone. Primidone raises electroshock or chemoshock seizure thresholds or alters the seizure pattern. Primidone resembles phenobarbital in many anticonvulsant effects, but it is much less potent than phenobarbital in antagonizing seizures. The anticonvulsant effects of primidone are attributed to both the drug and its active metabolites, principally phenobarbital. The mechanism of action is not

known exactly. However, it is known that these agents depress the sensory cortex, decrease motor activity, alter cerebellar function and produce drowsiness, sedation and hypnosis.

Indications and dosage

These drugs are indicated for the control of grand mal, psychomotor or focal epileptic seizures, either alone or with other anticonvulsants. Dosage for these drugs is highly individualized and must be slowly increased to achieve proper levels and, if therapy is discontinued, the dose must be tapered to prevent withdrawal. Primidone is available in 50 and 250 mg tablets and phenobarbital comes in 15, 30, 60, and 100 mg tablets; 15 and 20 mg/5ml elixir; and 30, 60, 65, and 130 mg/ml injection.

Contraindications

These drugs are contraindicated in patients who are sensitive to barbiturates, have impaired liver functions, or suffer from dyspnea or other respiratory diseases.

Warnings

Pregnancy – All barbiturates are in pregnancy category D. Barbiturates can cause fetal damage when administered to a pregnant woman. Studies suggest a connection between maternal consumption of barbiturates and a higher incidence of fetal abnormalities. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise her of the potential hazards to the fetus.

Barbiturates readily cross the placental barrier and are distributed throughout fetal tissues. Fetal blood levels approach maternal blood levels following parenteral use.

Withdrawal symptoms occur in infants born to mothers who receive barbiturates throughout the last trimester of pregnancy. Reports include the acute withdrawal syndrome of seizures and hyperirritability from birth to a delayed onset of up to 14 days.

Anticonvulsant use: Because of the strong possibility of precipitating status epilepticus with attendant hypoxia and risk to both mother and unborn child, do not discontinue anticonvulsants when used to prevent major seizures. However, consider discontinuing anticonvulsants prior to and during pregnancy when the nature, frequency and severity of the seizures do not pose a serious threat to the patient. It is not known whether even minor seizures constitute some risk to the embryo or fetus.

Lactation - Exercise caution when administering barbiturate to the nursing mothers, since small amounts are excreted in breast milk. Drowsiness in the nursing infant has been reported.

Drug interactions

Phenobarbital has many, many more drug interactions than primidone. This is probably due to phenobarbital being highly bound to plasma proteins. The next table lists drug interactions for phenobarbital and the following paragraph will discuss the primidone interactions.

Drugs that Phenobarbital Effects	Description
Acetaminophen	The risk of hepatotoxicity is increased
Anticoagulants	There is an increase in anticoagulant metabolism resulting in a decreased response.
Beta blockers	The effectiveness of beta blockers may be decreased.
Carbamazepine	Blood levels of carbamazepine may be decreased.
Clonazepam	The effectiveness of clonazepam may be decreased.
Contraceptives	Decreased contraceptive effect may occur.
Corticosteroids	Corticosteroid metabolism may be increased.
Theophylline	Theophylline levels are decreased.
Verapamil	Bioavailability is decreased.

Primidone blood levels are increased by hydantoins, isoniazid, and succinimide anticonvulsants.

Patient information

- Drowsiness, dizziness or muscular incoordination may occur initially, but these symptoms usually disappear with continued therapy.
- Observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity.
- If GI upset occurs, take with food.
- Do not discontinue medication abruptly or change dosage, except on advice of physician.
- Notify your physician if skin rash or fever occurs or if patient becomes pregnant.
- Patients should carry identification (Medic Alert) indicating medication usage and epilepsy.

Hydantoins

The primary site of action of the hydantoins appears to be the motor cortex, where the spread of seizure activity is inhibited. Possibly by promoting sodium efflux from neurons, hydantoins tend to stabilize the threshold against hyperexcitability caused by excessive stimulation or environmental changes capable of reducing membrane sodium gradient. This loss of overstimulation prevents cortical seizure foci from detonating adjacent cortical areas. Hydantoins reduce the activity of brain stem centers responsible for the tonic phase of grand mal seizures. The only hydantoin that we'll be discussing is phenytoin.

Phenytoin is available as phenytoin acid (chewable tablets, suspension) or phenytoin sodium (capsules, injection); phenytoin sodium contains 92 percent phenytoin.

Indications and dosage

Phenytoin is indicated for the control of grand mal and psychomotor seizures. Phenytoin is a drug that requires a level to be built up in the blood. This level is known as *steady state*. Dosage is individualized. Because of potential bioavailability differences between products, brand interchange is not recommended. Some providers like to use a loading dose for patients who require a rapid steady state and where IV administration is not desirable. After the steady state has been reached, the normal maintenance dose is 300 – 400 mg/day divided into three doses. There are extended release capsules available, but a patient must be well controlled before moving to once daily dosing with the extended release capsules.

Contraindications

People with certain heart problems and those sensitive to hydantoins should not use phenytoin.

Warnings

Since blood levels must be maintained, when therapy is discontinued, it must be tapered, or seizures may occur.

Pregnancy - Reports suggest an association between use of anticonvulsant drugs by women with epilepsy and an elevated incidence of birth defects in children born to these women. Data are more extensive with respect to phenytoin and phenobarbital; other reports indicate a possible similar association with other anticonvulsants. Other factors (e.g., genetics or the seizure disorder per se) may also contribute to the higher incidence of birth defects. The great majority of mothers receiving anticonvulsant medication deliver normal infants.

Lactation - These drugs are excreted in breast milk. Because of the potential for serious adverse reactions in nursing infants, decide whether to discontinue nursing or to discontinue the drug.

Drug interactions

This seems like it takes a step backward. The data presented in the following tables is more plain than before. It is without description. The important information in these tables is which drugs' effects are decreased by phenytoin and which drugs decrease or increase the effects of phenytoin.

Phenytoin Drug Interactions – Drug Effects Decreased by Phenytoin		
Acetaminophen	Haloperidol	Cyclosporine
Carbamazepine	Oral contraceptives	Furosemide
Cardiac glycosides	Quinidine	Levodopa
Corticosteroids	Theophylline	Mebendazole
Doxycycline	Valproic acid	Sulfonylureas
Estrogens		

Phenytoin Drug Interactions – Decreased Phenytoin Effects		
Through Increased Metabolism	Through Decreased Absorption	Through Unknown Reasons
Barbiturates	Antacids	Antineoplastics
Carbamazepine	Charcoal	Folic acid
Ethanol (chronic use)	Sucralfate	Nitrofurantoin
Theophylline		Pyridoxine

Drugs that Increase Phenytoin Effects	
Benzodiazepines	Cimetidine
Disulfiram	Ethanol (acute ingestion)
Fluconazole	Isoniazid
Metronidazole	Miconazole
Omeprazole	Succinimides
Trimethoprim	Valproic acid
Salicylates	Tricyclic antidepressants
Chlorpheniramine	Ibuprofen

Patient information

- Take phenytoin with food to reduce GI upset.
- Phenytoin suspension must be thoroughly shaken immediately prior to use.
- Do not discontinue phenytoin abruptly or change dosage, except on advice of physician.
- Maintain good oral hygiene (regular brushing and flossing) while taking phenytoin. Inform dentist of phenytoin usage.
- Patients should carry identification (Medic Alert) indicating medication usage and epilepsy.
- May cause drowsiness, dizziness or blurred vision; alcohol may intensify these effects. Observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity. Notify physician if drowsiness, slurred speech or impaired coordination (ataxia) occurs.
- Do not use capsules which are discolored.

Benzodiazepines

In two earlier lessons, we talked about benzodiazepines, the fact that they work through GABA on many neuroreceptors. In this case, the affected receptors are in the brain stem. We have already discussed diazepam under anti-anxiety drugs. It can also be used as an anticonvulsant. In this lesson we'll add clonazepam to the mix.

Indications and dosage

Clonazepam is indicated for certain specific types of seizures (too deep for us here). It may also be useful in patients with absence (petit mal) seizures who have failed to respond to succinimides. The initial dose of clonazepam should not exceed 1.5 mg/day in 3 divided doses. Dosage can be increased in increments of 0.5 to 1 mg every 3 days until seizures are adequately controlled or until side effects preclude any further increase. The maintenance dose of clonazepam must be individualized. Maximum recommended dosage is 20 mg/day.

Contraindications

Clonazepam is contraindicated in patients with sensitivity to any benzodiazepine, suffering from liver disease or closed-angle glaucoma.

Warnings

Pregnancy - All of the benzodiazepines are in pregnancy category D, except for clonazepam. Clonazepam does not have an official category assigned, but when you read any reference book on it, it is very close to a C

Lactation - Benzodiazepines are excreted in breast milk. Since neonates metabolize benzodiazepines more slowly than adults, accumulation of the drug and its metabolites to toxic levels is possible. Chronic diazepam use in nursing mothers reportedly caused infants to become lethargic and to lose weight; do not give to nursing mothers.

Drug interactions

If this table looks familiar, it's the same one from temazepam. The interactions for benzodiazepines are all the same.

Drug	Interaction
Theophylline	Theophylline antagonizes the effects of benzodiazepines
Digoxin	Benzodiazepines may increase blood levels and toxicity of digoxin.
Phenytoin	Benzodiazepines may increase blood levels and toxicity of phenytoin.

Patient information

- May cause drowsiness; avoid driving or other tasks requiring alertness.
- Avoid alcohol or other CNS depressants.
- May be taken with food or water if stomach upset occurs.
- Patients on long-term or high dosage therapy may experience withdrawal symptoms on abrupt cessation of therapy; do not discontinue therapy abruptly or change dosage except on advice of physician.
- Concomitant ingestion with antacids may alter the rate of absorption of these drugs (documented with diazepam and chlordiazepoxide).
- Anticonvulsant therapy patients should carry identification (Medic Alert) indicating medication usage and epilepsy.

Miscellaneous anticonvulsants

The last two drugs that we must look at in the anticonvulsant area are carbamazepine and divalproic sodium. These two are not related to any of the other anticonvulsants that we have discussed, nor are they similar to each other. Now, you know what that means; we'll be looking at these two drugs individually.

Carbamazepine

Carbamazepine is an anticonvulsant effective in the treatment of psychomotor and grand mal seizures. It is an iminostilbene derivative chemically related to the tricyclic antidepressants and

unrelated to other anticonvulsants. Its mechanism of action is unknown. It appears to act by reducing polysynaptic responses and blocking post-tetanic potentiation.

Indications and dosage

Carbamazepine is indicated for treating partial seizures with complex symptoms (psychomotor, temporal lobe). Patients with these seizures appear to show greatest improvement. Dosage for carbamazepine is individualized. A low initial daily dosage with gradual increase is advised. As soon as adequate control is achieved, dosage is reduced gradually to the minimum effective level. Carbamazepine is most effective when taken with meals. An initial dose of 200 mg twice daily, increased as necessary to control seizures, not to exceed 1200 mg/day is normal. For maintenance, the dosage is adjusted to the minimum effective level, usually 800 to 1200 mg daily. Extended release forms are available but shouldn't be used until the patient is well controlled.

Contraindications

Patients with a history of bone marrow depression, hypersensitivity to carbamazepine and tricyclic antidepressants, or who are using monoamine oxidase (MAO) inhibitors, should not use carbamazepine.

Warnings

Aplastic anemia and agranulocytosis have been reported in association with carbamazepine therapy. The risk of developing these reactions is 5 to 8 times greater than in the general population; however, the overall risk of these reactions in the untreated general population is low (approximately six and two patients per one million per year for agranulocytosis and aplastic anemia, respectively).

Pregnancy – Carbamazepine is in pregnancy category D. Carbamazepine can cause fetal harm when administered to a pregnant woman. Epidemiological data suggest that there may be an association between the use of carbamazepine during pregnancy and congenital malformations, including spina bifida. Use only when clearly needed and when the potential benefits outweigh the potential hazards to the fetus.

Lactation - Carbamazepine and its metabolite are transferred to breast milk. The estimated doses given to the newborn during breastfeeding are in the range of 2 to 5 mg daily for carbamazepine. Because of the potential for serious adverse reactions, decide whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Drug interactions

The next two tables list the carbamazepine drug interactions.

Drugs Affecting Carbamazepine	
Drug	Description
Barbiturates	Barbiturates may cause higher carbamazepine levels
Cimetidine	Carbamazepine levels may increase to toxic levels
Diltiazem	Carbamazepine levels may increase to toxic levels
Hydantoins	Carbamazepine levels may increase to toxic levels
Isoniazid	Carbamazepine toxicity, isoniazid toxicity, or hepatotoxicity may result
Macrolide antibiotics	Carbamazepine levels may increase to toxic levels
Propoxyphene	Carbamazepine levels may increase to toxic levels
SSRIs	Carbamazepine levels may increase to toxic levels
Tricyclic antidepressants	Carbamazepine levels may increase to toxic levels
Valproic acid	Carbamazepine levels may vary greatly, valproic acid levels are decreased
Verapamil	Carbamazepine toxicity has occurred within 36 – 96 hours

Drugs Affected by Carbamazepine	
Drug	Description
Anticoagulants	Effects of anticoagulants are decreased
Bupropion	Decreased bioavailability of bupropion by up to 90 percent
Contraceptives	Effectiveness of contraceptives is decreased
Doxycycline	Doxycycline half life is reduced
Haloperidol	Haloperidol levels and efficacy are reduced by up to 60 percent
Lithium	CNS toxicity may occur with concomitant therapy

Patient information

- Carbamazepine may produce drowsiness, dizziness or blurred vision; patients should observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity.
- Notify physician if any of the following occurs: Unusual bleeding or bruising, fever, sore throat, rash or ulcers in the mouth.
- Take carbamazepine with food.

Divalproex sodium

This last drug is actually a combination. Divalproex sodium is a stable coordination compound containing equal proportions of valproic acid and sodium valproate, both of which are used alone as anticonvulsants. Divalproex sodium also works with GABA. It seems to be related to increasing brain levels of GABA and inhibiting an enzyme which destroys GABA.

Indications and dosage

Divalproex sodium is indicated for use as a sole and adjunctive therapy in the treatment of simple and complex absence seizures and adjunctively in patients with multiple seizure types. When used as monotherapy, the dose is 10 to 15 mg/kg/day in divided doses which may be increased by 5–10 mg/kg/week until the seizures are controlled. When used as adjunctive therapy, divalproex sodium may be added to the patients regimen at a dosage of 10 to 15 mg/kg/day. The dosage may be increased by 5- 10 mg/kg/week to achieve an optimal response. Ordinarily, optimal response is achieved at doses of less than 60 mg/kg/day. There are numerous dosage forms and strengths which are available for divalproex sodium, too many to list here.

Contraindications

Of course, any patient sensitive to valproic acid shouldn't take divalproex sodium. Divalproex is also contraindicated in patients with hepatic disease or dysfunction.

Warnings

Hepatic failure resulting in fatalities has occurred in patients receiving valproic acid and its derivatives. The incidence of fatal hepatotoxicity decreases considerably in progressively older patient groups. These incidents usually have occurred during the first 6 months of treatment.

Pregnancy – Divalproex sodium is in pregnancy category D. The incidence of neural tube defects in the fetus may be increased in mothers receiving valproic acid during the first trimester. The CDC estimates the risk of valproic acid-exposed women having children with spina bifida to be 1 percent to 2 percent. This risk is similar to that for nonepileptic women who have had children with neural tube defects (anencephaly and spina bifida).

Administer antiepileptic drugs to women of child-bearing potential only if they are clearly shown to be essential in the management of their seizures; even minor seizures may pose some hazard to the developing embryo or fetus.

Lactation - Concentrations of valproic acid in breast milk are 1 percent to 10 percent of serum concentrations. It is not known what effect this would have on a nursing infant. Exercise caution when administering to a nursing woman.

Drug interactions

The next two tables give the drug interactions for divalproex sodium.

Drugs that Effect Divalproex Sodium	
Drug	Description
Charcoal	Valproic acid absorption is decreased
Cimetidine	Small decrease in clearance and increase in half life.
Erythromycin	May increase levels to toxicity

Drugs that are Effected by Divalproex Sodium	
Drug	Description
Clonazepam	May induce status absence in patients with absence seizure disorder
CNS depressants	Increase in CNS effects
Diazepam	Diazepam metabolism inhibited
Phenobarbital	Metabolism of both drugs is inhibited
Phenytoin	Increased action of phenytoin and decreased action of divalproex
Warfarin	Coagulation may be effected

Patient information

- If GI upset occurs, take divalproex sodium with food.
- Do not chew tablets or capsules; swallow whole to avoid irritation of mouth and throat.
- Patients should use caution while driving or performing other tasks requiring alertness, coordination or physical dexterity.

611. Antipsychotics

We touched on psychosis earlier. Psychosis is a term that was applied to any mental disorder, but recently has been limited to disturbances of such magnitude that there is personality disintegration and loss of contact with reality. The pathophysiology of psychosis is complex and not completely understood. Early theories focused solely on the involvement of the dopaminergic system in the etiology of this complex syndrome; however, serotonergic pathways have recently been implicated, and newer hypotheses address the interplay not only between these two systems but also the involvement of muscarinic, alpha-adrenergic and histaminic systems.

Antipsychotics can be grouped into several classes; the phenothiazines, structurally related thioxanthenes, butyrophenones, diphenylbutylpiperadines and the indolones. As a group, these agents are dopamine receptor antagonists. They also bind with varying affinities on nondopaminergic sites, such as cholinergic, alpha 1 -adrenergic and histaminic receptors, which can partially explain the varied side effect profiles for each agent. Typical antipsychotics are likely to induce side effects outside of the CNS and have similar efficacies when used in equipotent doses. Lower-potency agents tend to be more sedating and high-potency agents usually have a higher incidence of acute non-CNS side effects. Again, we don't have the time, space, or need to go into all of the antipsychotics. We're not even going to cover all of those classes that I mentioned earlier. Our focus will be on a few of the traditional medications used to treat this disorder and a new face or two that has been thrown into the mix. The antipsychotics that we'll cover are haloperidol, chlorpromazine, thioridazine, risperidone.

Drug	Equivalent Dose (mg)	Normal Adult Dose (mg)	Dosage Forms Available
Chlorpromazine	100	30 - 80	10, 25, 50, 100, 200 mg tablets; 30, 75, 150 mg SR capsules; 10 mg/5ml and 30 and 100 mg/ml syrup; 25, 100 mg suppositories; 25 mg/ml injection
Haloperidol	2	1 - 15	0.5, 1, 2, 5, 10, 20 mg tablets; 2, 5 mg/ml syrup, 50, 100 mg/ml injection
Risperidone	N/A	4 - 16	1,2,3,4 mg tablets 1 mg/ml syrup
Thioridazine	100	150 - 180	10, 15, 25, 50, 100, 150, 200 mg tabs; 30 and 100 mg/ml liquid, 25 mg/5 ml suspension

Indications

All of these drugs are indicated for the management of the manifestations of psychotic disorders. Specifically:

- Chlorpromazine – mania and manic-depressive disorder.
- Haloperidol – chronic schizophrenia, Tourette's syndrome, explosive hyperexcitability, and hyperactivity in children.
- Risperidone – no specifics given.
- Thioridazine – depression and anxiety, conduct disorders in children.

Contraindications

These drugs are contraindicated in patients who are comatose or in severely depressed states. Additionally, they shouldn't be used in patients who take other CNS depressants, suffer from bone marrow depression, liver damage, coronary artery disease, or severe hypertension or hypotension.

Warnings

Tardive dyskinesia (TD), a syndrome consisting of potentially irreversible, involuntary dyskinetic movements, may develop in patients treated with neuroleptic drugs.

These agents may impair mental or physical abilities, especially during the first few days. Drowsiness may occur during the first or second week, after which it generally disappears.

These drugs can lower the convulsive threshold and may precipitate seizures.

Pregnancy – All of the covered drugs are in pregnancy category C. Safety for use during pregnancy has not been established. Use only when clearly needed and when potential benefits outweigh potential hazards to the fetus.

Lactation - Chlorpromazine and haloperidol have been detected in breast milk. Although few cases are documented, a milk:plasma ratio of 0.5 to 0.7 or less is reported, representing a milk drug level of 290 mcg/ml and 2 to 23.5 mcg/ml, respectively. Safety for use in the nursing mother has not been established.

Drug interactions

Since this section has been pretty well combined, I'll do the same thing with the drug interactions. The following table gives the interactions for all of the drugs discussed. I'm going to follow the format of *Drug Facts and Comparisons* in presenting the information in the fact that I'll first list the precipitant drug (the one that causes the interaction), then the object drug (the one that is effected), and then I'll give a short description of the interaction.

Antipsychotic Drug Interactions		
Precipitant Drug	Object Drug	Description
All antipsychotics	Phenytoin	Phenytoin levels must be monitored, may increase or decrease
Chlorpromazine	Valproic acid	Valproic acid levels may be increased
Chlorpromazine and Thioridazine	Anorexants	Anorexiant effects may be decreased
Chlorpromazine and Thioridazine	Bromocriptine	Bromocriptine effectiveness may be inhibited
Chlorpromazine, Thioridazine and Haloperidol	Tri-cyclic antidepressants (TCAs)	TCA levels may be increased
Chlorpromazine and Thioridazine	Propranolol	Coadministration may result in increased levels of both drugs resulting in hypotensive episodes
Aluminum salts	Chlorpromazine and Thioridazine	Antacids containing aluminum may impair the absorption and reduce the effects of chlorpromazine and thioridazine
Anticholinergics	Chlorpromazine and Thioridazine	Antipsychotic effects are decreased and anticholinergic side effects are increased
Barbiturates	Chlorpromazine, Thioridazine and Haloperidol	Effectiveness of all four drugs is decreased
Carbamazepine	Haloperidol and Risperidone	Antipsychotic effectiveness is decreased
Charcoal	Chlorpromazine and Thioridazine	Charcoal prevents the absorption of these drugs reducing effectiveness and toxicity
Lithium	Chlorpromazine, Thioridazine and Haloperidol	May induce disorientation, unconsciousness and other side effects outside of the CNS
Meperidine	Chlorpromazine and Thioridazine	May cause excessive sedation and hypotension
Methyldopa	Haloperidol	Potentiates antipsychotic effects, maybe causing worse episode of psychosis
Phenytoin	Thioridazine and Haloperidol	Antipsychotic levels and effectiveness are decreased

Patient information

Because some patients exposed chronically to neuroleptics will develop symptoms outside the CNS, inform all patients in whom chronic use is contemplated, if possible, about this risk. The decision to inform patients or their guardians must obviously take into account the clinical circumstances and the patient's competence to understand the information.

These drugs may cause drowsiness; use caution while driving or performing other tasks requiring alertness. Avoid alcohol and other CNS depressants because of possible addictive effects and hypotension.

612. Antiemetic and antivertigo drugs

Drug-induced vomiting is generally stimulated through the chemoreceptor trigger zone (CTZ), which in turn stimulates the vomiting center (VC) in the brain. Nausea associated with motion sickness is initiated by stimulation of labyrinthine mechanism of the ear, which sends impulses to CTZ. The VC may also be stimulated directly (by GI irritation, motion sickness, vestibular neuritis, etc.). Increased activity of central neurotransmitters, dopamine in CTZ or acetylcholine in VC, appears to be a major mediator for inducing vomiting.

Patients undergoing cancer chemotherapy often experience nausea and vomiting so intolerable that they may refuse further treatment. Prophylaxis with an antiemetic drug before the patient receives chemotherapy and treatment afterward may enable the patient to overcome this unpleasant side effect and continue a potentially curative protocol.

Vertigo is a feeling of whirling or rotation accompanied by involuntary swaying, weakness and lightheadedness. Motion sickness, a functional disorder, is caused by repetitive angular, linear or vertical motion. Both of these conditions are characterized by lack of skin color, sweating, hyperventilation, nausea and vomiting.

The drugs that are effective as antiemetics are the antidopaminergic agents that are especially effective for drug-induced emesis. Anticholinergic agents may be more appropriate in motion sickness. With all of that said, we'll now look at some drugs. This lesson covers the anticholinergics as a group, then we'll look at antidopaminergics, and a newer group of drugs used almost exclusively with antineoplastics, the 5-HT₃ antagonists.

Anticholinergics

We've already discussed some things about anticholinergics. Above in the reading, it is stated that increased activity of acetylcholine at the VC causes vomiting. These drugs are anticholinergics, blocking the action of the acetylcholine – simple huh?

Indications and dosing

This table shows the antiemetic indications and dosing for the covered anticholinergics.

Drug	Antiemetic Dosing
Diphenhydramine	MS: 25 – 50 mg three or four times daily
Meclizine	MS: 25 – 50 mg 1 hour before travel, may repeat every 24 hours V: 25 – 100 mg/day in divided doses

NV = Nausea and Vomiting MS = Motion Sickness V = Vertigo

Antidopaminergics

Just as acetylcholine at the VC caused vomiting, dopamine action at the CTZ does too.

Indications and dosage

This table describes the indications and dosages for the antidopaminergic drugs.

Drug	Antiemetic Dosing
Promethazine	MS: 25 mg twice daily, 0.5 – 1 hr before travel, may repeat in 8 – 12 hours NV: 25 mg every 4 – 6 hours
Prochlorperazine	NV: 5 – 10 mg 3 – 4 times daily, 15 mg (SR) on arising and 10 mg (SR) every 12 hours

NV = Nausea and Vomiting MS = Motion Sickness V = Vertigo

Contraindications

Patients who have shown sensitivity to any antihistamine should not use these drugs. Also, patients with glaucoma, prostatic hypertrophy, or lower respiratory conditions should not use antihistamines.

Warnings

Promethazine may lower the seizure threshold; consider this when giving to people with known seizure disorders or when giving in combination with narcotics or local anesthetics that may also affect seizure threshold.

Pregnancy – These drugs fall into category C. Safety for use during pregnancy has not been established. Several possible associations with malformations have been found, but significance is unknown.

Lactation – Some antihistamines are excreted into breast milk. However, it isn't known if the ones that we discussed are. Caution should still be exercised.

Drug interactions

The main interaction is between these drugs and other CNS depressants. Additive CNS depressant effects may occur.

Patient information

- Inform your physician of a history of glaucoma, peptic ulcer, urinary retention or pregnancy before starting antihistamine therapy.
- Some antihistamines may cause nervousness, insomnia and dry mouth.
- Some antihistamines may cause drowsiness or dizziness; observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity. Avoid alcohol and other CNS depressants (e.g., sedatives, hypnotics, tranquilizers, antianxiety agents).

5-HT₃ receptor antagonists

This is a fairly new class of drugs, used pretty exclusively in chemotherapy patients. During chemotherapy, cells from the small intestine release serotonin, stimulating the 5-HT₃ receptors in the CTZ, stimulating vomiting. These antagonists block the messages from reaching the CTZ. You won't see these drugs in your pharmacy unless your facility performs chemotherapy and these drugs are mainly used on an in-patient basis. You just need to know that they exist and further studies in this area may turn up new uses for these drugs.

The 5-HT₃ receptor antagonists are indicated in the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic (emesis causing) cancer therapy, prevention of nausea and vomiting from radiotherapy, and prevention of postoperative nausea and vomiting (ondansetron only).

The 5-HT₃ receptor antagonists are:

1. Ondansetron.
2. Dolasetron.
3. Granisetron.

That's as deep as we really need to go into these drugs. You now have a good general knowledge of them!

613. Drugs for ADD/ADHD and Parkinson's disease

The drugs used to treat ADD/ADHD disorder include methylphenidate, pemoline, and dextroamphetamine. It isn't known how these drugs help with the symptoms of ADD/ADHD, but it is thought that somehow stimulation of the brain stem plays a part. I also added drugs to treat Parkinson's disease to this area because they are of such limited scope. The primary defect in Parkinsonism appears to be an imbalance of neurotransmitters (a lot of acetylcholine to little or no dopamine). The two drugs that can take care of this are the combination of carbidopa/levodopa and selegiline. This is another one of those cases where we have to look at each drug separately. We'll start with methylphenidate.

Methylphenidate

Methylphenidate is a mild CNS stimulant with actions similar to the amphetamines.

Indications and dosage

Methylphenidate is indicated as part of a total treatment program in children with a behavioral syndrome characterized by moderate to severe distractibility, short attention span, hyperactivity, emotional instability and impulsivity. The dosage for methylphenidate is individualized. It is administered in divided doses 2 – 3 times daily. The average dose is from 10 mg/day up to 60 mg/day. There is an SR dosage form of methylphenidate. Patients must be titrated to this dose.

Contraindications

Patients with marked anxiety, tension and agitation should not take methylphenidate because the drug may aggravate these symptoms. Also, patients with a hypersensitivity to methylphenidate, glaucoma, motor tics or a family history or diagnosis of Tourette's syndrome, should not use methylphenidate.

Warnings

Methylphenidate may lower the seizure threshold in patients with any seizure disorder.

Pregnancy – Methylphenidate is in pregnancy category C. Use methylphenidate in women of childbearing age only when clearly needed and when potential benefits outweigh potential hazards to the fetus. In the small numbers of patients reported who received methylphenidate during their pregnancy, no evidence of increased malformation rate was found.

Lactation – The safety of methylphenidate use in nursing women has not been established.

Drug interactions

Concomitant use of methylphenidate with phenytoin or tri-cyclic antidepressants may increase the levels and possible toxicity of the phenytoin or antidepressant.

Patient information

- Take the last daily dose early in the evening (prior to 6 p.m.) to avoid insomnia. It is often recommended that methylphenidate be taken 30 to 45 minutes before meals.
- May mask symptoms of fatigue, impair physical coordination or produce dizziness or drowsiness. Use caution while driving or performing other tasks requiring alertness.
- Notify physician of nervousness, insomnia, palpitations, vomiting, fever or skin rash.
- Do not crush or chew SR medication.

Pemoline

Pemoline is a CNS stimulant. Although structurally dissimilar from the amphetamines and methylphenidate, it has pharmacologic activity similar to that of other stimulants but with minimal sympathomimetic effects. Although the exact mechanism of action is unknown, pemoline may act through dopaminergic mechanisms.

Indications and dosage

Pemoline is indicated as part of a total treatment program in children with a behavioral syndrome characterized by moderate to severe distractibility, short attention span, hyperactivity, emotional instability and impulsivity. Dosing for pemoline is giving as a single daily dose in the morning. The recommended starting dose is 37.5 mg/day. If dosing needs to be increased, do so at 1 week intervals using increments of 18.75 mg until the desired response is obtained. Average doses are from 56 – 75 mg/day. The maximum dose is 112.5 mg/day.

Contraindications

Patients with liver problems or any known hypersensitivity to pemoline should not use pemoline.

Warnings

Pregnancy – Pemoline is in pregnancy category B. There are no adequate and well controlled studies in pregnant women. Use pemoline during pregnancy only if clearly needed.

Lactation - It is not known whether pemoline is excreted in breast milk. Exercise caution when administering pemoline to a nursing woman.

Drug interactions

There are no drug interactions noted for pemoline.

Patient information

This medication should be taken in the morning.

If dizziness occurs, use caution when performing tasks requiring alertness.

Dextroamphetamine

Dextroamphetamine is an amphetamine. Amphetamines are sympathomimetic amines with CNS stimulant activity.

Indications and dosage

Dextroamphetamine is indicated as an integral part of a total treatment program which includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with a behavioral syndrome characterized by moderate to severe distractibility, short attention span, hyperactivity, emotional instability and impulsivity. The dosing for dextroamphetamine is 5 mg once or twice daily. The dose may be increased in increments of 5 mg/day at weekly intervals until the best response is obtained. Dosages rarely exceed 40 mg/day. Dextroamphetamine is available in 5 and 10 mg tablets and 5, 10, and 15 mg extended release capsules.

Contraindications

Dextroamphetamine is contraindicated in patients with cardiovascular disease, hypertension, or hyperthyroidism.

Warnings

A tolerance and/or dependency can occur with this drug. If tolerance occurs, dextroamphetamine therapy should be discontinued.

Pregnancy – Dextroamphetamine is in pregnancy category C. Safety for use during pregnancy has not been established.

Lactation - Amphetamines are excreted in breast milk. Advise patients to discontinue nursing while taking amphetamines.

Drug interactions

Tricyclic antidepressants may decrease the effectiveness of dextroamphetamine.

Patient information

- Take early in the day (especially sustained release dosage forms) to avoid nighttime insomnia.
- Do not chew or crush sustained release or long-acting tablets.
- Do not increase dosage, except on physician's advice.
- May impair ability to drive or perform other tasks requiring alertness. May mask extreme fatigue and cause dizziness.
- May cause nervousness, restlessness, insomnia, dizziness, anorexia, dry mouth and GI disturbances. Notify physician if these effects become pronounced.

Carbidopa/Levodopa

These agents are used in combination since carbidopa inhibits decarboxylation of levodopa and makes more levodopa available for transport to the brain. We'll briefly look at each of their actions and then discuss the drug combination of the two.

Levodopa

The symptoms of Parkinson's disease are related to depletion of dopamine. Dopamine does not cross the blood-brain barrier; however, levodopa, the metabolic precursor of dopamine, does cross the blood-brain barrier. It is converted into dopamine in the brain cells. Therefore, blood dopamine is markedly increased, accounting for many of levodopa's pharmacologic and adverse effects.

Carbidopa

Carbidopa inhibits the conversion of peripheral levodopa. It does not cross blood-brain barrier and does not affect levodopa metabolism within the CNS. Since its inhibiting activity is limited to extracerebral tissues, administration of carbidopa with levodopa makes more levodopa available for transport to the brain.

Levodopa and carbidopa

The two chemicals are used together as the carbidopa helps make more levodopa available.

Indications and dosage

This combination is indicated in the treatment of Parkinson's disease. Dosing of this agent is complicated as the balance of the two medications is critical. The tablets come in two ratios, 1:4 and 1:10 with various strength combinations. Medications are usually marked in milligrams as fractions with the numerator being the amount of carbidopa and the denominator being the amount of levodopa. Normal dosing starts with a 25/100 mg tablet three times daily or a 10/100 mg tablet 3 – 4 times daily. If more carbidopa is needed, a switch from the 10/100 mg to the 25/100 tablet could be made. If more levodopa is needed, switch the 25/100mg tablet for the 25/100 or the 10/100 mg tablet. There is a controlled release tablet which is dosed twice daily. When switching strengths with the CR tablet, a three day interval should be adhered to .

Warnings

Certain adverse CNS effects occur at lower dosages and appear sooner during therapy when the sustained release form is used.

Drug interactions

The use of antacids may increase the bioavailability of levodopa increasing its efficacy. The following table lists the drugs that decrease levodopa's effects.

Drug	Interaction Description
Anticholinergics	Decreased intestinal absorption of levodopa may occur
Benzodiazepines	Levodopa's therapeutic value may be lessened
Hydantoins	Levodopa's effectiveness may be reduced
Pyridoxine	Levodopa's effectiveness is reduced
Tricyclic antidepressants	Decreased bioavailability of levodopa, hypertensive episodes have occurred

Patient information

- The effects of this drug may be delayed from several weeks to a few months.
- If GI upset occurs, notify your physician and take with food.

Selegiline

Selegiline is a derivative of phenethylamine. The mechanism of action in the adjunctive treatment of Parkinson's disease is not fully understood. Selegiline inhibits monoamine oxidase (MAO) type B activity and may act through other mechanisms to increase dopaminergic activity.

Indication and dosage

Selegiline is indicated as an adjunct in the management of Parkinsonian patients being treated with levodopa/carbidopa who exhibit deterioration in the quality of their response to this therapy. A dose of 10 mg/day in divided doses of 5 mg each taken at breakfast and lunch is used to begin therapy. This should allow for a reduction of 10 – 30 percent in the dose of carbidopa/levodopa.

Contraindications

Selegiline should not be used in patients using an opioid.

Warnings

The max dose of 10 mg/day must be observed. Side effects resembling non-selective MAO inhibitors may occur at higher doses.

Pregnancy – Selegiline is in category C. It is not known whether selegiline can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Use during pregnancy only if clearly needed.

Lactation - It is not known whether selegiline is excreted in breast milk.

Patient information

Patients should be advised of the possible need to reduce levodopa dosage after the initiation of selegiline therapy.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

607. Antianxiety agents

1. Which benzodiazepines are used to treat anxiety?
2. What are the indications for buspirone?
3. Which antihistamine is also used to treat anxiety?

608. Antidepressants

1. What are the three ways that tricyclic antidepressants (TCAs) work?
2. Why shouldn't TCAs be used in patients with a history of seizures?

3. How do SSRIs work?
4. How does cimetidine interact with SSRIs?
5. How is lithium unlike other antimaniac agents?
6. What warning is given concerning trazadone and patients recovering from myocardial infarction?

609. Hypnotics

1. What is the definition of a hypnotic?
2. How does temazepam cause sleep?

610. Anticonvulsants

1. How does primidone work?
2. Describe primidone and phenobarbital use in pregnant women.
3. How do hydantoins work?
4. What is *steady state*?
5. Why shouldn't clonazepam be given to nursing mothers?
6. What is the normal maintenance dose for carbamazepine?
7. What are the components of divalproex sodium?

611. Antipsychotics

1. What is the relationship between lower-potency antipsychotics and side effects?
2. What are the indications for haloperidol?
3. What is tardive dyskinesia?

612. Antiemetic and antivertigo drugs

1. What type of anti-emetic drug is more effective in motion sickness?
2. What is the role of serotonin in vomiting?

613. Drugs for ADD/ADHD and Parkinson's disease

1. Why shouldn't patients suffering from anxiety take methylphenidate?
2. What is the maximum daily dose of pemoline?
3. How do TCAs interact with dextroamphetamine?

Answers to Self-Test Questions**600**

1. The central nervous system and the peripheral nervous system.
2. Nerves that carry impulses to and from the brain.
3. Nerves that carry messages to and from the spinal cord.
4. From the central nervous system to the glands, the involuntary muscles located in the walls of tubes and hollow organs, and the heart.
5. Sympathetic and parasympathetic nervous systems.
6. A cell body, containing the nucleus, and nerve fibers.
7. The dendrites conduct impulses to the cell body, and the axons conduct impulses away from the cell body.
8. A bundle of nerve fibers, located outside the central nervous system, that directs impulses from one place to another.
9. Nerve fibers that are connected with receptors, for receiving stimuli. They conduct impulses to the brain and spinal cord.

10. Nerve fibers that carry impulses from the centers out to the muscles and glands.

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1. Cerebrum.
2. Brainstem.
3. The outer nerve tissue of the cerebral hemispheres (gray matter).
4. Frontal lobe, parietal lobe, temporal lobe, and occipital lobe.
5. In the temporal lobe.
6. In the front of the lowest part of the motor cortex of the frontal lobe.
7. In the brainstem.
8. To control the muscles of respiration in response to chemical and other stimuli.
9. The middle portion and two lateral hemispheres.
10. Four, they are called ventricles.
11. This study provides multiple x-ray pictures taken from different angles simultaneously. The information is organized, by means of a computer, and displayed as a photograph of the bone, soft tissue, and cavities of the brain.
12. The transfer and integration of messages that enter the spinal cord, so that a sensory (afferent) impulse entering the center becomes a motor (efferent) message leaving the cord.
13. Three layers of connective tissue surrounding the brain and spinal cord, forming a complete enclosure.
14. To cushion shocks that would otherwise injure the delicate structures of the CNS and to carry nutrients to the cells and transport waste products from the cells.

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1. To carry smell impulses from receptors in the nasal mucosa to the brain.
2. In the spinal cord with the cell bodies of the thoracolumbar area.
3. In the craniosacral area.
4. The action of glands, smooth muscles of hollow organs, and the heart.

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1. Inflammation of the brain.
2. Viruses and protozoa.
3. The stroke.
4. Brain damage occurring before or during the birth process.
5. Brain tumors are slightly more common in young and middle-aged adults.
6. The loss of the ability to speak or write, or the loss of the understanding of written or spoken language.
7. The virus enters the body through the nose and the throat. It multiplies in the GI tract and then travels to the CNS, possibly by way of the blood.
8. Loss of sensation and motion in the lower portion of the body.
9. The term "sclerosis" means hardening. Multiple sclerosis involves the entire spinal cord, in addition to the brain. The myelin (fat-like substance that forms a sheath around certain nerve fibers) disappears and the nerve axons themselves degenerate.
10. A disorder of the nervous system in which motor neurons are destroyed. Muscle atrophy and loss of motor control are the result of the progressive destruction of this disorder. This destruction continues until finally the person is unable to swallow, or talk.

604

1. An inflammation of the brain and spinal cord coverings caused by pathogenic bacteria, notably a diplococcus called the meningococcus.
2. Tears in the dural walls of the venous sinuses.
3. A shunt is created to drain excess CSF from the brain.
4. May be caused by increased pressure of the eye fluid on the nerves.

5. Paralysis of the muscles supplied by these fibers.
6. A facial paralysis due to damage to the facial (VII) nerve usually on one side of the face. This injury results in distortion of the face because of one-sided paralysis of the muscles of facial expression.
7. Nerve pain, particularly refers to a severe spasmodic pain affecting the fifth cranial nerve.
8. Inflammation of a nerve, and degenerative and other disorders involving the nerves.
9. A ruptured disk(s) between the lower lumbar vertebrae and arthritis of the lower portion of the spinal cord.
10. Shingles.

605

1. Bipolar disorder is a mental illness involving episodes of serious mania and depression.
2. Persistent, sad, anxious, or empty mood; feelings of hopelessness or pessimism; feelings of guilt, worthlessness, or helplessness; loss of interest or pleasure in ordinary activities; decreased energy, fatigue; being "slowed down"; sleep disturbances; loss of appetite and weight, or weight gain; thoughts of death or suicide, suicide attempts.
3. Anxiety is when a person becomes jittery, shakes, and can't stand still for no apparent reason.

606

1. Progressive deterioration of the nerve cells in the part of the brain that controls movement.
2. Any four of the 26 listed in the text such as: Muscle rigidity, stiffness, difficult bending arms or legs, unstable, loss of balance, gait changes, slow movements, shuffling, myalgia, shaking, tremors, changes in facial expression.
3. Inattention, distractibility, impulsivity, and hyperactivity.
4. Dopamine.
5. Diagnosis, appropriate treatment, vigilant monitoring, communication between physicians, caretakers, and schools, an on-going exchange of information.

607

1. Alprazolam, diazepam, lorazepam.
2. Management of anxiety disorders or short term relief of anxiety.
3. Hydroxyzine.

608

1. They block the amine pump, cause sedation, provide central and peripheral anticholinergic action.
2. They lower a person's seizure threshold.
3. Stop the presynaptic cell from reabsorbing the serotonin so that it remains at the receptor longer to work.
4. Cimetidine increases SSRI blood concentration by 50 percent.
5. Does not possess general sedative properties.
6. Trazodone may cause arrhythmia in these patients.

609

1. Any drug that causes insensitivity to pain by inhibiting afferent impulses or by inhibiting the receiving of sensory impression in the cortical center of the brain, causing unconsciousness.
2. It binds to receptors that cause sleep and inhibits GABA.

610

1. Primidone depresses the sensory cortex of the brain.
2. If a patient becomes pregnant while on these drugs, the provider should weigh the needs of the mother for the drug against the risk to the fetus. Therapy should not be discontinued during a pregnancy due to fetal withdrawals.
3. Hydantoins stabilize cells in the motor cortex to prevent excessive stimulation.
4. *Steady state* refers to when a drug has been taken long enough to build up steady levels in the blood.
5. It is passed to the infant through nursing, since it is metabolized slowly in infants, toxic levels may occur.

6. 800 – 1200 mg daily
7. Equal portions of valproic acid and sodium valproate.

611

1. They tend to be more sedating.
2. Chronic schizophrenia, Tourette's syndrome, explosive hyperexcitability, and hyperactivity in children.
3. TD is a syndrome consisting of potentially irreversible, involuntary dyskinetic movement that may develop in patients treated with neuroleptic drugs.

612

1. Anticholinergic agents.
2. During chemotherapy, cells from the small intestine release serotonin, stimulating the 5-HT₃ receptors in the CTZ, stimulating vomiting.

613

1. The CNS stimulation may aggravate the anxiety.
2. 112.5 mg/day.
3. TCAs decrease the effects of dextroamphetamine.

Unit Review Exercises

Note to Student: Consider all choices carefully, select the *best* answer to each question, and *circle* the corresponding letter. When you have completed all unit review exercises, transfer your answers to ECI Form 34, Field Scoring Answer Sheet.

Do not return your answer sheet to ECI.

1. (600) What part of the nervous system includes the brain and spinal cord?
 - a. Central.
 - b. Peripheral.
 - c. Sympathetic
 - d. Parasympathetic
2. (600) What type of nerve conducts impulses from the brain to the cell body?
 - a. Dendrite.
 - b. Axon.
 - c. Myelin.
 - d. Neurilemma.
3. (601) What is the largest part of the brain?
 - a. Cerebellum.
 - b. Cerebrum.
 - c. Medulla Oblongata.
 - d. Pons.
4. (601) What part of the brain controls voluntary actions?
 - a. Brainstem.
 - b. Cerebellum.
 - c. Cerebral cortex.
 - d. Frontal lobe.
5. (601) What part of the brain aids in controlling body temperature, water balance, sleep, and appetite?
 - a. Thalamus.
 - b. Hypothalamus.
 - c. Midbrain.
 - d. Pons.
6. (601) Which part of the brain contains the centers to regulate respiration, cardiac activity, and vasomotor response?
 - a. Pons.
 - b. Cerebellum.
 - c. Cerebral cortex.
 - d. Medulla oblongata.
7. (602) How many pairs of nerves branch off of the spinal cord?
 - a. 28.
 - b. 29.
 - c. 30.
 - d. 31.

8. (602) Which portion of the peripheral nervous system controls all of our conscious awareness of the external environment and motor activity?
 - a. Somatic.
 - b. Autonomic.
 - c. Sympathetic.
 - d. Parasympathetic.
9. (602) Which effect can be attributed to the parasympathetic nervous system?
 - a. Pupil dilation.
 - b. Bronchial tube constriction.
 - c. Blood pressure increase.
 - d. Peristalsis suppression.
10. (603) What spinal cord disorder involves the disappearance of myelin causing the nerve axons to degenerate?
 - a. Poliomyelitis.
 - b. Paraplegia.
 - c. Multiple sclerosis.
 - d. Amyotrophic lateral sclerosis.
11. (604) What brain disorder is caused by an obstruction of the flow of cerebrospinal fluid?
 - a. Meningitis.
 - b. Subdural hematoma.
 - c. Trigeminal neuralgia.
 - d. Hydrocephalus.
12. (605) What term is interchangeable with bipolar disorder?
 - a. Schizophrenia.
 - b. Manic-depressive illness.
 - c. Anxiety.
 - d. Chronic depression
13. (605) A decreased need for sleep, uncharacteristically poor judgment, and an unrealistic belief in one's abilities and power are symptoms of which psychotic disorder?
 - a. Schizophrenia.
 - b. Mania.
 - c. Anxiety.
 - d. Depression.
14. (606) Early treatment with what drug slows the progression of Parkinson's disease?
 - a. Selegiline.
 - b. Carbidopa.
 - c. Ethambutol.
 - d. Levodopa.
15. (606) What neurotransmitter has recently been discovered to be deficient in adults diagnosed with ADHD?
 - a. Serotonin.
 - b. Dopamine.
 - c. Norepinephrine.
 - d. Acetylcholine.

16. (607) To what neurotransmitter's receptor sites do benzodiazepines bind?
- Serotonin.
 - Dopamine.
 - Gamma-aminobutyrate.
 - Norepinephrine.
17. (607) Which medication increases the effects of benzodiazepines?
- Fexofenadine.
 - Carbamazepine.
 - Imipramine.
 - Fluoxetine.
18. (608) What interaction occurs when tricyclic antidepressants are given concomitantly with clonidine?
- Respiratory depression.
 - Increased toxic effects of clonidine.
 - Hypertensive crisis.
 - Extreme anticholinergic symptoms.
19. (608) Which antidepressant drug alters sodium transport in nerve and muscle cells and may reduce concentration of catecholamine neurotransmitters?
- Diazepam.
 - Hydroxyzine.
 - Fluoxetine.
 - Lithium.
20. (608) What adverse reaction may occur when trazadone is used in patients recovering from myocardial infarction?
- Arrhythmia.
 - Hypotension.
 - Edema.
 - Tachycardia.
21. (609) Which benzodiazepine is used strictly for sleep?
- Diazepam.
 - Temazepam.
 - Lorazepam.
 - Alprazolam.
22. (609) Into which pregnancy category does temazepam fall?
- A.
 - B.
 - X.
 - D.
23. (610) In what part of the brain do benzodiazepines exert their anticonvulsant activity?
- Midbrain.
 - Cerebral cortex.
 - Brainstem.
 - Motor cortex.

-
24. (610) To which class of antidepressant is carbamazepine related?
- a. Selective Serotonin Reuptake Inhibitors (SSRIs).
 - b. Tricyclic.
 - c. Monoamine Oxidase Inhibitors.
 - d. Lithium.
25. (611) What is the relationship between antipsychotic drug potency and side effects?
- a. Low potency drugs tend to be more sedating.
 - b. Low potency drugs have more non-CNS effects.
 - c. High potency drugs tend to be more sedating.
 - d. High potency drugs have less non-CNS effects.
26. (611) What antipsychotic is indicated for treatment of Tourette's syndrome?
- a. Chlorpromazine.
 - b. Risperidone.
 - c. Thioridazine.
 - d. Haloperidol.
27. (612) Diphenhydramine and meclizine produce their anti-emetic effects by inhibiting what neurotransmitter?
- a. Dopamine.
 - b. Norepinephrine.
 - c. Serotonin.
 - d. Acetylcholine.
28. (613) How does methylphenidate effect patients with a history of seizure disorder?
- a. It may lower the seizure threshold.
 - b. It may raise the seizure threshold.
 - c. CNS stimulant activity is increased.
 - d. CNS stimulant activity is decreased.
29. (613) Which class of medications may decrease the effectiveness of dextroamphetamine?
- a. Antihistamines.
 - b. Antineoplastics.
 - c. Tricyclic antidepressants.
 - d. Selective serotonin reuptake inhibitors (SSRI)

Student Notes

Unit 2. The Respiratory System

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RESPIRATION means “to breathe again.” The fundamental purpose of the respiratory system is to supply oxygen to the individual tissue cells and to remove their gaseous waste product, carbon dioxide. The pathway that air takes through our body to get oxygen into our blood is amazing. This section is broken into two parts. The first part we’ll look at the anatomy of the respiratory system and then we’ll dive in to seeing just how we breathe.

2-1. Anatomy and Physiology of the Respiratory System

The respiratory system is an intricate arrangement of spaces and passageways that serve to conduct air into the lungs. These spaces include the nasal cavities; the pharynx, which is common to the digestive and respiratory systems; the voice box, or larynx, the windpipe, or trachea and the lungs, with their tubes and air sacs. The entire system might be thought of as a pathway for air between the atmosphere and the blood (fig. 2-1).

614. Anatomy of the respiratory system

This lesson covers the basics. We’ll start with the nasal cavities, pharynx, larynx, trachea, and bronchi and then move on to the lungs themselves.

The nasal cavities

Air makes its initial entrance into the body through the openings in the nose called the nostrils. Immediately within are the two spaces known as the nasal cavities, located between the roof of the mouth and the cranium. These two spaces are separated from each other by a partition, the nasal septum. The septum and the walls of the nasal cavities are constructed of bone covered with mucous membrane. From the lateral (side) walls of each nasal cavity are three projections called the conchae. The conchae greatly increase the surface over which the air must travel on its way through the nasal cavities.

The lining of the nasal cavities contains many blood vessels; hence it is described as a vascular membrane. The blood brings heat and moisture to the mucosa. As much as a quart of liquid is secreted daily by this membrane. The advantages of breathing through the nasal cavities over breathing through the mouth are due to the various changes effected on the air as it comes in contact with the parts of the nose, particularly the lining. The following changes take place:

1. Foreign bodies, such as dust particles and pathogens, are removed by either being strained out by the hairs of the nostrils or being caught in the surface mucus.
2. The blood in the vascular mucosa warms the air.

3. The liquid secretions moisten the air.

Also included in the discussion of the nasal cavities are the sinuses, which are small cavities lined with mucous membrane, in the bones of the skull. The sinuses communicate with the nasal cavities, and they are highly susceptible to infection.

Another feature of the nasal cavities is a small duct communicating indirectly with the glands that produce tears. This is the nasolacrimal duct, and its presence explains why the nose runs when tears flow freely. The nasal cavities also contain the receptors for the sense of smell.

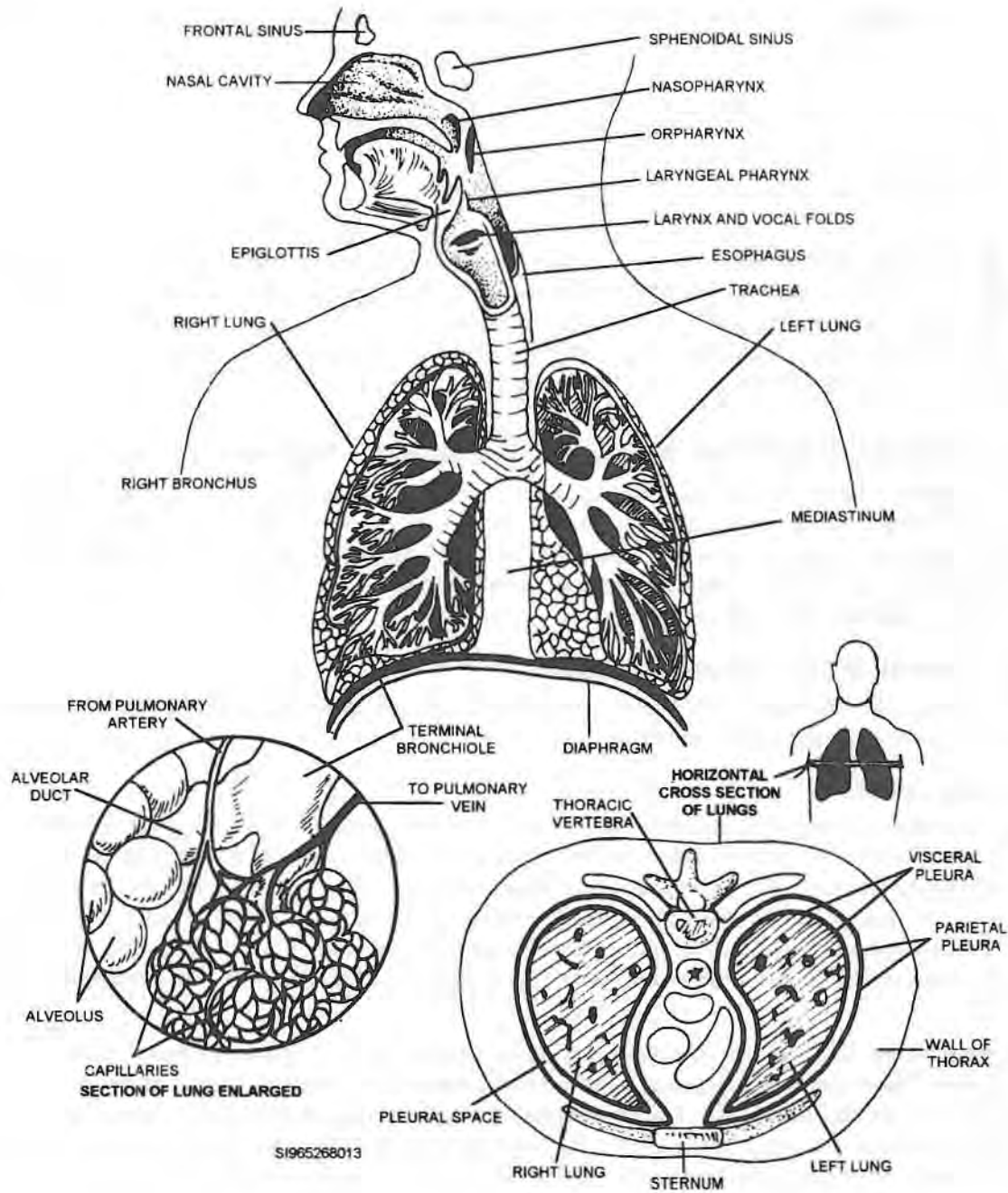


Figure 2-1. The respiratory system.

The pharynx

The muscular pharynx serves as a passageway for air into the respiratory tract, and for foods and liquids into the digestive system. The upper portion located immediately behind the nasal cavity is called the nasopharynx. The middle section located behind the mouth is called the oropharynx and finally the lowest portion is the laryngeal pharynx. This last section opens into two spaces:

- The air passageway into the larynx is toward the front.
- The food path, toward the back, enters the esophagus.

The space between the vocal cords is called the glottis, and the little leaf-shaped structure that closes this opening during swallowing is called the epiglottis. By the action of the epiglottis, food is kept out of the remainder of the respiratory tract. The epiglottis acts as a lid or trapdoor. As the larynx moves upward and forward during swallowing, the epiglottis moves downward, closing the opening into the larynx. During breathing, the epiglottis rises to allow air to pass downward. The larynx is lined with ciliated mucous membrane. The cilia trap dust and other particles, moving them upward to the pharynx to be expelled, by coughing, sneezing, or blowing the nose.

The trachea

The trachea is a tube that extends from the lower edge of the voice box to the center of the chest behind the heart. It has a framework of cartilage to keep it open. These cartilages, shaped somewhat like a tiny horseshoe or letter C, are placed near each other along the entire length of the trachea. All the open sections of these cartilages are at the back so that the esophagus can bulge into this region during swallowing. The purpose of the trachea is to conduct air between the larynx and lungs.

The bronchi

Near the center of the chest, behind the heart, the trachea divides into two bronchi. These two main air passageways enter the lungs, one on each side. The right bronchus is considerably larger in diameter than the left and extends downward in a more vertical direction. Therefore, if a foreign body is inhaled, it is likely to enter the right lung. Each bronchus enters the lung at a notch or depression called the hilus. In this same region, the blood vessels and nerves also connect with the lung.

The bronchi contain small bits of cartilage that give firmness to the walls and serve to hold the passageways open so that air can pass in and out easily. However, as the bronchi become smaller, the cartilage decreases in amount until finally, in the most minute subdivisions (bronchioles) there is no cartilage at all.

The lungs

The lungs are the organs in which external respiration takes place; that is, where blood and air meet through the medium of the extremely thin and delicate lung tissues. There are two lungs, set side by side in the thoracic cavity.

As soon as each bronchus enters the lung at the hilus, it immediately subdivides. These branches or subdivisions of the bronchi resemble the branches of a tree, hence the common name, bronchial tree. Each individual bronchus subdivides repeatedly, forming progressively smaller divisions. The smallest are called bronchioles.

At the end of each of the smallest subdivisions of the bronchial tree, called terminal bronchioles, there is a cluster of air sacs, resembling a bunch of grapes, known as alveoli. Each alveolus is a single-cell layer of squamous (flat) epithelium. This very thin wall provides an easy passage for the gases entering and leaving the blood as it circulates through the millions of tiny capillaries of the alveoli. Certain cells in the alveolar wall produce surfactant, a substance that prevents the alveoli from collapsing. There are millions of alveoli in the human lung. The resulting surface approximates 60 square meters, about three times as much lung tissue as is necessary for life. Surely, nature allowed an ample margin of safety! Because of the many air spaces, the lung is light in weight and, normally, a piece of lung tissue dropped into a glassful of water will float.

The lungs occupy a considerable portion of the thoracic cavity, which is separated from the abdominal cavity by the muscular partition known as the diaphragm. Each lung is enveloped in a sac of serous membrane called the pleura. The portion of the pleura attached to the chest wall is called parietal pleura, while that which is reflected onto the surface of the lung is called visceral pleura.

The pleural cavity around the lungs is an airtight space having a partial vacuum. The pressure in this space is less than the atmospheric pressure. The pressure inside the lungs is higher than in the surrounding pleural cavity.

The entire thoracic cavity is flexible, capable of expanding and contracting along with the lungs. Its interior is well sealed off from the outside by its layer of membrane; and, as we shall see, this is a feature of the mechanism of breathing.

Between the lungs is the mediastinum that contains the heart, great blood vessels, esophagus, and lymph nodes.

615. Respiratory system physiology

This lesson explains how we breathe. We'll cover ventilation, air movement, the exchange, and transport of gas. Then we'll look into the regulation of respiration and respiratory rates.

Ventilation

Ventilation is the movement of air into and out of the lungs. Breathing is the usual means of ventilating the lungs, but artificial respiration, as taught in first-aid classes, or use of various mechanical devices may be required to obtain adequate lung ventilation.

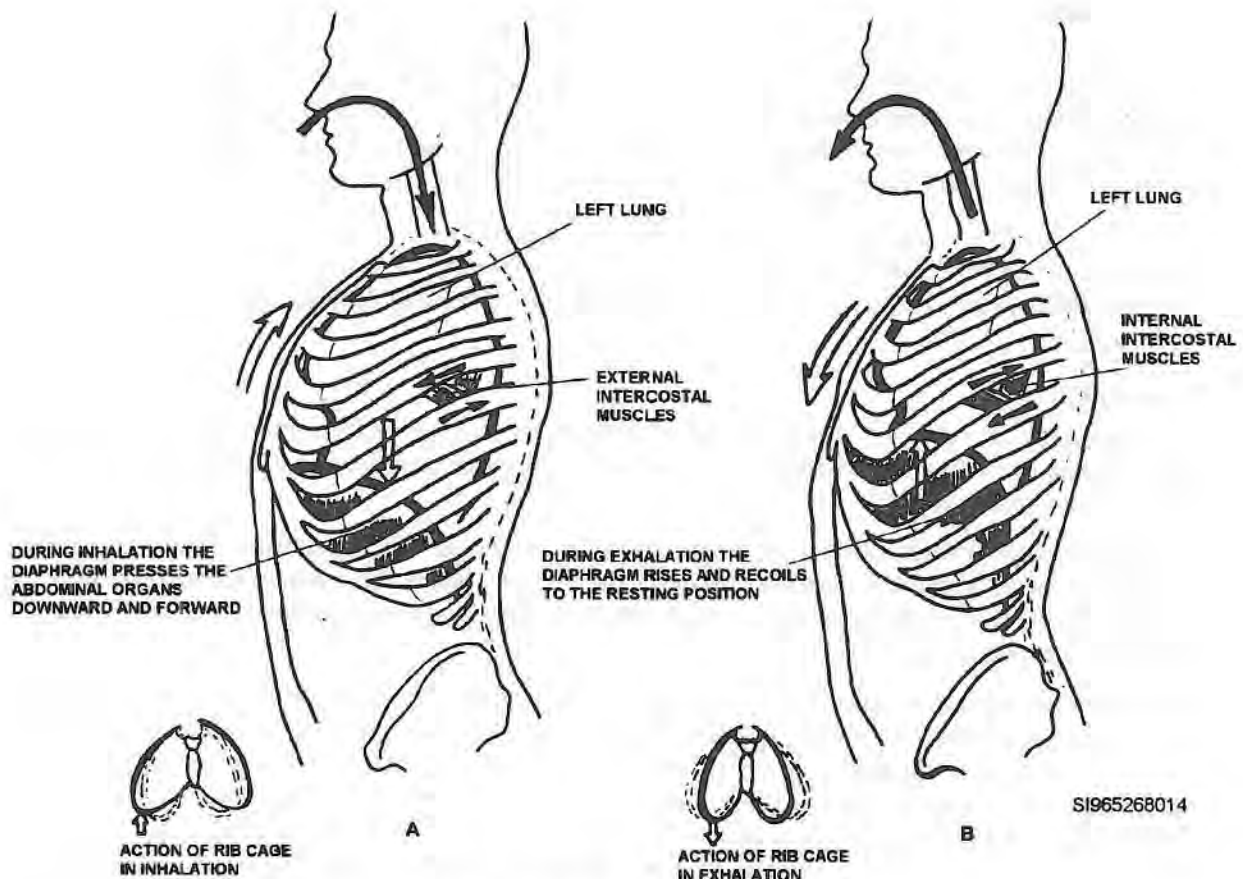


Figure 2-2. (A) Inhalation and (B) exhalation.

There are two phases of breathing:

1. Inhalation—drawing of air into the lungs.
2. Exhalation—expulsion of air from the lungs.

Inhalation is the active phase of breathing, since it is then that the respiratory muscles contract to enlarge the thoracic cavity. The diaphragm is a strong dome-shaped muscle attached around the base of the rib cage. The contraction and flattening of the diaphragm cause a piston-like downward motion that results in an increase in the vertical dimension of the chest. The rib cage also moves upward and outward owing to the action of the diaphragm with the assistance of the external intercostals and other muscles. During quiet breathing, the movement of the diaphragm accounts for 75 percent of the increase in thoracic volume.

Exhalation is the passive phase of breathing, since the muscles of respiration then relax, allowing the lungs and chest wall to return to their original position (fig. 2-2).

Air movement

Air enters the respiratory passages and flows through the ever-dividing tubes of the bronchial tree. As the air traverses this passage, it moves more and more slowly through the great number of bronchial tubes until there is virtually no forward flow as it reaches the alveoli. Here the air moves by diffusion, which soon equalizes any differences in the amounts of gases present. Each breath causes relatively little change in the gas composition of the alveoli, but normal continuous breathing ensures the presence of adequate oxygen and the removal of carbon dioxide.

Gas exchanges

The barrier that separates the air in the alveolus from the blood in the capillary is very thin and is ideally suited for the exchange of gases by diffusion. Normally, inspired air contains about 21 percent oxygen, while expired air has only 16 percent oxygen along with 3.5 percent carbon dioxide. A two-way diffusion takes place through the walls of the alveoli. Blood entering the lung capillaries is relatively lower in oxygen, which means that oxygen will diffuse from the alveolus, where its concentration is higher, into the blood. Carbon dioxide diffuses out of the blood into the air of the alveolus.

Gas transport

The oxygen that diffuses into the lung capillary blood is bound to the hemoglobin of the red blood cell. The hemoglobin becomes a brighter red as it combines with larger amounts of oxygen, so oxygenated blood is a scarlet color, while deoxygenated blood is a dusky crimson red. The arterial blood (in systemic arteries and pulmonary veins) is 97 percent saturated with oxygen, while venous blood (in systemic veins and pulmonary arteries) contains about 70 percent oxygen saturation. The bond between oxygen and hemoglobin is easily broken so oxygen can be readily released for use by the body cells. The carbon dioxide produced in the tissues is transported to the lungs in three ways:

1. Most is transported as a compound, known as bicarbonate, which is formed by the union of the gas carbon dioxide with water.
2. Some is dissolved in the plasma.
3. Some is also combined with protein substances in the blood plasma.

The bicarbonate compound is formed slowly in the plasma but much more rapidly inside the red blood cells where an enzyme called carbonic anhydrase increases the speed of the reaction. These larger amounts of bicarbonate formed in the red blood cells are returned to the plasma and then carried to the lungs. The bicarbonate releases carbon dioxide in the lungs for diffusion into the alveoli and exhalation.

Regulation of respiration

Regulation of respiration is a complex process, which must keep pace with the moment-to-moment changes in cellular oxygen requirements and carbon dioxide production. Regulation depends primarily upon the respiratory control centers located in the medulla and pons of the brain stem. Respiration is regulated so that the levels of oxygen, carbon dioxide, and acid are kept within certain limits. The control centers regulate the rate, depth, and rhythm of respiration. From the respiratory center in the medulla, motor nerve fibers extend into the spinal cord. From the cervical (neck) part of the cord, these nerve fibers continue through the phrenic nerve to the diaphragm. Unlike the heart, the diaphragm does not continue to function if it is cut off from its nerve supply. The diaphragm and the other muscles of respiration are voluntary in the sense that they can be regulated by messages from the higher brain centers, notably the cortex. It is possible for a person deliberately to breathe more rapidly or more slowly, or to hold his breath and not breathe at all for a time. Usually, we breathe without thinking about it, while the respiratory centers in the medulla and pons do the controlling.

Of vital importance in the control of respiration are the chemoreceptors. These receptors are found in structures called the carotid and aortic bodies, as well as in the medulla of the brain stem. We have noted that carbon dioxide is carried in the form of a compound-bicarbonate. This compound releases acid, so that one of the effects of an increase in the production of carbon dioxide is an increase in acidity (lower pH). The carotid bodies are located near the bifurcation of the common carotid arteries, while the aortic bodies are located on or near the aortic arch. These bodies contain many small blood vessels and sensory neurons, which are sensitive to a decreased oxygen supply as well as to increases in carbon dioxide and acid. Impulses are sent to the brain from the receptors in the carotid and aortic bodies. The receptor cells in the medulla are affected by the concentrations of carbon dioxide and acid in the fluids related to it.

Respiratory rates

Normal rates of breathing vary from 12 to 20 times per minute for adults. In children, rates may vary from 20 to 40 times a minute, depending on age and size. In infants, the respiratory rate may be more than 40 times per minute. To determine the respiratory rate, the healthcare worker counts the client's breathing for at least 30 seconds, observing in such a way that the person is unaware that a count is being made. Changes in respiratory rates are important in various disorders and should be carefully recorded.

Abnormal respiration

The following is a list of terms describing symptoms that refer to abnormal respiration:

1. Hyperpnea – over breathing due to abnormally rapid respiratory movements. This refers to an increase in depth as well as rate of respiration.
2. Apnea – temporary cessation of breathing.
3. Dyspnea – difficult or labored breathing.
4. Cheyne-Stokes respiration – a type of rhythmical variation in the depth of respiratory movements found in certain critically ill persons.

Situations that occur in relation to changes in respiration may include the following:

- Cyanosis is a bluish color of the skin and mucous membranes caused by an insufficient amount of oxygen in the blood.
- Hypoxia and anoxia are often used interchangeably to mean reduced oxygen supply to the tissues.
- Suffocation is the stoppage of respiration, often the result of a mechanical blockage of the respiratory passages. Suffocation can cause asphyxia, which is a lack of oxygen in the inspired air.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

614. Anatomy of the respiratory system

1. Where are the nasal cavities located?
2. What separates the two nasal cavities?
3. What is the nasolacrimal duct?
4. What term describes the upper portion of the pharynx that is located behind the nasal cavity?
5. What is the purpose of two spaces found in the laryngeal pharynx?
6. What is the purpose of the trachea?
7. What term describes the smallest subdivision of each individual bronchus?
8. What are alveoli?
9. What substance prevents the alveoli from collapsing and where is it produced?
10. What is the portion of the pleura that is attached to the chest wall called?

615. Respiratory system physiology

1. What is ventilation?
2. What are the two phases of breathing?

3. What percentage oxygen is in arterial blood? Venous blood?
4. What are the three ways that carbon dioxide produced in the tissues is transported to the lungs?
5. Where are the chemoreceptors that control respiration located?
6. What is the normal respiratory rate of an adult? Child?
7. What term describes a temporary cessation of breathing?

2-2. Conditions Associated with the Respiratory System

Respiratory system problems are some of the worst that we can have. If it is difficult for you to breathe, then it's difficult to do pretty much anything. This section covers disorders from the common cold to asthma, pneumonia, and emphysema. The section is divided into two lessons, conditions affecting the upper respiratory system and those affecting the lower respiratory system.

616. Conditions affecting the upper respiratory system

Many conditions affect the upper respiratory system. Some of them are pathological while some are more physical. First, I guess that I'll define "upper respiratory system." The upper respiratory system includes the nose, throat, and larynx. The trachea and lungs make up the "lower respiratory system," which will be discussed later. The upper respiratory conditions that we'll be discussing are sinusitis, nasal polyps, deviated septum, nosebleeds, the common cold, allergies, and influenza.

Sinusitis and nasal polyps

"I have sinus" is an expression that many people use to indicate disease of the sinuses. The sinuses are located close to the nasal cavities and, in one case, near the ear. Infection may easily travel into these sinuses from the mouth, nose, and throat along the mucous membrane lining. The resulting inflammation is called sinusitis. Chronic sinus infections may cause changes in the epithelial cells, resulting in tumor formations. Some of these growths have a grape-like appearance and cause obstruction of the air pathway. These tumors are called polyps.

Deviated septum

The partition that separates the two nasal spaces from each other is called the nasal septum. Since many of us have minor structural defects, it is not surprising that the nasal septum is rarely exactly in the mid-line. If it is markedly to one side, it is described as a deviated septum. In this condition, one nasal space may be considerably smaller than the other. If such a person has an attack of hay fever or develops a cold with the accompanying swelling of the mucosa, this smaller nasal cavity may be completely closed. Sometimes, the septum is curved in such a way that both nasal cavities are occluded, forcing the person to breathe through their mouth. Such an occlusion may also prevent proper drainage from the sinuses and aggravate a case of sinusitis.

Nosebleeds

The most common cause of nosebleed is an injury or blow to the nose. Other causes include inflammation and ulceration, following a persistent discharge from a sinus. Growths including polyps, can also be a cause of nosebleeds. Rarely, will an abnormally high blood pressure cause the blood vessels in the nasal lining to break, resulting in a varying degree of hemorrhage. To stop the nosebleed, the victim should remain quiet with their head slightly elevated. Pressure applied to the nostril, as well as a cold compress place on the nose is usually helpful. In some cases, it may be necessary to insert a plug into the bleeding side in order to encourage adequate clotting. If these methods fail, a physician should be consulted.

The common cold and allergies

These two ailments affect the upper respiratory system but may also affect the lower as well. The cold virus causes the body to excrete copious amounts of mucous to try and expel it. This mucous and the resulting irritation clogs and swells nasal passageways making nasal breathing difficult if not impossible. Allergies have the same result, however they tend to cause inflammation of the passageway by activating a histamine response. More is discussed about this inflammatory response in the lesson discussing asthma.

Influenza

Influenza, or "the flu," is an acute, contagious disease characterized by an inflammatory condition of the upper respiratory tract accompanied by generalized aches and pains. It is caused by a virus and may spread to the sinuses as well as downward to the lungs. Inflammation of the trachea and bronchi causes the characteristic cough of influenza and the general infection brings about an extremely weakened condition of the victim. The great danger of influenza is its tendency to develop into a particularly severe form of pneumonia. At intervals in history, there were tremendous epidemics of influenza in which millions of people died. Vaccines have been effective, though the immunity is of short duration.

617. Conditions associated with the lower respiratory system

When we talk about the lower respiratory system; we mean the trachea and lungs. Conditions affecting this area of the body can be life threatening. When you can't breathe through your nose you can just breathe through your mouth. That option is not available with the lower respiratory tract. The conditions that we'll look at are asthma, chronic obstructive airway disease, emphysema, bronchitis, pneumonia, tuberculosis, pleurisy, and lung cancer.

Asthma

Asthma is an inflammatory disease of the airways. The immunologic and subsequent inflammatory reactions in the airways produce contraction of smooth muscle (e.g., bronchospasm), swelling of the airway wall, mucus secretion, and structural changes. These pathological effects result in airflow limitation and increased airway responsiveness to a variety of stimuli, which, in turn, cause the characteristic symptoms of asthma. The magnitude of the inflammatory reaction correlates with the severity of symptoms.

Patients may experience a sense of suffocation and have labored breathing (dyspnea). A lot has been written about the part that psychological factors play in causing asthma. It would seem advisable to leave the decision concerning the possible causes in the hands of the family physician or the specialist he/she may recommend. Individuals vary considerably, and most cases of asthma present a multiplicity of problems.

Mast cells and eosinophils are the essential effector cells of the inflammatory response. When these cells are activated, they synthesize leukotriene from arachidonic acid, which is subsequently converted to three leukotriene metabolites. These three cysteinyl leukotrienes are mediators of inflammation and can produce many of the symptoms of asthma. Leukotriene biosynthesis appears to

be self-perpetuating in that LTE_4 , the end product of cysteinyl leukotriene metabolism, participates in the recruitment of eosinophils into the airways, which, after activation by cytokines, generate more of these inflammatory mediators. Eosinophils also release proteins that damage the epithelial lining of the airways resulting in an increase in airway responsiveness.

Diagnosis

Establishing the diagnosis is critical to successfully dealing with asthma. This is especially so because of the frequency with which asthma has historically been misdiagnosed. Particularly, but not exclusively in children, the symptoms resulting from airway inflammation associated with asthma have been misdiagnosed as pneumonia and bronchitis. This leads to ineffective and unnecessary use of antibiotics while exposing the patient to the problems of ongoing disease. *Asthma should therefore be considered in the presence of the following clinical presentations:*

- Recurrent or chronic lower respiratory wheezing.
- Recurrent or chronic coughing.
- Repeated diagnoses of bronchitis (in children and nonsmokers).
- Repeated diagnoses of pneumonia.

The diagnosis is most efficiently confirmed by demonstrating the complete response of acute symptoms, when present, to an inhaled β_2 -agonist and/or a 5 to 10 day course of high-dose oral corticosteroids. Patients not clearly made asymptomatic with these measures should be referred to an appropriate subspecialist for reevaluation of the diagnosis.

Classification by clinical pattern

Managing asthma requires identification of the following clinical patterns:

Intermittent—patients with episodic illness interspersed with extended symptom-free periods. These are most commonly triggered by viral respiratory infections or exposure to a specific allergen (e.g., cat dander in a cat-sensitive patient).

Chronic—patients with virtually daily symptoms without extended symptom-free periods in the absence of continuous medication.

Seasonal allergic—patients with virtually daily symptoms during an inhalant allergy season; this is most commonly from outdoor molds that grow on decaying vegetation from early spring through late fall with peaks particularly in the spring and fall. These patients do not have chronic symptoms during other seasons when the allergen to which they are sensitive is not present. For example, a patient with grass pollen-induced asthma may have chronic symptoms during the spring when grass pollen is in the air but have intermittent symptoms during summer, fall, and winter.

It is important to note that severity, as assessed by degree of disease, is independent of clinical pattern. Intermittent disease may be life-threatening and chronic disease may be relatively benign.

There is some overlap among these since patients with chronic disease often have intermittent exacerbations from viral respiratory illness, and patients with chronic disease may have seasonal allergic exacerbations. Nonetheless, identification of the clinical pattern leads logically to a therapeutic strategy.

Therapeutic strategies

Therapeutic strategies fall into two categories:

1. *Intervention*—measures to stop acute symptoms.
2. *Maintenance*—measures to prevent symptoms.

All patients require availability of efficient and effective intervention measures. These should be available at home and the patient/families should be taught when and how to apply them. Patients

with chronic disease additionally need maintenance medication to prevent their daily symptoms. Patients with seasonal allergic disease may require maintenance medication only seasonally, and patients with chronic disease may require seasonal increases in their maintenance medication.

Intervention for exacerbations

- A Short-acting Inhaled β_2 -selective agonist.
- A short course of oral corticosteroids.

Maintenance therapy

- A Long-acting Beta agonist.
- Mast cell stabilizer
- Inhaled corticosteroids.
- Xanthine-derivative bronchodilator.
- Leukotriene inhibitors/antagonists.

Nonpharmacological measures

Identification of triggers of asthma and avoidance measures

Triggers of asthma such as passive exposure to cigarette smoke and allergens should be identified and the patient given advice on how to avoid them. If a patient with asthma smokes, they should be referred to a smoking cessation program. If care givers or other members of the household smoke, they should be encouraged to discontinue smoking. If they cannot stop, they should only smoke outside the house and never in an automobile in which the patient with asthma rides.

All patients requiring maintenance medication for chronic asthma should be evaluated for sensitivity to allergens in the home environment. Avoidance measures should be instituted when possible. For example, if the patient is allergic to house dust mites, their mattress should be covered with a special cover that seals in the mites and they should use a pillow and bedding that can be washed at $>130^\circ\text{F}$ once a week. If they are sensitive to animals, the animal should be removed from the home and the patient should not go into homes in which an animal lives. If the family is unwilling to remove a dog or cat from the home, keeping the animal out of the patient's bedroom and washing it twice a week may decrease the effects on the patient. Several studies indicate that removing the patient from allergen exposure results in less symptoms and a decrease in medication requirements. On the other hand, failure to reduce exposure to allergens can result in the need for higher doses of inhaled corticosteroids and more frequent short courses of daily prednisone.

Home monitoring of lung function

Measurement of the peak expiratory flow rate (PEFR) with an inexpensive handheld peak flow meter provides an objective measure of lung function. It is useful to guide therapy but few patients routinely use a peak flow meter, especially when they are feeling good. However, if it is prescribed for short periods while increasing medication to gain control or while weaning medication in the well controlled patient to determine the minimal amount of medication required, many patients will adhere to the regimen. It is particularly useful for patients who don't feel symptoms until their lung function is dangerously low. Also, patients may be willing to measure their peak flow during exacerbations if they are given an action plan to use in response to a threshold measurement. For example, a patient can be given instructions to call their physician or start a short course of prednisone when the PEFR drops below a predetermined value, and doesn't improve after the use of an inhaled bronchodilator. Such a plan will decrease costly emergency department visits and hospitalizations for asthma.

Chronic obstructive airways disease

Chronic obstructive airways disease (COAD) refers to conditions of chronic airflow limitation. Other terms include chronic obstructive pulmonary disease (COPD) and chronic obstructive lung disease (COLD). All are characterized by a reduction in air outflow, measured as impaired expiratory flow,

that doesn't change much over several months. COAD is termed as reversible if patients exhibit significant improvement when treated with bronchodilators.

COAD is the fifth leading cause of death in the United States. It affects over 15 million people nationwide, causing significant disability and over 99,000 deaths annually. It is not uncommon to encounter COAD with other chronic illnesses.

COAD is represented mainly by emphysema and chronic bronchitis, but also includes peripheral airway disease and asthmatic bronchitis. The pathophysiology of COAD is characterized by both acute and chronic inflammation, as well as changes in cellular growth. This leads to tissue destruction, structural changes, smooth muscle hypertrophy, and scarring. Patients with COAD will exhibit varying degrees of bronchial hyperreactivity and reversibility of obstruction. There are three stages of the disease. First, bronchial changes of enlarged mucous glands, inflammation, and bronchial wall thickening, which is typical of chronic bronchitis. Second, the alveolus become inflamed and enlarged. Finally, inflammation, fibrosis, and narrowing of small airways contribute to increased airway resistance and obstruction. The consequences of the changes are worsened by obstruction, hyperinflation of the lungs, increased sputum production, recurrent respiratory infections and poor gas exchange. End results include respiratory muscle fatigue, ventilatory disorders, cardiovascular damage, and poor quality of life.

Diagnosis and categorization

COAD is diagnosed using pulmonary function tests. The main indication of the disease is the measurement of forced expiratory volume (FEV). The measurement is made comparing the volume expired in one second (FEV₁) versus the total forced vital capacity for a normal breathing patient of the same height, weight, and age (FVC). A patient is considered to have COAD when FEV₁ is less than 75 percent of FVC. Mild obstruction is characterized by a ratio of 60 percent to 75 percent, moderate 50 percent to 60 percent, and severe obstruction to airflow occurs when the ratio is less than 50 percent.

Emphysema

Emphysema results from the physical changes of the lung tissue characterized by abnormal permanent enlargement of the air spaces distal to the terminal bronchiole, along with destruction of the alveolar walls. It is the destruction of the alveoli that results in the loss of elasticity and structural support resulting in obstruction and airway collapse during exhalation. With chronic symptoms, patients' bodies adapt and use accessory muscles of respiration causing a prolonged expiratory phase.

There are two types of emphysema, defined by their areas of involvement. Centriacinar emphysema is found predominantly in the proximal part of the lobe, is associated with cigarette smoking, and is normally diagnosed around age 60. Panacinar emphysema involves the entire lung and is associated with an enzyme deficiency, a genetic defect. This type of emphysema accounts for 2 percent of all cases and the disease is diagnosed as early as age 20.

Chronic bronchitis

Chronic bronchitis is normally seen as excessive mucus production and secretion resulting in airflow obstruction secondary to inflammation and edema. Inflammation and edema of mucosa and mucus glands found in the small and medium size airways of the bronchial tree result in copious production of thick secretions. The increased mucus is an excellent media for recurrent bronchial infections resulting in further damage. Airflow obstruction results from airway narrowing from edema of bronchial walls and occlusion by increased mucus secretion. Repeated infections result because of the inability to clear the mucus and mucous plugs.

Characteristically, chronic bronchitis patients appear at 45 to 65 years old. They complain of a chronic, productive cough, moderate dyspnea, and recurrent respiratory infections. This patient is often obese and suffers from abnormally low oxygenation of arterial blood, causing cyanosis. Later

stages of the disease include increased red cell production (polycythemia), and congestive heart failure secondary to pulmonary hypertension.

Therapeutic strategies

General management principles are directed toward educating the patient about his condition, minimizing the progression of airflow limitation, and optimizing functional abilities. Proper coughing techniques, chest percussion, and aggressive hydration are important strategies for the COAD patient.

Medication therapy must be carefully selected.

1. Bronchodilators can increase airflow in patients with reversible obstruction and reduce dyspnea.
2. Oral corticosteroids help, but the risk may outweigh the benefits.
3. Theophylline is frequently used in COAD for its effects on diaphragm function.

Of course, any COAD patient who smokes is strongly encouraged to get smoking cessation therapy.

Pneumonia

Pneumonia is an inflammation of the lungs in which the air spaces become filled with fluid. A variety of organisms including staphylococci, streptococci, *Legionella pneumophila* (as Legionnaire's disease), chlamydiae, or viruses may be responsible. Many of these pathogens may be carried by a healthy person in the mucosa of the upper respiratory tract. If the person remains in good health, these pathogens may be carried for an indefinite period with no ill effect. However, if the individual's resistance to infection is lowered, the pathogens then may invade the tissues and cause disease. Exposure to inclement weather for long periods of time, alcoholism, malnutrition, a severe injury, or other debilitating or weakening conditions may cause a susceptibility to pneumonia.

There are two main kinds of pneumonia as determined by the method of lung involvement and other factors—lobar pneumonia and bronchopneumonia. With lobar pneumonia, an entire lobe of the lung is infected at one time. The organism is usually a pneumococcus, although other pathogens also may cause this disease. The *Legionella* organism is the causative agent of a severe lobar pneumonia that occurs mostly in localized epidemics. Bronchopneumonia, in which the disease process is scattered here and there throughout the lung. The cause may be a staphylococcus, a gram-negative proteus, or colon bacillus (not normally pathogenic), or a virus. Bronchopneumonia most often is secondary to an infection or to some agent that has lowered the individual's resistance to disease. This is the more common form of pneumonia.

A characteristic of most types of pneumonia is the formation of a fluid, or exudate in the infected alveoli; this fluid consists chiefly of serum and pus cells, products of infection. Some red blood cells may be present, as indicated by red streaks in the sputum. Sometimes so many air sacs become filled with fluid that the victim finds it hard to absorb enough oxygen to maintain life.

Tuberculosis

Tuberculosis is an inflammation caused by the bacillus *mycobacterium tuberculosis*. Although the tubercle bacillus may invade any tissue in the body, the lung is the usual site. Tuberculosis remains a leading cause of death from communicable disease primarily because of the relatively large numbers of cases among recent immigrants and poor population groups in metropolitan areas.

The lungs, with the pleuras, are the organs affected most often by tuberculosis. The bacillus can be spread in a number of ways, chiefly by inhalation. The sputum deposited by a person who carries the organism dries out; and the bacilli, which are extremely hardy, are carried about for long periods of time in the dust of the air from which they are inhaled by another individual. This organism withstands exposure to many disinfectants, but it is vulnerable to sunlight. Therefore, we might expect to find the greatest frequency of tuberculosis to be among the poorer inhabitants of the large

cities, where disease and malnutrition are common and where there is a maximum of crowding and a minimum of fresh air and sunlight.

In addition to the lungs, many other organs may become infected by tubercle organisms. The lymph nodes in the thorax, especially those surrounding the trachea and the bronchi, frequently are involved. Tuberculous pleurisy (inflammation of the pleura) with fluid formation is fairly common. The fluid may collect in the pleural cavity, and such a collection is called an effusion. The fluid presses against the pleura and compresses the lung. The fluid may be absorbed over a period of time, if it is not removed artificially to relieve pressure against the lung. Chronic hoarseness may be due to tuberculosis (or cancer) of the larynx. Other organs that may be infected by tubercle organisms include the kidneys, certain tubes of the reproductive system and, particularly in children, the bones of the vertebral column. Occasionally, vast numbers of the organisms may enter the bloodstream and cause a rapidly fatal tuberculosis.

Drugs are used quite successfully in many cases of tuberculosis. However, this chemotherapy may have the undesirable effect of producing resistant strains of bacteria. These resistant organisms can be transmitted to additional victims, who then cannot be treated effectively with these particular medications. Best results have been obtained by the use of a combination of several drugs, along with prompt, intensive, and uninterrupted treatment once such a program is begun. Such therapy is usually continued for a minimum of 12 to 18 months, therefore, close supervision by the healthcare practitioner is important. Adverse drug reactions are rather common, necessitating changes in the drug combinations.

Lung cancer

The death rate due to cancer of the lungs has increased more than 25 times in males, and more than doubled in females in the last 45 years. It is considerably higher in industrial areas. By far, the most important cause of lung cancer is cigarette smoking. Additionally, smokers who are exposed to toxic chemicals or particles in the air have an even higher rate of lung cancer. Smoking has also been linked with an increase in chronic obstructive pulmonary disease and cancers of respiratory passages.

Early lung cancer has few symptoms. However, it may be discovered during a routine chest x-ray examination. Too often, emphasis upon the danger of exposure to radiation from x-ray machines can frighten people away from routine chest x-ray examination thus prevent an early diagnosis of lung cancer. Early detection is absolutely essential if any possibility of a cure is to be maintained. Modern x-ray machines in competent hands pose such slight danger, at least to those over 40 years old, that this would be greatly offset by the advantages of discovering a tumor while it is still small enough to be completely removed. A common form of lung cancer is bronchogenic carcinoma, so-called because the malignancy originates in a bronchus. The tumor may grow until the bronchus is blocked, cutting off the supply of air to that lung. The lung then collapses, and the secretions trapped in the lung spaces become infected, with a resulting pneumonia or the formation of a lung abscess. Such a lung cancer can also spread to cause secondary growths in the lymph nodes of the chest and neck as well as in the brain and other parts of the body. The only treatment that offers a possibility of cure, before secondary growths have had time to form, is to remove the lung completely. This operation is called a pneumonectomy. Malignant tumors of the stomach, breast, prostate gland, and other organs may spread to the lungs, causing secondary growths.

Pleurisy

Pleurisy is inflammation of the pleura, and it usually accompanies a lung infection, particularly pneumonia and tuberculosis. This condition can be quite painful, because the inflammation produces a sticky exudate that roughens the pleura of both the lungs and chest wall; when the two surfaces rub together during respiration, the roughness causes acute irritation. If the two surfaces stick together, this condition is called an adhesion. Infection of the pleura also causes an abnormal flow of pleural fluid. This may accumulate in the pleural cavity in such large amounts that the lung will be

compressed, and the patient cannot obtain enough air. Withdrawal of the fluid by chest tube or syringe may be necessary.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

616. Conditions affecting the upper respiratory system

1. What is sinusitis?
2. What term describes the nasal septum if it is located markedly to one side of the nasal spaces?
3. What is influenza?

617. Conditions affecting the lower respiratory system

1. What are Mast cells and how do they affect respiratory inflammation?
2. What are the three classifications of asthma?
3. What is the fifth leading cause of death in the United States?
4. What causes emphysema?
5. Other than the lungs, what organs may be affected by tuberculosis?

2-3. Drugs Used to Treat Conditions of the Respiratory System

There are quite a few drugs that are used in the respiratory system. In this section we'll consider different dosage forms of the antihistamines and corticosteroids that we looked at earlier for topical use. We'll look at some old standards of respiratory care, expectorants, anti-tussives, and decongestants. The other drugs that we'll cover are bronchodilators, leukotriene inhibitors/antagonists, and mast cell stabilizers. There's a lot of stuff to cover, so let's get going.

618. Bronchodilators

Many respiratory tract disorders involve inflammation of the bronchiole. If this passageway is inflamed, the amount of room for air to pass is lessened. Bronchodilators do exactly as their name

implies. Bronchodilators are divided into two basic categories—sympathomimetics and xanthine derivatives.

Sympathomimetics

Sympathomimetics relieve reversible bronchospasm associated with asthma, bronchitis, or emphysema. This bronchodilation may also facilitate expectoration. Sympathomimetic bronchodilators stimulate alpha-adrenergic receptors, β_1 and β_2 receptors. It is the β_2 receptor stimulation that produces the bronchial dilation and vasodilation with the greatest benefit and minimal side effects. This fact makes the sympathomimetic agents the primary drug used to treat respiratory conditions.

Indications

Sympathomimetic bronchodilators are indicated for the relief of reversible bronchospasm associated with acute and chronic bronchial asthma, exercise-induced bronchospasm, bronchitis, emphysema, bronhiectasis, or other obstructive pulmonary diseases. The next table gives the pertinent information about the sympathomimetic bronchodilators.

Sympathomimetic	Route	Onset (mins)	Duration (hrs)	Dosed	Age	Main Side Effect
Albuterol	PO	within 30	4–8	qid	>2	CNS stimulation
	Inh	within 5	3–8	q4h	>4	
Metaproterenol	PO	aprox 30	4	tid-qid	>6	Tachycardia
	Inh	5–30	2–6		>12	
Pirbuterol	Inh	within 5	5	q4–6h	>12	CNS (tremor)
Salmeterol	Inh	within 20	12	bid	>12	Headache
Terbutaline	PO	30	4–8	q4–6h	>12	CNS (tremors)
	SC	5–15	1.5–4			
	Inh	5–30	3–6			
Isoproterenol	SL	aprox 30	1–2	up to 5 times daily	any	Cardiovascular palpitations
	IV	immediate	<1			
	Inh	2–5	0.5–2			
Ephedrine	PO	within 60	3–5	2–3 times daily	any	None listed
	SC	>20	<1			
	IM	10–20	<1			
	IV	-	-			
Epinephrine	SC	5–15	1–4	4–6 times daily	any	Palpitations Nervousness
	IM	-	1–4			
	Inh	1–5	1–3			

Contraindications

Patients suffering from hypersensitivity to sympathomimetics, cardiac arrhythmias associated with tachycardia, tachycardia or heart block caused by digitalis intoxication, angina, narrow angle glaucoma should not use sympathomimetic bronchodilators.

Warnings

Sympathomimetics may produce CNS stimulation and include jitteriness and hyperactivity in children.

Pregnancy - All sympathomimetic bronchodilators except terbutaline are in pregnancy category C. Terbutaline is category B. All β_2 sympathomimetics inhibit uterine contractions. Other side effects include increased heart rate, transient hyperglycemia, hypokalemia, cardiac arrhythmias, and increased fetal heart rate.

Lactation – Terbutaline and epinephrine are excreted into breast milk. The needs of the mother should be assessed before deciding to discontinue these medications.

Salmeterol is the only long acting bronchodilator discussed. It is not to be used to treat/relieve acute asthma symptoms. It is not to be used more than twice daily. Patients who add salmeterol to their treatment regime should discontinue regular short acting bronchodilator use and be instructed to use the short acting only for symptomatic relief if they develop symptoms during salmeterol use.

Drug Interactions

The following table lists medications that interact with Sympathomimetic Bronchodilators.

Drug	Interaction
Theophylline	All sympathomimetics may enhance effectiveness, possible toxicity
Lithium	Decreases sympathomimetics effectiveness
Oxytocic drugs	May cause hypertension
Tricyclic antidepressants	May cause dysrhythmia
MAO inhibitors	Headache, severe hypertension
Hypoglycemics	Diabetics may require increased doses of hypoglycemics
Digoxin	Digoxin levels may be decreased

Patient information

Inhalation

- Patient instructions are available with products. Many patients do not use metered-dose inhalers correctly, even after repeated instructions. Do not assume the patient understands the use of inhaled drugs and the proper administration technique. Use verbal instructions as well as an actual demonstration if possible. Repeat instructions at follow-up visits.
- Have patient tilt head back and keep the metered dose inhaler mouthpiece » 2 inches (or 2 finger widths) from open mouth or place the mouthpiece between open lips. Spacer devices are also available to aid the patient in proper administration of the drug. The patient should press down on the canister, breathe in slowly, hold breath for at least 10 seconds or as long as comfortable, then exhale. Administer pressurized inhalation during the second half of inspiration as the airways are open wider and the aerosol distribution is more extensive.
- Do not exceed recommended dosage; excessive use may lead to adverse effects or loss of effectiveness. Do not stop or adjust the dose.
- Do not change brands without consulting the physician or pharmacist.
- If more than one inhalation per dose is necessary, wait at least one full minute between inhalations (administer second inhalation at 3 to 5 minutes for isoproterenol and epinephrine, 2 minutes for metaproterenol).
- Notify physician of failure to respond to usual dosage or of dizziness or chest pain.
- Isoproterenol may cause the patient's saliva to turn pinkish-red.
- Salmeterol - Shake well before using. Salmeterol is not meant to relieve acute asthmatic symptoms, which should be treated with an inhaled, short-acting bronchodilator. The bronchodilator action usually lasts for at least 12 hours; therefore it should not be used more often than every 12 hours. While using salmeterol, seek medical attention immediately if the short-acting bronchodilator treatment becomes less effective for symptom relief, if more inhalations than usual is needed, or if more than the maximum number of inhalations of short-acting bronchodilator treatment prescribed for a 24-hour period is needed. If the patient uses > 4 inhalations per day of a short-acting beta 2 -agonist on a regular basis, or if more than one canister (200 inhalations per canister) is used in an 8-week period, then the patient should see the physician for re-evaluation of treatment. When using salmeterol to prevent

exercise-induced bronchospasm, administer the dose at least 30 to 60 minutes before exercise.

Oral

- Do not exceed prescribed dosage. If GI upset occurs, take with food.
- Sublingual tablets (Isuprel). Do not swallow; allow to dissolve under tongue.
- May cause nervousness, restlessness, insomnia (especially ephedrine); if these effects continue after reducing dosage, notify physician.
- Notify physician if palpitations, tachycardia, chest pain, muscle tremors, dizziness, headache, flushing or difficult urination (ephedrine) occurs, or if breathing difficulty persists.

Xanthine Derivatives

Xanthine derivatives are all different forms of theophylline. Theophylline directly relaxes the smooth muscle of the bronchi and pulmonary blood vessels, and stimulates the CNS. It is also a central respiratory stimulant. Theophylline has a potent effect on diaphragmatic contractility. This means that it can reduce the fatigability of diaphragm muscles allowing persons with COAD to breathe easier.

Indications

Theophylline is indicated for symptomatic relief or prevention of bronchial asthma and reversible bronchospasm associated with chronic bronchitis and emphysema.

Contraindications

Patients who display a hypersensitivity to this drug or suffer from peptic ulcer disease, untreated seizure disorder should not use any theophylline derivative.

Dosing

Theophylline can be used for patients of any age. Dosing is individualized and based on pulmonary improvement and/or clinical response. Dosages are calculated based on lean body weight, since theophylline doesn't distribute through fatty tissue.

Theophylline Maintenance Dosing

Patient Group	Maintenance Dosing
Children 1–9 years old	4mg/kg q6h
Children 9–16 and young adult smokers	3mg/kg q6h
Otherwise healthy non-smoking adults	3mg/kg q8h
Older patients	2mg/kg q8h
Patients with CHF	1–2 mg/kg q12h

Warnings

Excessive doses of theophylline may cause severe toxicity with ventricular arrhythmia, convulsion, or death. Normal doses may even cause an arrhythmia, dysrhythmia, or tachycardia.

Pregnancy and Lactation - Theophylline is in pregnancy Category C. Theophylline is distributed in breast milk and may cause irritability or other toxic signs in infants.

Adverse reactions

Theophylline may cause nausea, vomiting, diarrhea, induced gastroesophageal reflux, palpitations, tachycardia, hypotension, life-threatening ventricular arrhythmia, and tachypnea.

Interactions

Many drugs interact with theophylline. The following tables list the more prevalent ones.

Drugs that Decrease Theophylline Levels		
Barbiturates	Ketoconazole	Sympathomimetics (β -agonists) ¹
Charcoal	Rifampin	Carbamazepine ¹
Hydantoins	Loop diuretics	Isoniazid ¹

Drugs that Increase Theophylline Levels		
Allopurinol	Calcium channel blockers	Oral contraceptives
Thyroid hormones	Sympathomimetics (β -agonists) ¹	Corticosteroids
Beta blockers	Carbamazepine ¹	Quinolones
Ephedrine	Cimetidine	Macrolides
Isoniazid ¹		

¹ May increase or decrease theophylline levels.

Drugs that Theophylline Affects	
Medication	Interaction
Benzodiazepines	Theophylline may reverse sedation caused by benzodiazepines
Beta-agonists	These act synergistically with theophylline
Lithium	Reduced lithium plasma levels
Ranitidine	May increase ranitidine levels, increasing toxic effects
Tetracyclines	Increases theophylline adverse reactions

Patient information

- If GI upset occurs with liquid or nonsustained release forms, take with food.
- Do NOT chew or crush enteric coated or sustained release tablets or capsules.
- Take at the same time, with or without food, each day.
- Notify physician if nausea, vomiting, insomnia, jitteriness, headache, rash, severe GI pain, restlessness, convulsions or irregular heartbeat occurs.
- Avoid large amounts of caffeine-containing beverages, such as tea, coffee, cocoa and cola drinks or large amounts of chocolate; these products may increase side effects.

619. Corticosteroids

The discussion of corticosteroids (steroids) is broken into two parts. First, inhaled corticosteroids used in maintenance therapy and second, systemically administered corticosteroids. In general, steroids are used pharmacologically for their anti-inflammatory effects. They reduce inflammation by stabilizing leukocytes so that they don't release a destructive acid. If released, the acid causes phagocyte build up in the area and an edema (swelling). Steroids suppress the immune system by reducing activity in the lymph system. We often see young patients growth retarded with prolonged steroid use because at pharmacologic doses, systemically administered steroids suppress the release of corticotropin from the pituitary gland causing the hypothalamus-pituitary-adrenal axis (HPA) to be suppressed. Continued suppression of the HPA causes adrenal cortex atrophies.

Inhaled corticosteroids

Inhaled corticosteroids have proven to be exceptionally helpful in treating asthma, but reviews are mixed and studies show that only 10 percent of patients with COAD benefit from corticosteroid use.

Indications

Corticosteroids are indicated in the maintenance and prophylactic treatment of asthma. The next table provides dosing information on each of the inhaled corticosteroids. Relative potency is based on skin vasoconstrictive effects. Systemic absorption is given as percent of drug affecting the HPA.

Oral Inhalation Corticosteroid Comparison Chart					
Drug	Dosage Forms	Adult Dose	Pediatric Dose	Relative Potency	Systemic Absorption
Beclomethasone	MDI 42µg/puff	2-3 puffs tid-qid	1-2 puffs tid-qid	500	<5%
Dexamethasone	MDI 100 µg/puff	2 puffs tid-qid	2 puffs tid-qid	0.8	80%
Flunisolide	MDI 250µg/puff	2 puffs bid (max 8/day)	1-2 puffs bid (max 4/day)	100	20%
Triamcinolone	MDI 100 µg/puff	2 puffs tid-qid (max 16/day)	1-2 tid-qid (max 12/day)	100	0%
Budesonide	MDI 50 µg/puff Turbohaler 100 µg/inhal	400-600 µg/day in 2-4 doses	200-400 µg/day in 2-4 doses	1000	10%
Fluticasone	Diskhaler 50,100, 200 µg	100-1000 µg bid	50-100 µg bid	1000	1%

Contraindications

Corticosteroids are contraindicated for the relief of acute bronchospasm and in those patients who have shown any hypersensitivity to corticosteroids.

Warnings

Oral, pharyngeal, or laryngeal fungal infections may occur with corticosteroid use.

Pregnancy – Corticosteroids are in category C. Studies in animals have resulted in significant birth defects. There are no well controlled studies in pregnant women. Use these agents during pregnancy only if the benefit clearly justifies the potential risk to the fetus. Observe infants born of mothers who received substantial doses during pregnancy for adrenal insufficiency.

Lactation - Systemic glucocorticoids are excreted in breast milk. It is unknown whether inhaled corticosteroids are excreted in breast milk. Decide whether to discontinue nursing or to discontinue the drug.

Adverse Reactions – Light headedness, irritation of the nose and throat, flu-like symptoms, respiratory infections, pharyngitis, sinusitis, nausea.

Patient information

- Patient instructions are available with product.
- Rinse mouth with water without swallowing after each dose to reduce the risk of oral candidiasis. If the infection develops, treat with appropriate therapy. Corticosteroid therapy may need to be interrupted.
- Instruct patients whose systemic corticosteroids have been reduced or withdrawn to carry a warning card indicating the need for supplemental systemic steroids in the event of stress or severe asthmatic attack that is unresponsive to bronchodilators.

- Advise patients not to stop therapy abruptly. If discontinuation is necessary, contact the physician immediately.
- Medication is for preventive therapy only; do NOT use to abort an acute asthmatic attack; use at regularly scheduled intervals as prescribed, even if asymptomatic.
- Warn people who are on immunosuppressant doses of corticosteroids to avoid exposure to chickenpox or measles. Advise patients to seek medical advice without delay if they are exposed.
- Advise patients receiving bronchodilators (e.g., isoproterenol, metaproterenol, albuterol) by inhalation to use the bronchodilator several minutes before the corticosteroid inhalant to enhance penetration of the steroid into the bronchial tree and reduce potential toxicity from the inhaled fluorocarbon propellants in the 2 aerosols.
- Notify physician if sore throat or sore mouth occurs.

Systemically administered corticosteroids

Systemically administered corticosteroids are found both naturally occurring and synthetically produced. The natural steroids include hydrocortisone and cortisone. They are used for replacement therapy and as anti-inflammatories. Prednisone, prednisolone, and fludrocortisone are synthetic steroids with the same glucocorticoid and mineralocorticoid properties as the natural steroids. Triamcinolone, dexamethasone, methylprednisolone, and betamethasone are grouped together as synthetic steroids with only glucocorticoid properties and are used for their potent anti-inflammatory effects.

Indications

There are numerous indications for systemic steroid use. Focusing on the respiratory system, bronchial asthma and tuberculosis are the main two indications. COAD is an unlabeled use of systemic steroids.

Administration

The adrenal cortex produces most of its corticosteroids between 2 and 8 a.m. Corticosteroid therapy has the least suppression of the adrenal cortex when given during the maximum production time. Therefore, steroids should be given in the morning.

The exact dosage given is specific to the disease and to the patient. Each dosage must be individualized! After a favorable response has been achieved, the dose should be lowered to the minimum that is required to sustain the state of being. If the patient has been on the medication for longer than 7–10 days, the steroid dosage must be tapered. Abruptly discontinuing the steroid could cause a sudden reappearance of severe manifestations of the disease.

Alternate day therapy is a specific dosing regimen where twice the usual daily dose is given every other morning. This dosing is usually reserved for patients requiring chronic steroid administration. The alternate day gives the adrenal cortex a chance to recover from the steroid administration while the anti-inflammatory effects of the drug are still being felt.

Glucocorticoids		
Short Acting	Intermediate Acting	Long Acting
Cortisone	Triamcinolone	Dexamethasone
Hydrocortisone	Prednisone	Betamethasone
	Methylprednisolone	
	Prednisolone	

Contraindications

Individuals with systemic fungal infections or sensitivity to any of these drugs should not use corticosteroids.

Warnings

Corticosteroids may mask the signs of infection and decrease resistance to prevent spreading of newly acquired infections.

Corticosteroids may exacerbate systemic fungal infections.

Due to the mineralcorticoid properties of some of the corticosteroids, the retention of salt and water may elevate blood pressure.

Pregnancy – Corticosteroids are in category C. Studies in animals have resulted in significant birth defects. There are no well controlled studies in pregnant women. Use these agents during pregnancy only if the benefit clearly justifies the potential risk to the fetus. Observe infants born of mothers who received substantial doses during pregnancy for adrenal insufficiency.

Lactation - Systemic glucocorticoids are excreted in breast milk. Decide whether to discontinue nursing or to discontinue the drug.

Drug interactions

Drugs That Increase Corticosteroid Activity	Drugs That Decrease Corticosteroid Activity
Oral Contraceptives	Barbiturates
Cholestyramine	Hydantoins
Estrogens	Ephedrine
Ketoconazole	Rifampin
Macrolide Antibiotics	

Drug Effects Increased by Corticosteroids	Drug Effects Decreased by Corticosteroids
Cyclosporin	Isoniazid
Digitalis Glycosides	Salicylates
Potassium Depleting Agents (diuretics)	Somatrem

Patient information

- Steroid use may cause GI upset; take with meals or snacks. Take single daily or alternate day doses in the morning prior to 9 a.m. Take multiple doses at evenly spaced intervals throughout the day.
- Patients on chronic steroid therapy should wear or carry identification to that effect.
- Notify physician if unusual weight gain, swelling of the lower extremities, muscle weakness, black tarry stools, vomiting of blood, puffing of the face, menstrual irregularities, prolonged sore throat, fever, cold or infection occurs.
- Signs of adrenal insufficiency include fatigue, anorexia, nausea, vomiting, diarrhea, weight loss, weakness, dizziness and low blood sugar. Notify physician promptly if these symptoms occur following dosage reduction or withdrawal of therapy.

620. Mast cell stabilizers (MCS) and leukotriene inhibitors/antagonists

This next lesson covers two types of drugs that are seeing increased usage. These classes of drugs work by breaking the chain of inflammation. Both mast cells and leukotrienes must be activated in order for bronchial inflammation to occur and be potentiated. We'll start out discussion of these groups with the mast cell stabilizers.

Mast cell stabilizers (MCS)

Mast cell stabilizers act directly on the cells in the lung mucosa. MCSs prevent the release of histamine from affected cells stopping excess secretions and inflammation before it starts. MCSs have no direct antihistamine, anticholinergic, anti-inflammatory, or corticosteroid-like effects. Recent studies have shown that MCSs may have some bronchodilating effects, but the mechanism is unknown.

Indications

Mast cell stabilizers are indicated in the management of severe, perennial asthma, symptomatic prevention of allergic rhinitis, and allergic ocular disorders. There are two MCSs currently on the market. Cromolyn sodium and Nedocromil sodium. Nedocromil sodium is only available as an MDI (MCSs have almost no oral absorption and require contact with mucosa to work). Cromolyn sodium is available in an MDI, nebulizer solution, and inhalation capsule. All dosage forms of MCSs are administered QID.

NOTE: Oral cromolyn is available, but seldom used. 100mg oral cromolyn capsules are indicated for prevention of GI reactions to food allergies.

Contraindications

The use of either of these drugs is contraindicated in patients that have shown hypersensitivity to either agent or are having an acute bronchospasm.

Warnings

MCSs must be used at regular intervals to be effective. Patients should be told not to expect immediate symptomatic relief. Two to four weeks of therapy may be required to provide optimal results.

Pregnancy – Both of these drugs are in pregnancy category B. Safety for use during pregnancy has not been established. Use only when clearly needed and when potential benefits outweigh the potential hazards to the fetus.

Lactation – Safety for use in the nursing mother has not been established. Exercise caution when these drugs are administered to a nursing woman.

Adverse reactions – Headache and dizziness seem to be the major adverse reactions to MCSs.

Drug interactions

MCSs are generally well tolerated. Concomitant use with isoproterenol may increase fetal risk during pregnancy. No other drug interactions are noted.

Patient information

Inhalation or nasal:

- Do not discontinue therapy abruptly except on advice of physician. Notify physician if coughing or wheezing occurs.

Nasal solution:

- Stop using nasal spray when symptoms worsen, new symptoms emerge, or there is no improvement within 2 weeks. Other medications (e.g., allergy medications) may be used safely with cromolyn nasal solution.
- Directions for use - Blow nose before administering spray. Hold pump with thumb at bottom and nozzle between fingers. If this is the first time using the pump, prime it by spraying 5 times into the air until the appearance of a fine mist. If the pump has not been used for 14 days, spray 2 times into the air before using again. Insert nozzle into nostril, spray upward

while breathing through the nose. Repeat in other nostril. Keep clean by wiping nozzle. If used > 12 weeks, consult a physician.

Aerosol:

- Directions for use - Remove cap from mouthpiece and shake the inhaler with canister in place for 5 to 10 seconds. Breathe out to the end of a normal breath. Place mouthpiece into mouth or position mouthpiece 2 to 3 times finger width from open mouth. Slightly tilt head back. Breathe in through mouth slowly for 3 to 5 seconds and press the top of the canister at the same time. Remove inhaler from mouth and hold breath for » 10 seconds; allow at least 1 minute between inhalations (puffs).

Nebulizer solution:

- Do not swallow solution because it is poorly absorbed orally. Empty the ampule into a power-driven nebulizer as directed. Do not mix different types of medications without permission from your health care provider.
- Directions for use - Assemble the face mask or mouthpiece and connect the tubing from the port to the compressor. Sit in an upright and comfortable position. Put the mask over nose and mouth (making sure it properly fits to prevent mist from going into the eyes); or, if a mouthpiece is used, place it into mouth. Turn on compressor and take slow, deep breaths. If possible, hold breath for 10 seconds before slowly exhaling. Continue until medication chamber is empty.

Oral:

- The effect of therapy depends upon administration at regular intervals as directed.
- Take at least 30 minutes before meals. Break open ampule(s) and squeeze liquid contents into a glass of water. Do not mix with fruit juice, milk, or foods. Stir solution and drink all of the liquid.

Leukotriene receptor inhibitors/antagonists

Leukotrienes are substances that induce numerous biological effects on the smooth muscles of the lungs. Leukocyte adhesion and eosinophil migration caused by leukotrienes contribute to and perpetuate inflammation, edema, and mucus secretion. Leukotrienes are also known as the "slow-releasing substances of anaphylaxis." Medications are available, which compete for receptor sites with the leukotrienes and inhibit their formation. Unless noted, information given these drugs is for both the inhibitor and antagonist.

Indications

Leukotriene receptor inhibitors/antagonists are used for the prophylaxis and chronic treatment of asthma in adults and children. The table below lists the drugs, their class, and dosage.

Drug	Class	Dosage
Zileuton	Inhibitor	600 mg tablet QID
Zafirlukast	Antagonist	20 mg tablet, BID on an empty stomach
Montelukast	Antagonist	Adult: 10 mg tablet Q PM Pediatric: 5mg chewable Q PM

Contraindications

Hypersensitivity to this class of drug and patients suffering with liver function problems should not use these medications.

Warnings

Inhibitors: These are not indicated for the relief of acute bronchospasm, treatment can be continued during exacerbations. Hepatotoxicity, low occurrence of decreased white blood cell count

Antagonists: These are not indicated for the relief of acute bronchospasm, treatment can be continued during exacerbations. Older patients may incur mild respiratory infections.

Pregnancy - Both of the antagonists are in category B. The inhibitor is pregnancy category C.

Lactation - All three of the drugs are excreted in breast milk.

Drug Interactions

Zileuton – Doubles the effects of propranolol and theophylline and significantly increases the effects of warfarin.

Zafirlukast – Significantly increases the effects of warfarin. Aspirin increases plasma levels of Zafirlukast by about 45 percent. Erythromycin and Theophylline decrease the effects of Zafirlukast by 30–40 percent.

Montelukast – No significant drug interactions have been noted.

Patient information

- Advise patients to take leukotriene antagonists/inhibitors daily as prescribed, even when they are asymptomatic, as well as during periods of worsening asthma, and to contact a physician if the asthma is not well controlled.
- Advise patients that leukotriene antagonists/inhibitors are not for the treatment of acute asthma attacks. Patients should have appropriate short-acting inhaled beta-agonist medication available to treat asthma exacerbations.
- Advise patients using leukotriene antagonists/inhibitors to seek medical attention if short-acting inhaled bronchodilators are needed more often than usual or if more than the maximum number of inhalations of short-acting bronchodilator treatment prescribed for a 24-hour period are needed.
- Instruct patients receiving leukotriene antagonists/inhibitors not to decrease the dose or to stop taking any other anti-asthma medications unless instructed by a physician.
- Instruct patients who have exacerbations of asthma after exercise to continue to use their usual regimen of inhaled beta-agonists as prophylaxis unless otherwise instructed by a physician. All patients should have a short-acting inhaled beta-agonist available for rescue.

621. Antihistamines and decongestants

I think that we're all familiar with antihistamines and decongestants. In that case, we don't need much introduction. We'll just jump into the antihistamines!

Antihistamines

We've discussed antihistamines a couple of times before this, H-2 blockers in the digestive system, as anti-emetics in the central nervous system, and going way back to the integumentary system we used antihistamines for their topical antipruritic activity. This will be, what I think is the traditional view of antihistamines. The stopping of allergic reaction and inflammation throughout the respiratory system. Antihistamines are divided into two basic groups, first generation and second generation. These designations pretty much refer to sedation. First generation antihistamines have much more sedating effects than the second generation antihistamines, which are reported to have none at all. We'll start with the older, first generation antihistamines chlorpheniramine, diphenhydramine, clemastine, and hydroxyzine.

First generation antihistamines

Antihistamines are reversible, competitive H₁ receptor antagonists, which reduce or prevent most of the physiologic effects that histamine normally induces at the H₁ receptor site. They do not prevent histamine release nor bind with histamine that has already been released. Antihistaminic effects

include inhibition of respiratory, vascular and GI smooth muscle constriction; decreased capillary permeability, which reduces the wheal, flare and itch response; and decreased histamine-activated exocrine secretions (saliva and tears for example). First-generation antihistamines bind non-selectively to central and peripheral H₁ receptors and can result in CNS stimulation or depression. The following table lists the first generation antihistamines which we'll be covering.

Drug	Dose (mg)	Dosing interval (hrs)	Antihistaminic activity
Chlorpheniramine	4	4 – 6	Moderate
Diphenhydramine	25 – 50	6 – 8	High
Clemastine	1	12	Low to moderate
Hydroxyzine	25 – 100	4 – 8	Moderate

Indications

As a group, these agents are used for the relief of manifestations of immediate-type hypersensitivity reactions. The varying degrees of anticholinergic, antihistaminic and antimuscarinic activity make many antihistamines useful as sedatives, antiemetics, antitussives, antiparkinson agents, adjuncts to pre- or post-operative analgesic therapy and agents to combat motion sickness.

Contraindications

Antihistamines are contraindicated in patients with a hypersensitivity to specific or structurally related antihistamines, in newborn or premature infants, and nursing mothers. Also patients suffering from narrow-angle glaucoma, peptic ulcer, symptomatic prostatic hypertrophy, bladder neck obstruction, and lower respiratory tract symptoms (including asthma) should not use antihistamines.

Warnings

In general, antihistamines are not recommended to treat lower respiratory tract symptoms (e.g., emphysema, chronic bronchitis, asthma) because their anticholinergic effects may thicken secretions and impair expectoration.

Pregnancy – Chlorpheniramine, diphenhydramine, and clemastine are in category B. Hydroxyzine is in category C. Safety for use during pregnancy has not been established. Several possible associations with malformations have been found, but significance is unknown. Use only when clearly needed and when the potential benefits outweigh the potential hazards to the fetus. Do not use during the third trimester; newborn and premature infants may have severe reactions (e.g., convulsions) to some antihistamines.

Lactation – Although quantitative determinations of antihistaminic drugs in breast milk have not been reported, qualitative tests have documented the excretion of diphenhydramine in breast milk. Because of the higher risk of adverse effects for infants generally, and for newborns and prematures in particular, antihistamine therapy is contraindicated in nursing mothers.

Drug interactions

The only drug interaction for the first generation antihistamines is that of alcohol and other CNS depressants. Due to the anticholinergic effects of antihistamines, CNS depressant effects may be additive.

Patient information

- Inform physician of a history of glaucoma, peptic ulcer, urinary retention or pregnancy before starting antihistamine therapy.
- Some antihistamines may cause nervousness, insomnia and dry mouth.
- Some antihistamines may cause drowsiness or dizziness; observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity. Avoid alcohol and other CNS depressants (e.g., sedatives, hypnotics, tranquilizers, antianxiety agents).

- Some antihistamines may cause GI upset; take with food. Avoid prolonged exposure to sunlight; some agents may cause photosensitivity.
- Do not crush or chew sustained release preparations.

Second generation antihistamines

The second generation antihistamines have also been called the *non-sedating* antihistamines. The less sedating effects of these drugs seems to be because they act on peripheral receptors, not penetrating the blood-brain barrier. The second generation antihistamines are fexofenadine, loratadine, and cetirizine. I'll try to make a long story short by saying that the indications and contraindications for these drugs are the same as the first generation antihistamines. The next table lists the particulars for each of the medications.

Drug	Dose (mg)	Dosing Interval (hrs)	Antihistaminic Activity
Cetirizine	5 – 10	24	moderate to high
Fexofenadine	60	12	moderate to high
Loratadine	10	24	moderate to high

Warnings

Pregnancy and Lactation– These second generation antihistamines are in category B. They also are passed into breast milk. Specifically, breastmilk concentrations of loratadine are close to those found in the mother's blood. Because of the higher risk of adverse effects for infants generally, and for newborns and prematures in particular, antihistamine therapy is contraindicated in nursing mothers.

Drug interactions

Loratadine is the only second generation antihistamine with listed interactions. They are listed in the following table.

Drug	Interaction Description
Azole antifungals	Loratadine levels and actions may be increased
Cimetidine	Loratadine levels and actions may be increased
Macrolide antibiotics	Loratadine levels and actions may be increased

Patient information

- Inform physician of a history of glaucoma, peptic ulcer, urinary retention or pregnancy before starting antihistamine therapy.
- Some antihistamines may cause nervousness, insomnia and dry mouth.
- Some antihistamines may cause drowsiness or dizziness; observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity. Avoid alcohol and other CNS depressants (e.g., sedatives, hypnotics, tranquilizers, antianxiety agents).
- Some antihistamines may cause GI upset; take with food.
- Avoid prolonged exposure to sunlight; some agents may cause photosensitivity.

Decongestants

Decongestants stimulate α -adrenergic receptors of vascular smooth muscle (vasoconstriction, pressor effects, nasal decongestion), although some retain β -adrenergic properties (e.g., ephedrine, pseudoephedrine). Other α effects include contraction of the GI and urinary sphincters, mydriasis and decreased pancreatic β cell secretion. The α -adrenergic effects cause intense vasoconstriction when applied directly to mucous membranes. Systemically, the products have similar effects and decongestion occurs without drastic changes in blood pressure, vascular

redistribution or cardiac stimulation. Constriction in the mucous membranes results in their shrinkage; this promotes drainage, thus improving ventilation and the stuffy feeling.

Decongestants are sympathomimetic amines administered directly to swollen membranes (e.g., via spray, drops) or systemically via the oral route. They are used in acute conditions such as hay fever, allergic rhinitis, sinusitis and the common cold to relieve membrane congestion.

Oral agents are not as effective as topical products, especially on an immediate basis, but generally have a longer duration of action, cause less local irritation and are not associated with rebound congestion.

The drugs that we'll cover in this class are phenylpropanolamine, pseudoephedrine, and oxymetazoline.

Indications

As mentioned above, these drugs are available orally and topically. Indications are listed for both of the routes of administration. The table after the indications lists our decongestants, their route of administration and usual adult dose.

Oral decongestants are used for temporary relief of nasal congestion due to the common cold, hay fever or other upper respiratory allergies, and nasal congestion associated with sinusitis. They are also used to promote nasal or sinus drainage and in to give relief of eustachian tube congestion.

Topical decongestants are used for symptomatic relief of nasal and nasopharyngeal mucosal congestion due to the common cold, sinusitis, hay fever or other upper respiratory allergies. They are also used as adjunctive therapy of middle ear infections by decreasing congestion around the eustachian ostia. Nasal inhalers may relieve ear block and pressure pain in air travel.

Decongestant	Route	Usual Adult Dose
Phenylpropanolamine	Oral	25 mg every 4 hours or 50 mg every 8 hours
	Oral SR	75 mg every 12 hours
Pseudoephedrine	Oral	60 mg every 4 – 6 hours
	Oral SR	120 mg every 12 hours
Oxymetazoline	Topical	2 – 3 sprays twice daily

Contraindications

Patients whom have shown any hypersensitivity or idiosyncrasy to sympathomimetic amines manifested by insomnia, dizziness, weakness, tremor or arrhythmias should not use decongestants. More specifically, patients with severe hypertension and coronary artery disease should not use any oral form of decongestant. Children should not be given the sustained release dose of any of the medications and nursing mothers should avoid the sustained release formula of phenylpropanolamine.

Drug interactions

The next table lists the drug interactions associated with the covered nasal decongestants.

Precipitant Drug	Affected Drug	Interaction Description
Indomethacin	Phenylpropanolamine	Using these together may lead to an increase in blood pressure.
Methyldopa	Decongestants	Using these together may lead to an increase in blood pressure.
Phenylpropanolamine	Bromocriptine	Side effects of bromocriptine may be increased, patient may experience tachycardia and other cardiac dysfunction.
Phenylpropanolamine	Caffeine	Caffeine levels and toxic effects may be increased
Decongestants	Theophylline	Theophylline levels may be decreased with toxicity enhanced.

Patient information

- Patients with hypertension or other cardiovascular diseases, hyperthyroidism, diabetes mellitus or prostatic hypertrophy should use decongestants only with medical advice.
- Topical:
 - Notify physician of insomnia, dizziness, weakness, tremor, irregular heart beat.
 - Do not exceed recommended dosage and do not use longer than 3 to 5 days.
 - Stinging, burning, sneezing, increased nasal discharge or drying of the nasal mucosa may occur.
 - Do not share container with other patients. Do not allow tip of container to touch the nasal passage. Discard after medication is no longer required.
 - Proper use - Spray - Keep head upright. Sniff hard for a few minutes after use.
 - Drops - Recline on a bed and hang your head over the edge; remain in this position for several minutes after using the drops, turning the head from side to side.
 - Inhalers - Warm in the hand before use. Wipe the inhaler after each use.
- Oral - Do not exceed recommended dosage; higher doses may cause nervousness, dizziness or sleeplessness.
- If symptoms do not improve within 7 days or are accompanied by a high fever, consult physician before continuing use.

622. Expectorants, antitussives, and combination products

This is the last lesson for this unit. It's kind of a catch-all lesson to clean up the little areas that don't have much information. Our slimmed-down formularies don't leave much room for these products because the majority of them are available over-the-counter. What we're going to cover is what the DOD Basic Core Formulary mandates be stocked in your pharmacy and a couple of extra medications that our pharmacist staff feel that is important for you to know. With all of that said, let's see what "comes-up" with the expectorants.

Expectorants

The only expectorant that warrants coverage is guaifenesin. Guaifenesin is claimed to enhance the output of respiratory tract fluid by reducing adhesiveness and surface tension facilitating the removal of viscous mucus. As a result, nonproductive coughs become more productive and less frequent.

Indications and dosage

Guaifenesin is indicated for the symptomatic relief of respiratory conditions characterized by dry, nonproductive cough and in the presence of mucus in the respiratory tract. Guaifenesin can be used in patients of all ages (over 2 years old). The dosing is:

- Adults and children (≥ 12): 100 to 400 mg every 4 hours. Do not exceed 2.4 g/day.
- Children (6 to 12): 100 to 200 mg every 4 hours. Do not exceed 1.2 g/day.
- Children (2 to 6): 50 to 100 mg every 4 hours. Do not exceed 600 mg/day.

Guaifenesin is available in multiple strengths and dosage forms. It is also often used in combination with decongestants.

Contraindications

The only contraindication to guaifenesin use is in patients who are sensitive to it.

Warnings

Guaifenesin is not for persistent cough such as occurs with smoking, asthma or emphysema, or where cough is accompanied by excessive secretions.

The main reference used in pharmacies does not assign a pregnancy category to guaifenesin. Thinking back to an earlier lesson, we must assume that it is in category C. Risks cannot be ruled out. Human studies are lacking and animal studies are either positive for fetal risk or lacking. Potential benefits may justify potential risks.

Drug interactions

There are no drug interactions listed for this medication.

Patient information

- This medication should be taken with large quantities of water to ensure proper action.
- If a cough persists for more than one week, or is accompanied by fever, rash, or persistent headache, consult a physician.

Antitussives

By definition, antitussives relieve cough. They work either on the cough center of the brain or in the receptors in the respiratory passages. Antitussives are broken down into two categories, narcotic and nonnarcotic.

Narcotic antitussives

The only narcotic antitussive that we'll cover is codeine. Codeine has good antitussive activity; side effects are infrequent at the usual antitussive dose. The dose required to suppress coughing is lower than the dose required for analgesia.

Indications and dosage

Codeine is indicated for suppression of cough induced by chemical or mechanical respiratory tract irritation. Codeine may be used in patients from 2 years old. The dosing is:

- Adults - 10 to 20 mg every 4 to 6 hours. Maximum 120 mg/day.
- Children - 6 to 12 years - 5 to 10 mg every 4 to 6 hours. Maximum 60 mg/day.
- Children - 2 to 6 years - 2.5 to 5 mg every 4 to 6 hours. Maximum 30 mg/day.

Codeine is available in both tablet and liquid form and in combination with many other drugs.

Contraindications

Codeine is contraindicated in patients with sensitivity to it or in women in labor who may deliver prematurely.

Warnings

Due to the respiratory depressant effects of codeine products, extreme caution should be used in giving codeine to asthma patients. Codeine may also raise cerebrospinal fluid pressure and should not be used if a patient has a head injury.

Pregnancy – Codeine falls into category C. Dependence has been reported in newborns whose mothers took opiates regularly during pregnancy. Withdrawal signs include irritability, excessive crying, tremors, hyperreflexia, fever, vomiting and diarrhea. Signs usually appear during the first few days of life. Use during pregnancy only if the potential benefits outweigh the potential hazards to the fetus.

Lactation – Codeine is excreted into breast milk. The levels are not significant with normal use, but codeine has abuse potential and levels in nursing mothers abusing codeine may harm an infant.

Drug interactions

Codeine interacts and potentiates the actions of other CNS depressants (other opiates, phenothiazines, tricyclic antidepressants, tranquilizers) and alcohol.

Patient information

- Codeine may impair the mental or physical abilities required for the performance of potentially hazardous tasks. Observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity.
- The concomitant use of alcohol or other CNS depressants, including sedatives, hypnotics, antidepressants, tranquilizers, phenothiazines and antihistamines, may have an additive effect.
- May produce orthostatic hypotension (dizziness, lightheadedness when rising quickly from a sitting or lying position) in some ambulatory patients.
- Do not take for persistent or chronic cough, such as occurs with smoking, asthma or emphysema; or where cough is accompanied by excessive secretions, except under supervision of physician.
- May cause dry mouth or constipation.
- May cause GI upset; take with food or milk.

Nonnarcotic antitussives

We'll cover dextromethorphan and benzonatate. These two work very differently and need to be covered separately.

Dextromethorphan

Dextromethorphan is an isomer of codeine. It lacks analgesic and addictive properties. Its cough suppressant action is due to a central action on the cough center in the medulla. Dextromethorphan 15 to 30 mg equals 8 to 15 mg codeine as an antitussive.

Indications and dosage

Dextromethorphan is indicated to control nonproductive cough. It is available in lozenges and liquid both normal and sustained release. It can be used in children from 2 years. The dosing is:

Liquid, lozenges and syrup:

- Adults and children (> 12 years of age) 10 to 30 mg every 4 to 8 hours. Do not exceed 120 mg in 24 hours.
- Children (6 to 12 years) - 5 to 10 mg every 4 hours or 15 mg every 6 to 8 hours. Do not exceed 60 mg in 24 hours.
- Children (2 to 6 years) - 2.5 to 7.5 mg every 4 to 8 h. Do not exceed 30 mg/day.

Sustained action liquid:

- Adults 60 mg every 12 hours.
- Children (6 to 12 years) - 30 mg every 12 hours.
- Children (2 to 5 years) - 15 mg every 12 hours.

Contraindications

Patients with a sensitivity to this medication should not use it.

Warnings

Do not use dextromethorphan for persistent or chronic cough (e.g., smoking, asthma, emphysema) or cough accompanied by excessive secretions. Persons with high fever, rash, persistent headache, nausea or vomiting should use dextromethorphan only under medical supervision.

Pregnancy – Dextromethorphan falls into category C. There are no studies to substantiate any other category.

Lactation – There is no discussion on the effects of dextromethorphan in lactating women.

Drug interactions

There are no major interactions with dextromethorphan.

Patient information

- Shake liquid forms of dextromethorphan well.
- Do not exceed recommended dosage.
- Take with a large glass of water.
- If cough lasts more than one week or is accompanied by a rash, fever, or headache, notify your physician.

Benzonatate

Benzonatate is related to tetracaine. It anesthetizes stretch receptors in respiratory passages, lungs and pleura, dampening their activity, and reducing the cough reflex at its source. It has no inhibitory effect on the respiratory center of the brain in the recommended dosage. The onset of action is 15 to 20 minutes and effects last 3 to 8 hours.

Indications and dosage

Benzonatate is indicated for the symptomatic relief of cough. Benzonatate comes in 100 mg capsules. This is convenient because the dose for benzonatate is 100 mg three times daily.

Contraindications

Any patient who is sensitive to benzonatate or related compounds such as tetracaine should not use this medication.

Warnings

Local anesthesia: Release of benzonatate in the mouth can produce a temporary local anesthesia of the oral mucosa. Swallow the capsules without chewing.

Pregnancy – Benzonatate is in pregnancy category C. It is not known whether the drug can cause fetal harm or can affect reproduction capacity. Give benzonatate to a pregnant woman only if clearly needed.

Lactation - It is not known whether this drug is excreted in breast milk. Exercise caution when administering it to a nursing woman.

Drug interactions

There are no listed drug interactions with benzonatate.

Patient information

Do not chew or break capsules; swallow whole.

Combination products

Combination products are frequently used in respiratory conditions. All of the products work well, however, there are some problems with combination products. First, the patient may not need all of the components of the combination product. A cough and cold preparation may contain acetaminophen and dextromethorphan. If the patient is suffering only from a cough, the acetaminophen is not needed. Secondly, the patient may need all of the components of the combination product but may need them in different strengths or at different intervals. Use the dextromethorphan combination again. The dosing on dextromethorphan is every 4–8 hours. If the combination product contains other long acting ingredients dosed strictly at 8 hours then a patient who needs the dextromethorphan every 4 hours is out of luck! Most of the combination products that we dispense in our pharmacies are available over the counter (OTC).

Groupings

Respiratory combination products are grouped based on the components of their formulations. Some of the more common combination product groupings and their products are:

Antiasthmatic combinations

This combination contains xanthine derivatives and sympathomimetics for bronchodilation. These products may also contain expectorants to facilitate the movement of mucus.

Drug (mg)	Drug (mg)	Dose
Theophylline (300)	Guaifenesin (180)	16 mg/kg/day or 400 mg theophylline/day divided dose every 8 hours
Theophylline (120)	Ephedrine (22.5)	1 – 2 tabs every 4 hours, up to 3 doses daily

Drug (mg)	Drug (mg)	Drug (mg)	Dose
Theophylline (65)	Ephedrine (24)	Phenobarbital (24)	1 tablet 3 – 4 times daily (otc)
Dyphylline (150)	Ephedrine (24)	Guaifenesin (300)	10 – 20 ml every 6 hours

Upper respiratory combinations

These combinations are used primarily for relief from symptoms associated with colds, upper respiratory infections and allergic conditions. These can be decongestant combinations, antihistamine and analgesic combinations, decongestant and antihistamine combinations, and many more.

There are literally hundreds of these combinations. Most of them contain either pseudoephedrine or phenylpropanolamine as the decongestant, diphenhydramine, chlorpheniramine, brompheniramine, clemastine, or loratadine as an antihistamine, and some contain guaifenesin as an expectorant in various strengths and releases to meet the needs of multiple symptoms. Some also contain acetaminophen or ibuprofen to provide analgesia.

Cough preparations

These include an antitussive or expectorant, but may also contain ingredients for relief of other symptoms. These can be expectorants combined with either narcotic or nonnarcotic antitussive. Again, there are too many of these to list. Any combination of narcotic or nonnarcotic antitussive along with guaifenesin and sometimes even chlorpheniramine or diphenhydramine can be found.

Warnings for these categories are the same as for their individual components. The drowsiness side effects of the antihistamines can sometimes be offset by the actions of the sympathomimetics.

Pregnancy and lactation – Women who use these combinations should be aware of ingredients and take precautions for each.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

618. Bronchodilators

1. What are the indications for sympathomimetic bronchodilators?
2. How does salmeterol differ from the other bronchodilators discussed?

3. What are xanthine derivatives?
4. How is theophylline dosing based?

619. Corticosteroids

1. How is potency of corticosteroids based?
2. Why should systemic corticosteroids be given in the morning?
3. Why shouldn't systemic corticosteroids be used by patients suffering from systemic fungal infections?

620. Mast cell stabilizers and leukotriene inhibitors/antagonists

1. How do mast cell stabilizers work?
2. How long must a patient take mast cell stabilizers before feeling optimal benefits?
3. What drug interactions are given for Zileuton?

621. Antihistamines and decongestants

1. What are the two basic groups of antihistamines?
2. What are the antihistaminic effects of the first generation antihistamines?
3. Why are antihistamines not recommended to treat lower respiratory tract symptoms?
4. What is another name for the second generation antihistamines?
5. How do nasal decongestants work?

622. Expectorants, antitussives, and combination products

1. How does guaifenesin enhance the output of the respiratory tract fluid?
2. What are the two areas where antitussives produce their action?
3. Why should asthmatics be cautious when using codeine?
4. Which nonnarcotic antitussive is an isomer of codeine?
5. How does benzonatate work?
6. What are two problems with combination respiratory products?
7. What are the three groupings of combination products?

Answers to Self-Test Questions**614**

1. Between the roof of the mouth and the cranium.
2. The nasal septum.
3. A small duct that communicates indirectly with the glands that produce tears.
4. Nasopharynx.
5. The air passageway into the larynx is the space toward the front, and the food path, located toward the back, enters the esophagus.
6. To conduct air between the larynx and the lungs.
7. Bronchiole.
8. A cluster of air sacs, resembling grapes, at the end of each of the smallest subdivisions of the bronchial tree.
9. Surfactant. It is produced in certain cells in the alveolar wall.
10. Parietal pleura.

615

1. The movement of air into and out of the lungs.
2. Inhalation – drawing of air into the lungs; exhalation – expulsion of air from the lungs.
3. Arterial blood is 97 percent saturated with oxygen and venous blood contains about 70 percent oxygen.
4. Most is transported as a compound, known as bicarbonate, some is dissolved in plasma, some is combined with protein substances in the blood plasma.
5. In the carotid and aortic bodies, and in the medulla of the brain stem.

6. An adult is 12 to 20 times per minute; a child is 20 to 40 times per minute.
7. Apnea.

616

1. An inflammation caused by infection of the sinuses.
2. Deviated septum.
3. Influenza is an acute contagious disease characterized by an inflammatory condition of the upper respiratory tract accompanied by generalized aches and pains.

617

1. Along with eosinophils, mast cells are the essential effector cells of the inflammatory response. When these cells are activated, they synthesize leukotriene from arachidonic acid, mediating inflammation.
2. Asthma is classified by three clinical patterns, intermittent, chronic, and seasonal allergies.
3. Chronic Obstructive Airway Disease (COAD).
4. Physical changes of the lung tissue characterized by abnormal permanent enlargement of the air spaces distal to the terminal bronchiole and destruction of the alveolar walls.
5. Other organs affected by tuberculosis are: lymph nodes in the thorax, the pleura, the larynx, kidneys, reproductive system, and vertebral bones.

618

1. Relief of reversible bronchospasm associated with acute and chronic bronchial asthma, exercise induced bronchospasm, bronchitis, emphysema, bronchiectasis, or other obstructive pulmonary diseases.
2. Salmeterol is long acting. It is not to be used to treat or relieve acute asthma symptoms.
3. Xanthine derivatives are all different forms of theophylline.
4. Dosing is individualized and based on pulmonary improvement and clinical response.

619

1. Relative potency is based on skin vasoconstrictive effects.
2. Because of the actions of the adrenal cortex. The cortex produces most of its corticosteroids between 2 and 8 a.m. Morning administration has the least suppression of the adrenal cortex.
3. Corticosteroids may mask the signs of infection and decrease resistance to prevent spreading of newly acquired infections.

620

1. MCSs prevent the release of histamine from affected cells, stopping excess secretions and inflammation before it starts.
2. 2 – 4 weeks of therapy may be required to provide optimal results.
3. Zileuton doubles the effects of propranolol and theophylline, and significantly increases warfarin's effects.

621

1. First and second generation.
2. Inhibition of respiratory, vascular and GI smooth muscle constriction, decreased capillary permeability, and decreased exocrine secretions.
3. Their anticholinergic effects may thicken secretion and impair expectoration.
4. Non-sedating.
5. Decongestants stimulate alpha-adrenergic receptors of vascular smooth muscle causing vasoconstriction resulting in membrane shrinkage and promoting drainage.

622

1. It reduces adhesiveness and surface tension facilitating the removal of viscous mucus.
2. At the cough center of the brain or in the receptors in the respiratory passages.
3. Because of the respiratory depressant effects of codeine.
4. Dextromethorphan.

5. It anesthetizes stretch receptors in the respiratory passages, lungs and pleura.
6. The patient may not need all of the components of the combination drug and the patient may need all of the components, but at different strengths or intervals.
7. Upper respiratory combinations, antiasthmatic combinations, and cough preparations.

Do the unit review exercises before going to the next unit.

Unit Review Exercises

Note to Student: Consider all choices carefully, select the *best* answer to each question, and *circle* the corresponding letter.

30. (614) What structure keeps food from entering the respiratory tract?
 - a. Glottis.
 - b. Epiglottis.
 - c. Pharynx.
 - d. Larynx.
31. (614) What is the name of the cluster of air sacs at the end of the bronchial tree?
 - a. Epithelium.
 - b. Bronchioles.
 - c. Alveoli.
 - d. Pleura.
32. (615) Through what process is oxygen and carbon dioxide exchanged in the lungs?
 - a. Diffusion.
 - b. Dilution.
 - c. Dissolution.
 - d. Decarboxylation.
33. (615) Chemoreceptors that control respiration are sensitive to what compound?
 - a. Oxygen.
 - b. Nitrous oxide.
 - c. Carbon monoxide.
 - d. Carbon dioxide.
34. (616) What term is used to describe a septum which is markedly to one side?
 - a. Alveolar.
 - b. Polyp.
 - c. Off-centered.
 - d. Deviated
35. (616) What is the most common cause of nosebleed?
 - a. High blood pressure.
 - b. Polyps.
 - c. Injury.
 - d. Ulceration.
36. (617) Which two types of cells are the essential effector cells of the inflammatory response in asthma?
 - a. Mast cells and leukotrienes.
 - b. Mast cells and eosinophils.
 - c. Eosinophils and leukotrienes.
 - d. Eosinophils and histamines.
37. (617) Which lower respiratory disease is characterized by abnormal permanent enlargement of the air spaces distal to the terminal bronchiole, along with destruction of the alveolar walls?
 - a. Chronic bronchitis.
 - b. Asthma.
 - c. Emphysema.
 - d. Chronic obstructive airway disease.

38. (618) Which bronchodilator *is not* used to relieve acute asthma symptoms?
- Terbutaline.
 - Salmeterol.
 - Ephedrine.
 - Isoproteranol.
39. (618) What caution should be given to nursing mothers concerning theophylline use?
- Theophylline is safe and not excreted into breast milk.
 - Theophylline is excreted into breast milk and is unsafe, discontinue nursing.
 - Theophylline is excreted into breast milk with no effects on the nursing infant.
 - Theophylline is excreted into breast milk and may cause irritability in nursing infants.
40. (619) Which statement is true concerning inhaled corticosteroids and chronic obstructive airway disease (COAD)?
- Corticosteroids benefit only 10 percent of COAD patients.
 - Corticosteroids are the drug of choice in treating COAD.
 - Corticosteroids have no effect on COAD.
 - Corticosteroid use exacerbates COAD.
41. (619) What reaction may occur in a patient who has been taking systemically administered corticosteroids for longer than 7 to 10 days abruptly discontinues the medication?
- Nothing, abrupt discontinuance is normal.
 - The disease may reappear more severely.
 - Acute anaphylactic shock may occur.
 - The patient will continue to improve as the corticosteroids linger in their system.
42. (620) Why are mast cell stabilizers only used by inhalation?
- Gastric enzymes destroy the active agent.
 - They require contact with mucosa to work.
 - The half-life is too short to be stable through the intestine.
 - They irritate the esophagus too much to be taken orally.
43. (620) Which statement is correct concerning leukotriene inhibitors and acute asthma attacks?
- They effectively treat acute attacks.
 - They exacerbate acute attacks.
 - They have no effects on acute attacks.
 - They have only minor effects on acute attacks.
44. (621) What action occurs when decongestants come into contact with mucosa?
- Vasoconstriction.
 - Drying.
 - Vasodilation.
 - Increased secretions.
45. (622.) Why must benzonatate capsules be swallowed whole?
- The enteric capsule is meant to be dissolved in the intestine.
 - Capsule contents may irritate the esophagus.
 - Release in the mouth may produce local anesthesia.
 - The medication is only absorbed through gastric mucosa.

Student Notes

Unit 3. The Sensory System

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“SENSE” can be defined as “the interpretation, by the specialized areas of the cerebral cortex, of an impulse originating from the receptors which are designed to report changes taking place either within the body or outside of it.” What a mouthful! Sensory receptors are specialized tissues on the endings of the dendrites of afferent neurons. Some receptors are designed to respond only to special stimuli (sound waves, light rays), while others respond to general sensations, such as pain or pressure.

3-1. Anatomy and Physiology of the Sensory System

Many attempts have been made to classify our senses. Thus far, there has been no completely satisfactory classification of the senses. A partial list is given here:

1. Visual sense—from receptors in the eye.
2. Hearing sense—from receptors in the ear.
3. Taste sense—from the tongue receptors.
4. Smell sense—from receptors in the upper nasal cavities.
5. Pressure, heat, cold, pain, and touch senses—from the skin.
6. Position and balance sense—from the muscles, the joints, and the semicircular canals in the ear.
7. Hunger and thirst sense—from various internal parts of the body.

The following lessons discuss the eye, the ear, and other organs of special sense.

623. Eyes and ears

This lesson covers many topics concerning the eyes. Sight is probably the most important of all of our senses. When we get to the ears, we'll get into their three major parts.

The eyes

It's hard to imagine living without sight. For one thing, you wouldn't be able to read these CDCs! This lesson covers such topics as protection of the eyeball and its parts; eyeball coats, light rays pathway, eye muscles, the eye's nerve supply; the conjunctival sac and the lacrimal apparatus (fig. 3-1).

Protection of the eyeball and its parts

The eye develops, within the embryo, as an outpocketing of the brain. It is a very delicate organ, and nature has conveniently protected it by means of the following structures:

- More than half of the dorsal part of the eyeball is protected by the skull bones that form the eye orbit (cavity).
- The eye is protected anteriorly by the lids and eyelashes.
- Our tears wash away small foreign objects that may enter the eye.

An epithelial membrane lined sac separates the front of the eye from the eyeball proper. It also aids in the destruction of some of the pathogenic bacteria that can enter from the outside.

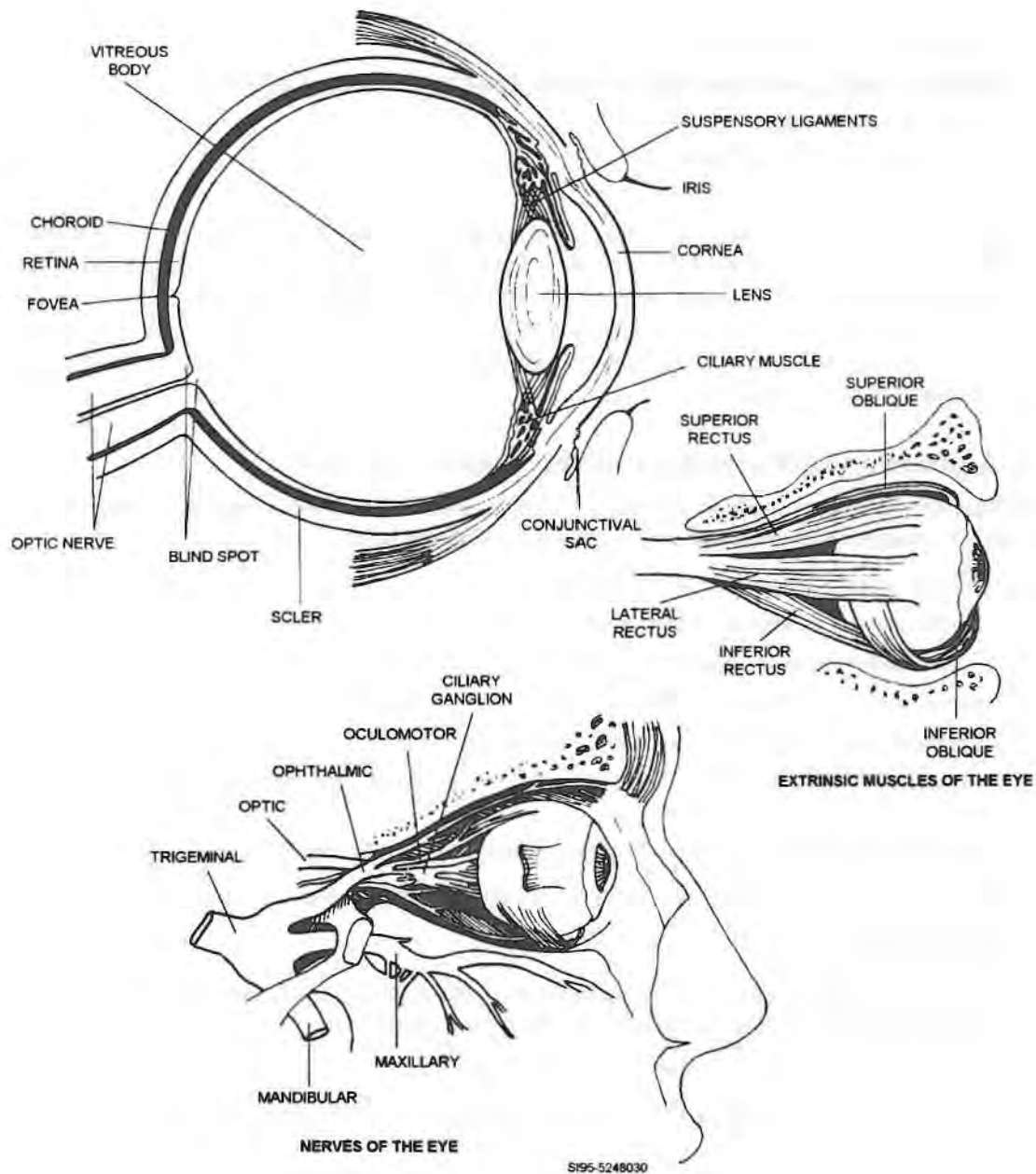


Figure 3-1. The eye.

The eyeball's coats

There are three separate coats or tunics for the eyeball: the *sclera*, *choroid* and *retina*. The *sclera*, the outermost layer, is made of firm, tough connective tissue. Commonly, it is referred to as the white of the eye. The *choroid*, the second tunic of the eyeball, is composed of a delicate network of connective tissue. This connective tissue is interlaced with many blood vessels, and this layer contains a great deal of dark brown pigment. In comparison, the choroid is similar to the dull black lining of a camera. It prevents incoming light rays from scattering and reflecting off the inner surface of the eye. The innermost coat, the *retina*, includes ten layers of nerve cells. This includes the end organs commonly

called the rods and cones. The rods and cones are the receptors for the sense of vision. The rods are sensitive to white and black, and the cones are sensitive to color. As far as we know, there are three types of cones, each of which is sensitive to red, green, or blue. Persons who don't have all three cones are totally color blind; others missing one type of cone are partially color blind. Color blindness occurs almost exclusively in males and is an inherited condition.

Light rays' pathway

Light rays pass through a series of transparent, colorless eye parts. During this journey they undergo a process of bending called *refraction*. The refracting of these light rays enables light from a very large area to be focused upon a very small surface, the retina, where the receptors are located. The following are, in order from the outside in, the transparent refracting parts, or *media*, of the eye:

1. *Cornea*—a forward continuation of the outer coat. But, it is transparent and colorless, whereas the sclera is opaque and white.
2. *Aqueous humor*—a watery fluid that fills most of the eyeball in front of the lens. This fluid helps to maintain the slight forward curve in the cornea.
3. *Crystalline lens*—a circular structure made of a jelly-like material.
4. *Vitreous body*—a jelly-like substance that fills the entire space behind the lens and keeps the eyeball in its spherical shape.

Cornea

Oftentimes, the cornea is referred to as the “window” of the eye. It has a slight forward bulge, and is the most important refracting structure. Scar formation on the cornea may be caused by injury due to foreign objects or by infection. Scar formation leaves an area of opacity that light rays cannot pass through. If this type of injury involves the central area in front of the pupil (the hole in the center of the colored part of the eye), the result might be blindness. “Eye Banks” store corneas obtained from donors, and corneal transplantation is becoming a fairly common procedure.

Aqueous humor and crystalline lens

The next light-bending medium is the aqueous humor, followed by the crystalline lens. The crystalline lens has two bulging surfaces. Therefore, it may be best described as *biconvex*. The crystalline lens, during youth, is elastic. Therefore, its thickness can be readily adjusted according to the need for near or distance vision. As we age, the crystalline lens loses its elasticity and consequently its ability to adjust by thickening. This results in what is known as *presbyopia*.

Vitreous body

This is the last of the transparent refracting parts of the eye. Similar to the aqueous humor, the vitreous body is important in maintaining the ball-like shape of the eyeball, and it also aids in refraction. An injury resulting in the loss of an appreciable amount of this jelly-like vitreous material collapses the eyeball. In these cases, the eyeball must be removed in an operation called *enucleation*.

The eye's muscles

Inside the eyeball itself, the muscles are *intrinsic muscles*, while others, attached to the bones of the eye orbit, as well as to the sclera, are *extrinsic muscles*.

Intrinsic muscles

The intrinsic muscles are located in two circular structures: the *iris* and the *ciliary body*.

Iris

The iris is the colored or pigmented portion of the eye. It is composed of two types of muscles. The central opening of the eye is called the pupil. The pupil's size is governed by the action of these two sets of muscles. One is arranged in a circular fashion, while the other extends in a radial manner resembling the spokes of a wheel.

The iris's purpose is to regulate the amount of light entering the eye. When a strong light is flashed in the eye, the circular muscle fibers of the iris, which form a sphincter, contract and consequently reduce the size of the pupil. On the other hand, if the light is very dim, the radial involuntary muscles of the iris, which are attached at the outer edge, contract, pulling the opening outward, and thereby enlarging it. Pupillary enlargement is known as *dilation*.

The pupil changes size, also, according to whether one is looking at a near object or a distant one. When viewing an object that is near the pupil becomes smaller, viewing an object that is far away causes it to enlarge.

Ciliary body

The ciliary body is shaped somewhat like a flattened ring with a hole the size of the outer edge of the iris. This muscle alters the shape of the lens during the process of accommodation.

The ciliary body's muscle resembles the radial muscle of the iris, in direction and method of action. As the ciliary muscle contracts, it removes the tension on the suspensory ligament of the lens. The elastic lens then recoils and becomes thicker in much the same way that a rubber band thickens if the pull on it is released. As the ciliary body relaxes, the lens becomes flattened. These actions change the refractive ability of the lens.

The process known as *accommodation* involves coordinated eye changes, enabling one to focus on near objects. During accommodation, the ciliary body contracts, thereby thickening the lens. In addition, the circular muscle fibers of the iris contract to decrease the size of the pupillary opening.

Extrinsic muscles

There are six extrinsic muscles connected with each eye. They are ribbon-like and extend forward from the apex of the orbit behind the eye ball. One end of each muscle is attached to a bone of the skull, and the other end is attached to the sclera. These muscles pull on the eyeball in a coordinated fashion, causing the two eyes to move together in order to center on one visual field. There is another muscle, located within the orbit, which is attached to the upper eyelid. As this muscle contracts, it keeps the eye open.

The eye's nerve supply

There are two sensory nerves that supply the eye: the *optic nerve (cranial nerve II)* and the *ophthalmic branch of the trigeminal nerve (cranial nerve V)*. The optic nerve carries visual impulses initiated by the rods and cones in the retina to the brain. It originates in the retina, a little toward the medial or nasal side of the eye. Visual impulses are transmitted from the retina, to the occipital lobe of the cortex. No cones or rods are found in the retina near the area of the optic nerve fibers. Therefore, this part, which is a circular white area, the blind spot, known as the *optic disk*. The *fovea centralis*, is a very small depressed area in the retina. It is the point of our most acute vision. The other sensory nerve—the ophthalmic branch of the trigeminal nerve (cranial nerve V)—carries impulses of pain, touch, and temperature from the eye and surrounding parts.

There are three nerves that carry *motor fibers* to the muscles of the eyeball. The *oculomotor nerve (cranial nerve III)* is the largest. It supplies both voluntary and involuntary motor fibers to all the muscles of the eyeball but two. The *trochlear (cranial nerve IV)* and the *abducens (cranial nerve VI)* each supply one voluntary muscle.

Conjunctival sac and lacrimal apparatus

The sac that lines the eyelid and covers the anterior part of the sclera, protecting the eyeball from drying is known as the *conjunctiva*. The *lacrimal gland* produces tears, serving to keep the conjunctival sac moist. Correspondingly, as tears flow from the lacrimal gland, which is located in the upper part of the orbit, across the eye, the fluid carries away small particles that have entered the conjunctival sac. Then, these tears are carried into ducts near the nasal corner of the eye, where they

drain into the nose via the *nasolacrimal duct*. Excessive amounts of tears causes a “runny nose”; a large overproduction of tears results in tears spilling over onto the cheeks.

The ear

The ear is a sense organ, related to both hearing and equilibrium. It is divided into three main sections (fig. 3-2):

1. The **external ear** includes the outer projection and a canal.
2. The **middle ear** is an air space containing three small bones.
3. The **internal ear** is the most important part, since it contains the sensory end organs or receptors for hearing and equilibrium.

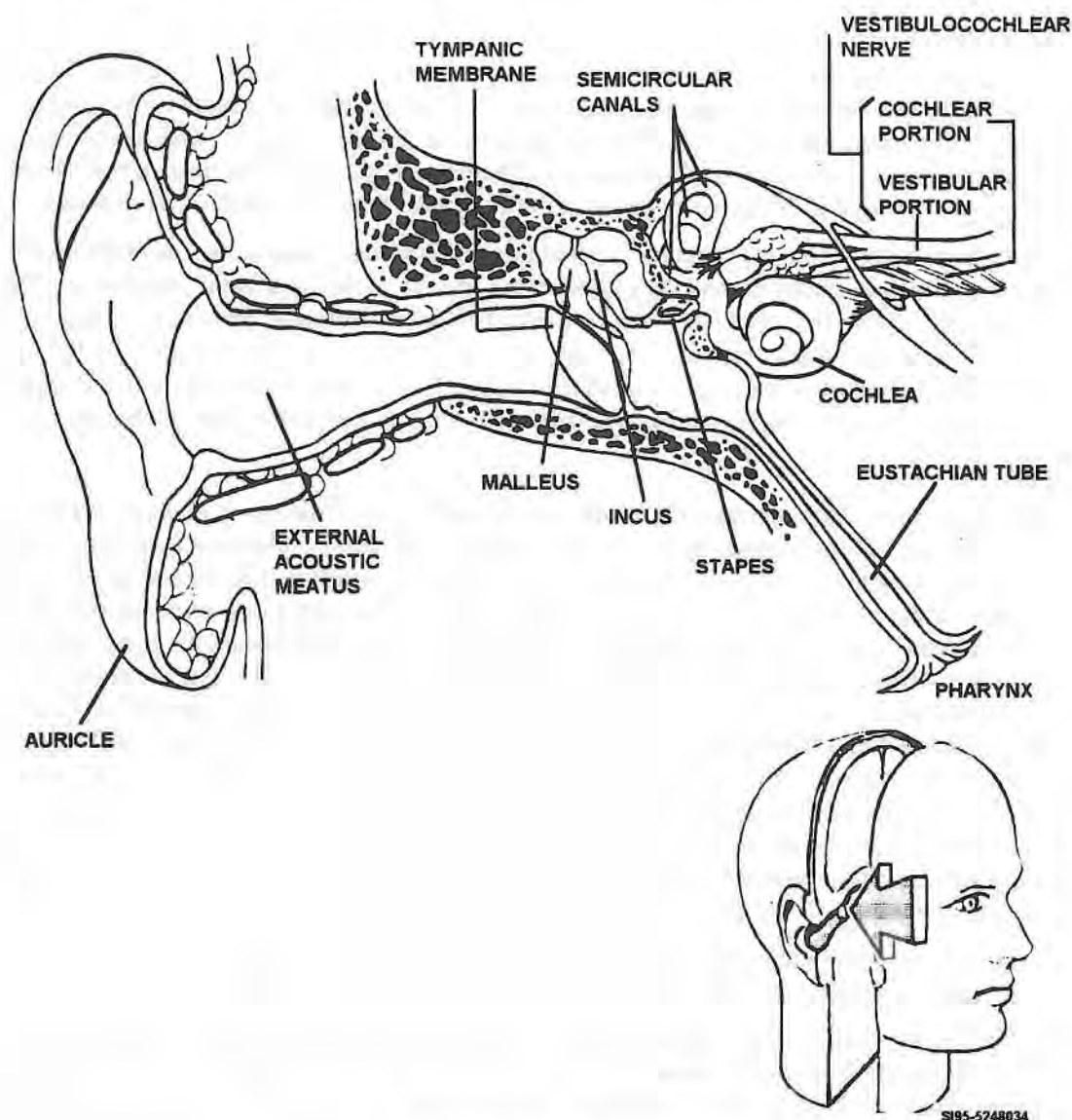


Figure 3-2. The Ear.

External ear

The *pinna*, or the *auricle*, is the projecting part of the ear. From a functional point of view, it is no doubt of little importance in the human. Then follows the opening itself, the *external auditory canal*.

This canal extends medially for about 1 inch or more, depending on which wall of the canal is measured. The skin lining this tube is very thin, and in the first part of the canal contains many *ceruminous* glands. The *cerumen*, or wax, may become dried and impacted in the canal and must be removed. The same kinds of disorders that involve the skin elsewhere also may affect the skin of the external auditory canal: eczema, boils, and other infections.

The *tympanic membrane*, or eardrum, lies at the end of the auditory canal. It serves as a boundary between the external auditory canal, or *meatus*, and the middle ear cavity. It may be injured by bobby pins, toothpicks, or other objects inserted into the ear. Ordinarily the air pressure on the two sides of the tympanic membrane is equalized by means of the *eustachian* tube connecting the middle ear cavity and the throat, or pharynx. This allows the eardrum to vibrate freely with the incoming sound waves.

Middle ear

This cavity is a small, flattened space that contains air and three small bones, or *ossicles*. Air enters the cavity from the pharynx through the eustachian, or auditory, tube. The mucous membrane of the pharynx is continuous through the eustachian tube into the middle ear cavity, and infection may travel along the membrane, causing middle ear disease. There is an opening at the back of the middle ear cavity into the mastoid air cells, with spaces inside the mastoid process of the temporal bone.

The three ossicles are joined in a manner so that they amplify the sound waves received by the tympanic membrane (eardrum) and then transmit the sounds to the fluid in the internal ear. The handle-like part of the first bone, or *malleus*, is attached to the tympanic membrane, while the head-like portion connects with the second bone, which is called the *incus*. The innermost of the ossicles is shaped somewhat like a stirrup and is called the *stapes*. The stapes is connected with the membrane of the *oval window* which, in turn, vibrates and transmits these waves to the fluid of the internal ear.

Internal ear

The internal portion is the most complicated and important part of the ear. It consists of three separate spaces hollowed out inside the temporal bone. This part of the ear is called the *bony labyrinth*, and it contains three divisions. One is the *vestibule*, next to the oval window. The second and third divisions of the bony labyrinth are the *cochlea* and the *semicircular canals*. All three divisions contain a fluid called *perilymph*. The *cochlea* is a bony tube shaped like a snail shell toward the front, and the semicircular canals are bony processes toward the back. In the fluid of the bony semicircular canals are the *membranous canals*, which contain another fluid called *endolymph*. Likewise, a *membranous cochlea* is situated in the perilymph of the bony cochlea, and it also is filled with endolymph. The organ of hearing consists of receptors connected with nerve fibers in the *cochlear nerve* (a part of the acoustic nerve); it is located inside the membranous cochlea, or *cochlear duct*. Sound waves enter the external auditory canal and cause the tympanic membrane to vibrate. These vibrations are amplified by the ossicles and transmitted by them to the perilymph. They then are conducted by the perilymph through the membrane to the endolymph.

The waves of the endolymph stimulate the tiny hairlike receptors, which, in turn, initiate nerve impulses that are conducted to the brain.

Other sensory receptors in the internal ear include those related to equilibrium, which are in the semicircular canals. The *membranous canals* are connected with two small sacs in the vestibule, and one of these sacs contains sensory end organs for obtaining information with relation to the position of the head. Nerve fibers from these sacs and from the canals form the vestibular nerve which joins the cochlear nerve to form the *vestibulocochlear* (acoustic) *nerve*, the latter being the eighth cranial nerve.

624. Other organs of special sense

Taste sense

The sense of taste involves receptors in the tongue and two different nerves that carry taste impulses to the brain. The taste receptors are known as *taste buds* and are located along the edges of small depressed areas called *fissures*. Taste buds are stimulated only if the substance to be tasted is in solution (liquid). Tastes have been described as essentially of four kinds:

1. Sweet tastes are most acutely experienced at the tip of the tongue.
2. Sour tastes are most effectively detected by the taste buds located at the sides of the tongue.
3. Salty tastes, as in the case of sweet tastes, are most acute at the tip of the tongue.
4. Bitter tastes are detected at the back part of the tongue.

The nerves of taste include the facial and the glossopharyngeal. The interpretation of taste impulses probably is accomplished by the lower front portion of the brain, although there may not be a sharply separate taste or *gustatory* center.

Sense of smell

The sensory end organs, or receptors, for smell are located in the olfactory *epithelium* of the upper part of the nasal cavity. Because they are high in the nasal cavity, an animal or a person “sniffs” in order to bring the gases responsible for an odor upward in the nose. The pathway of the impulses from the receptors for smell is the *olfactory nerve*. This leads to the olfactory center in the brain. The interpretation of smell is closely related to the sense of taste. The smell of foods is just as important in stimulating appetite and the flow of digestive juices as is the sense of taste.

Hunger and appetite

Hunger is the desire for food and can be satisfied with the ingestion of a filling meal. Hunger is regulated by centers in the hypothalamus which can be modified by input from higher brain centers. Therefore, cultural factors and memories of past food intake can influence hunger. Strong, mildly painful contractions of the empty stomach may stimulate a feeling of hunger. Messages received by the hypothalamus reduce hunger as the food is chewed and swallowed, and begins to fill the stomach. The short-term regulation of food intake works to keep the amount of food taken in within the limits of that which can be processed by the intestine. The long-term regulation of food intake maintains appropriate blood levels of certain nutrients. Appetite differs from hunger in that, although it is basically a desire for food, it often has no relationship to the need for food. Hunger may have been relieved by an adequate meal, but the person may still have an appetite for additional food. A loss of appetite is called *anorexia*, and may be due to a great variety of physical and mental disorders. Since the hypothalamus and the higher brain centers are involved in the regulation of hunger, it is likely that emotional and social factors contribute to the development of anorexia.

Sense of thirst

Depletion of body water and changes in the concentration of body fluids lead to stimulation of the thirst center in the hypothalamus. The individual becomes aware of a desire for water. Dryness of the mouth also causes a sensation of thirst. When excessive thirst is due to excessive urine loss, as in diabetes, the condition is called *polydipsia*.

General senses

As opposed to the *special* senses, in which the receptors are limited to a relatively small area in the body, the *general* sensory receptors are scattered throughout the body. These include pressure, heat, cold, pain, touch, position, and balance senses, all of which are rather widely distributed.

Pressure sense

It has been found that even though the skin is anesthetized, there still is consciousness of pressure. These end organs for deep sensibility are located in the subcutaneous and deeper tissues. They are sometimes referred to as receptors for deep touch.

Temperature sense

Heat and cold receptors have separate nerve fiber connections. Each has its type of end organ structure peculiar to it, and the distribution of each varies considerably. A warm object stimulates only the heat receptors, while a cool object affects only the cold terminals. As in the case of other sensory receptors, continued stimulation results in adaptation; that is, the receptors adjust themselves in such a way that one does not feel a sensation so acutely if the original stimulus is continued. For example, the initial immersion of a hand in hot water may give rise to an uncomfortable sensation, however, if the immersion is prolonged, the water very soon will not feel as hot as it did at first (even if it has not cooled appreciably).

Sense of touch

The touch receptors are small, rounded bodies called *tactile corpuscles*. They are found mostly in the dermis and are especially numerous and close together in the tips of the fingers and the toes. The tip of the tongue also contains many of these receptors, so it's very sensitive to touch; whereas the back of the neck is relatively insensitive.

Pain sense

Pain is the most important protective sense. The receptors for pain are the most widely distributed sensory end organs. They are found in the skin, the muscles, and the joints, and to a lesser extent in most internal organs (including the blood vessels and viscera). Pain receptors are not oval bodies as are many of the other sensory end organs, but apparently are merely branchings of the nerve fiber, called *free nerve endings*. *Referred pain* is a term used in cases in which pain that seems to be in an outer part of the body, particularly the skin, actually originates in an internal organ located near that particular area of skin. These areas of referred pain have been mapped out on the basis of much experience and many experiments. It has been found, for example, that liver and gallbladder disease often cause referred pain in the skin over the right shoulder. Spasm of the coronary arteries that supply the heart may cause pain in the left shoulder and the left arm. One reason for this is that some neurons have the twofold duty of conducting impulses both from visceral pain receptors and from pain receptors in neighboring areas of the skin. The brain cannot differentiate between these two possible sources; but since most pain sensations originate in the skin, the brain automatically assigns the pain to this more likely place of origin.

Pain sense differs from other senses in that continued stimulation does not result in adaptation. This is nature's way of being certain that the warnings of the pain sense are heeded. Sometimes the cause cannot be remedied quickly, and occasionally not at all. Then it is necessary to relieve pain. Some pain relief methods that have been found to be effective include the following:

- *Application of cold*—especially crushed ice in ice caps, for headaches; or in bags for localized areas of injury or inflammation; or cold compresses made by wringing out a towel (or gauze for small compresses) in cold water.
- *Pressure*—applied to the site of pain or to certain other locations in the body can provide pain relief.
- *Analgesic drugs*—which are mild pain relievers. Examples are *acetaminophen* and *aspirin*.
- *Narcotic drugs*—which produce stupor and sleep. These are often very effective pain relievers. An example of a narcotic drug is morphine.

- *Anesthetics*—which may be either local (i.e., that render only a certain area insensitive) or general, producing total unconsciousness. These are used largely to prevent pain during surgery.
- *Endorphins* and *enkephalins* are substances that are associated with the control of pain. The endorphins and enkephalins are under intensive study, and several theories have been proposed about the circumstances that can cause them to be released from the hypothalamus and the pituitary.

Sense of position

Receptors located in muscles, tendons and joints relay impulses that aid in judging the position and changes in the locations of parts with respect to each other. They also inform the brain of the amount of muscle contraction and tendon tension. These rather widely spread end organs, which are known as *proprioceptors*, are aided in this function by the semicircular canals and related internal ear structures. Information received by these receptors is needed for coordination of muscles and is important in such activities as walking, running, and many more complicated skills such as playing a musical instrument. These muscle sense end organs also play an important part in maintaining muscle tone and good posture, as well as allowing for the adjustment of the muscles for the particular kind of work to be done. The nerve fibers that carry impulses from these receptors enter the spinal cord and ascend to the brain in the posterior part of the cord.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

623. Eyes and ears

1. What is the outermost layer of the eyeball?
2. What is "aqueous humor?"
3. What is the purpose of the iris?
4. What is the "lay term" for tympanic membrane?
5. How does air enter the middle ear?
6. Which middle ear ossicle is shaped like a stirrup?

624. Other organs of special sense

1. What form must a substance be in to stimulate the taste buds?

2. Where in the nasal cavity are the sensory end organs for smell located?
3. What term describes excessive thirst due to excessive urine loss, as in diabetes?
4. What is the most important protective sense?

3-2. Sensory System Conditions and the Drugs Used to Treat the Conditions

At sometime in your life, you have most likely had an eye infection, suffered from eyestrain, or known someone who is blind. These are some of the more common eye disorders discussed in this section. We also discuss some common ear disorders. There are a wide variety of drugs used to treat conditions associated with the sensory system. We obviously cannot discuss all of them here. (Lucky for YOU). Most of the drugs used for the sensory organs are used in other areas of the body and simply put into a vehicle to get it into these organs. For example, some of the same steroids that were used topically or for the respiratory system can be put into the eyes and ears.

625. Eye and ear disorders

Eye disorders

There are numerous types of eye disorders caused by a multitude of pathogens. We do not have room to discuss each one, but will touch briefly on the most common ones.

Conjunctivitis

Conjunctivitis is the inflammation of the membrane lining the eyelids and covering the front of the eyeball. This condition may be acute or chronic. It may also be caused by a variety of irritants and pathogens. I am sure you have heard the term "pink eye." Pink eye is an acute conjunctivitis that is very contagious. It is caused by cocci or bacilli in most cases. Irritants like the wind and excessive glare can sometimes cause an inflammation, in turn, causing a susceptibility to bacterial infection. In cases of the contagious epidemic form, children should be kept home until the infection has gone away.

Trachoma

This infection is sometimes called *granular conjunctivitis*. Trachoma is caused by the *chlamydia trachomatis* bacterium. Formerly, this disease was quite common in the mountains of southern United States, and among native Americans. Trachoma is still very prevalent in the Far East, Egypt, and in southern Europe. It is characterized by the formation of granules on the lids. These may cause such serious irritation of the cornea that blindness may result. The use of antibiotic drugs and better hygiene has reduced the prevalence and seriousness of this infection.

Ophthalmia neonatorum

When a woman has a gonococcal infection, her newborn infant may contract an eye infection. This infection is called *ophthalmia neonatorum*. The bacterium enters the conjunctival sac of the fetus as it proceeds through the birth canal during the delivery process. Babies at risk for the development of ophthalmia neonatorum achieve prevention by the application of an appropriate antiseptic solution or ointment to the conjunctiva just after birth. As a matter of fact, all newborn babies receive a prophylactic application of an antiseptic solution or ointment.

Other infections

The choroid coat, ciliary body, iris, and other parts of the eyeball can become infected by various organisms. These disorders are likely to become serious. Fortunately, they are not very common in most people. Syphilis spirochetes, tubercle bacilli, and a variety of cocci may cause these very painful infections. These infections sometimes follow sinus infections, tonsillitis, conjunctivitis and other disorders, where the infecting agent may be spread to nearby structures. Patients with these types of infections are normally placed in the care of an *ophthalmologist*. An ophthalmologist is a health care provider specializing in the diagnosis and treatment of disorders of the eye.

Cataracts

Cataract formation is the most frequent cause of blindness. A cataract is an opacity of the lens or its capsule. Sometimes the areas of opacity can be seen through a pupil that becomes greatly enlarged because of the reduction in the amount of light that can reach the retina. In other cases, there is very gradual loss of vision, and frequent changes in glasses may aid in maintaining useful vision for some time. Removal of the lens may restore some vision, but the addition of eyeglasses or a contact lens usually is required to achieve satisfactory visual acuity, as well as binocular vision, which is, for example, needed for driving a car. Most persons affected will need reading glasses for close work. Surgical techniques are now available to implant an artificial lens; this procedure has been successful in restoring normal vision.

Glaucoma

A second, very important cause of blindness is *glaucoma*—a condition characterized by excess pressure of the aqueous humor. This fluid is being produced constantly from the blood, and after circulation through the eye it drains out a small hole in the bottom of the eye and is reabsorbed into the bloodstream. Interference with the drainage of this fluid to the bloodstream leads to an increase in pressure inside the eyeball. The pressure pushes on the optic disc and causes it to “cup”. The cupped tissue is necrotic. Similar to cataracts, glaucoma usually progresses rather slowly, with vague visual disturbances and gradual impairment of vision. Halos around lights, headaches, and the need for frequent changes of glasses (particularly by people over 40) are symptoms that should be investigated by an ophthalmologist. There are different forms of glaucoma. First, closed or narrow angle glaucoma results from the drainage hole being closed or obscured. In open angle glaucoma, drainage is satisfactory, but an overabundance of aqueous humor is produced. In this case, pressure builds up because only so much humor can go down the drain at a time. Each type of glaucoma requires different management. Because continued high pressure of the aqueous humor may cause destruction of the optic nerve fibers, it is important to obtain continuous treatment, beginning early in the disease, to avoid blindness.

Diabetes

In the United States, diabetes as a cause of blindness is increasing. Disorders of the eye directly related to diabetes include:

- *Optic atrophy*—where the optic nerve fibers die.
- *Cataracts*—occur earlier and with greater frequency among diabetics.
- *Diabetic retinopathy*—where the retina can be damaged by blood vessel hemorrhages and other causes.
- *Atherosclerosis*—fatty deposits in the arteries, diabetics are extremely susceptible to atherosclerosis.

Retinal detachment

Retinal detachment may be a slow developing disorder or it may occur suddenly. In this condition, the retina becomes detached from the underlying layer as a result of trauma or an accumulation of fluid or tissue between the layers. If left untreated, complete detachment can occur, resulting in

blindness. Surgical treatment includes a sort of “spot welding” with an electric current or a weak laser beam. A series of pinpoint scars (connective tissue) develop to reattach the retina.

Ear disorders

Pressure changes

Sudden great changes in the pressure on either side of the tympanic membrane may cause excessive stretching and inflammation of the membrane. There can even be perforation of the tympanic membrane to relieve the pressure.

Otitis media

Otitis media is an infection of the middle ear cavity and is rather common. A variety of bacteria as well as viruses may cause otitis media. It is also a frequent complication of measles, influenza, and other infections, especially those of the pharynx. Transmission of pathogens from the pharynx to the middle ear happens more often in children, partially because the eustachian tube is shorter and more horizontal in the child. On the other hand, in the adult the tube is longer and tends to slant down toward the pharynx. Antibiotic drugs have reduced complications and have caused a marked decrease in the amount of surgery done to drain middle ear infections. However, in some cases, pressure from pus or exudate in the middle ear can be relieved only by cutting the tympanic membrane, a procedure called a *myringotomy*.

Hearing loss

Hearing loss may be partial or complete. When the loss is complete, the condition is called deafness. The two main types of hearing loss are *conduction* deafness and *nerve* deafness.

Conduction deafness is due to interference with the passage of the sound waves from the outside to the inner ear. There may be obstruction of the external canal by wax or a foreign body. Blockage of the eustachian tube prevents the equalization of air pressure on both sides of the tympanic membrane, which, in turn, decreases the ability of the membrane to vibrate. Another cause of conduction deafness is damage to the tympanic membrane and ossicles resulting from chronic otitis media or from *otosclerosis*, an hereditary disease that causes bone changes in the stapes that prevent its normal vibration. Surgical removal of the diseased stapes and its replacement with an artificial device allows conduction of sound from the ossicles to the oval window and the cochlea.

Nerve deafness is due to disorders of the sensory mechanism affecting the cochlea, the vestibulocochlear nerve, or the brain areas concerned with hearing. This disorder may result from prolonged exposure to loud noises, to the use of certain drugs for long periods of time, or to various infections and toxins.

626. Ophthalmic and otic preparations

These are the two main categories that we'll be looking at. Many of the ophthalmic and otic preparations that we have in our pharmacies are medications that are used elsewhere in the body and are just formulated for use in the eyes and ears. We'll be covering just the medications that aren't covered in other units. Let's start with the eyes.

Ophthalmic preparations

The ophthalmic preparations that we're going to cover are the glaucoma agents including dipivefrin, the beta-blockers, and the miotics. We'll also look at vasoconstrictors and briefly touch on mydriatics.

Medications used to treat glaucoma

The beta blockers and miotics are broad categories that are commonly used to treat glaucoma. Dipivefrin doesn't fall into either of these categories and will be covered separately. With all of that said, I think that we should start with Dipivefrin.

Dipivefrin

Dipivefrin is a prodrug of epinephrine and is converted to epinephrine in the eye. It has the same therapeutic effects as epinephrine with fewer local and systemic side effects. Epinephrine, a direct-acting sympathomimetic agent, acts on α and β receptors. Topical application causes conjunctival decongestion (vasoconstriction), transient mydriasis (pupillary dilation) and reduction in intraocular pressure (IOP). IOP reduction is primarily due to reduced aqueous production and increased aqueous outflow.

Indications and dosage

Dipivefrin is indicated as initial therapy or in addition to other antiglaucoma agents for the control of IOP in chronic open-angle glaucoma. It is available in a 0.1 percent liquid in 5, 10, and 15 ml bottles. The dosage of Dipivefrin is one drop instill into the eye(s) every 12 hours.

Contraindications

Patients who have shown a sensitivity to Dipivefrin or any of its components should not use it. Also, patients who suffer from narrow angle glaucoma should not use Dipivefrin.

Warnings

Pregnancy – Dipivefrin is in category B. There are no adequate and well controlled studies in pregnant women.

Lactation – It is not known whether this drug is excreted in breast milk.

Drug interactions

There are no listed drug interactions for Dipivefrin.

Patient information

- Slight stinging or burning on initial instillation may occur.
- Do not try to "catch up" on missed doses by applying more than one dose at a time.

Ophthalmic beta blockers

The two drugs that are discussed here are Betaxolol and Timolol. These two drugs are noncardioselective beta 1 and beta 2 blockers. They do not have any sympathomimetic activity. The beta blockers reduce IOP by a reduction in aqueous production.

Drug	Strength	Dose
Betaxolol	0.25% and 0.5%	1 – 2 drops twice daily
Timolol	0.25% and 0.5%	1 drop twice daily until controlled, then 1 drop daily

Indications

Both of these agents are indicated for the treatment of ocular hypertension and chronic open-angle glaucoma. They may be used alone or in combination with other antiglaucoma drugs.

Contraindications

Patients with bronchial asthma, a history of bronchial asthma or severe chronic obstructive pulmonary disease; sinus bradycardia; hypersensitivity to any component of the products should not use these medications.

Warnings

These agents may be absorbed systemically. The same adverse reactions found with systemic β -blockers may occur with topical use. For example, severe respiratory reactions and cardiac

reactions, including death due to bronchospasm in asthmatics, and rarely, death associated with cardiac failure, have been reported with topical beta-blockers.

Pregnancy – Since no adequate studies have been performed on these drugs, they fall into category C.

Lactation – It isn't known if Betaxolol is excreted into breast milk. Timolol however is. Because of the potential for serious adverse reaction in nursing infants, a decision must be made to discontinue nursing or discontinue the medication based on the importance of the medication to the mother.

Drug interactions

The following table lists the interactions for ophthalmic beta blockers.

Drug	Reaction
Oral beta blockers	The use of topical beta blockers may potentiate and be additive on those of systemic beta blockers.
Quinidine	Bradycardic effects may be potentiated.
Verapamil	Bradycardic effects may be potentiated.

Patient information

Patients should be aware that transient stinging/discomfort is relatively common and that they should notify their physician if severe.

Miotics

The direct-acting miotics are parasympathomimetic (cholinergic) drugs which duplicate the muscarinic effects of acetylcholine. When applied topically, these drugs produce pupillary constriction, stimulate the ciliary muscles and increase aqueous humor outflow facility. Miosis, produced through contraction of the iris sphincter, causes increased tension on the scleral spur (reducing outflow resistance) and opening of the trabecular meshwork spaces facilitating outflow. With the increase in outflow facility, there is a decrease in intraocular pressure (IOP). The only miotic that we'll be discussing is pilocarpine.

Indications and dosage

Pilocarpine is indicated to decrease elevated IOP in glaucoma, especially open-angle glaucoma. Patients may be maintained on pilocarpine as long as intraocular pressure (IOP) is controlled and there is no deterioration in the visual fields. Pilocarpine is available in numerous strengths from 0.25 percent up to 10 percent. Pilocarpine is dosed initially at one or two drops 3 to 4 times daily. The frequency of instillation and the concentration are determined by patient response. Individuals with heavily pigmented irides may require higher strengths.

Contraindications

Patients sensitive to pilocarpine, or those who have a condition where constriction is undesirable should not use pilocarpine.

Warnings

Pregnancy and lactation – Pilocarpine is in category C because safety for use during pregnancy has not been established. It is not known whether these drugs are excreted in breast milk; exercise caution when administering to a nursing woman.

Drug interactions

There are no listed interactions for pilocarpine.

Patient information

- May sting upon instillation, especially first few doses.
- May cause headache, browache and decreased night vision. Use caution while night driving or performing hazardous tasks in poor light.
- To avoid contamination, do not touch tip of container to any surface. Replace cap after using. Keep bottle tightly closed when not in use. Discard solution after expiration date.

Vasoconstrictors

The action of these drugs is pretty obvious. Although they aren't listed as the main drugs to treat glaucoma, one of them, phenylephrine does work and is indicated for that. The three drugs that we'll discuss here are phenylephrine, oxymetazoline, and naphazoline. The second two will be discussed together.

Phenylephrine, Oxymetazoline, and Naphazoline

These are sympathomimetic agents. The effects of sympathomimetic agents on the eye include: Pupil dilation, increase in outflow of aqueous humor and vasoconstriction, relaxation of the ciliary muscle and a decrease in the formation of aqueous humor. Strong vasoconstriction preparations (phenylephrine 2.5 percent and 10 percent) cause vasoconstriction and pupillary dilation for diagnostic eye exams, during surgery. Weak sympathomimetic solutions (phenylephrine 0.12 percent, naphazoline and oxymetazoline) are used as ophthalmic decongestants (vasoconstriction of conjunctival blood vessels) for symptomatic relief of minor eye irritations.

Indications and dosage

Phenylephrine has different indications for its different strengths. They are:

For the 2.5 percent and 10 percent – Decongestant and vasoconstrictor and for pupil dilation in uveitis (posterior synechiae), open- angle glaucoma, refraction without cycloplegia, prior to surgery, ophthalmoscopic examination, diagnostic procedures (funduscopy).

For the 0.12 percent – A decongestant to provide relief of minor eye irritations.

Dosing also is different for the varied indications and strengths:

Vasoconstrictors and pupil dilation – Apply a drop of topical anesthetic. Follow in a few minutes by 1 drop of the 2.5 percent or 10 percent phenylephrine. The anesthetic prevents stinging and consequent dilution of solution by lacrimation. It may be necessary to repeat the instillation after 1 hour, again preceded by a topical anesthetic.

Glaucoma - Instill 1 drop of 10 percent solution on the upper surface of the cornea as often as necessary. The 2.5 percent and 10 percent solutions may be used in conjunction with miotics in patients with open-angle glaucoma.

Minor eye irritations - Instill 1 or 2 drops of the 0.12 percent solution in eye(s) up to 4 times daily as needed.

Oxymetazoline comes in 0.025 percent and is dosed at 1 – 2 drops in affected eye(s) every 6 hours.

Naphazoline in prescription strength is 0.1 percent and is dosed as 1 – 2 drops in the conjunctival sac of affected eye(s) every 3 – 4 hours

Contraindications

A hypersensitivity to the drug and narrow-angle glaucoma are the contraindications for phenylephrine, oxymetazoline and naphazoline.

Warnings

Pregnancy and lactation – These drugs are in category C. Safety for use during pregnancy is not established. Use only if clearly needed and if the potential benefits outweigh potential hazards to the fetus. Safety for use during breastfeeding has not been established. Use caution when administering to a nursing woman.

Drug interactions

When using this drug, caution should be used in patients taking beta-blockers. The systemic effects of the beta-blockers may occur more readily.

Patient information

- Do not use beyond 48 to 72 hours without consulting a physician.
- If irritation, blurring or redness persists, or if severe eye pain, headache, vision changes, floating spots, dizziness, decrease in body temperature, drowsiness, acute eye redness or pain with light exposure occur, discontinue use and consult a physician.

Cycloplegic Mydriatics

This grouping of drugs won't be dispensed from your pharmacy too often. Most of their use is in the clinic setting. The mydriatics cause pupil dilation, mainly for examination purposes. The mydriatics act as anticholinergic agents. Anticholinergic agents block the responses of the sphincter muscle of the iris and the muscle of the ciliary body to cholinergic stimulation, producing pupillary dilation (mydriasis) and paralysis of the ability to focus on close objects (cycloplegia). The next table gives some important information about the cycloplegic mydriatics.

Drug	Mydriasis		Cycloplegia		Available solution
	Peak action (min)	Recovery (days)	Peak action (min)	Recovery (days)	
Homatropine	40 – 60	1 – 3	30 – 60	1 – 3	2% – 5%
Scopolomine	20 – 30	3 – 7	30 – 60	3 – 7	0.25%
Tropicamide	20 - 40	0.25	20 - 35	0.25	0.5% - 1%

Indications

These drugs are indicated for cycloplegic refraction and for dilating the pupil in inflammatory conditions of the iris.

Contraindications

If a patient has a tendency toward glaucoma or has glaucoma, these drugs should not be used.

Warnings

As stated above, these medications should be avoided in patients with glaucoma. They may cause a glaucoma attack.

Pregnancy – These medications have been classified into category C. Safety for use during pregnancy has not been established. Give to a pregnant woman only if clearly needed.

Lactation - Homatropine may be detectable, in very small amounts, in breast milk. Although this is controversial, according to the American Academy of Pediatrics, these agents are compatible with breastfeeding.

Drug interactions

There are no drug interactions listed for these medications.

Patient information

- To avoid contamination, do not touch dropper tip to any surface . Replace cap after using.
- May cause blurred vision. Do not drive or engage in any hazardous activities while the pupils are dilated .
- May cause sensitivity to light . Protect eyes in bright illumination during dilation.
- Keep out of the reach of children . These drugs should not be taken orally . Wash your own hands and the child's following administration .
- If eye pain occurs, discontinue use and consult physician immediately.

Other ophthalmic preparations

We have already covered NSAIDS and steroids, and we'll cover antibiotics later in this course. All of these drugs have specific ophthalmic indications that aren't covered in their respective sections. The indications for these medications are probably obvious to you by this point in your training. NSAIDS and steroids are used to treat inflammation of the internal parts of the eye or conjunctiva when a systemic agent isn't appropriate. That statement also holds true for the antibiotics. Sometimes you need to place the medication right where the infection is, or the systemic affects of the drug may be undesirable. Also note that these medications are often found in combination with each other, especially the steroids and antibiotics. This combination would be indicated for steroid-responsive ocular conditions where a steroid is indicated and the risk of bacterial infection exists. The following table lists some of the medications that you may see in these classes.

NSAID	Steroid	Antibiotic
Flurbiprofen	Prednisolone	Erythromycin
Diclofenac	Dexamethasone	Gentamycin
Ketorolac		Tobramycin
		Bacitracin
		Ciprofloxacin
		Norfloxacin
		Ofloxacin

Otic preparations

The otic preparations that we'll discuss can be divided into three groups, steroid and antibiotic combinations, antibiotics, and miscellaneous. These three areas will be discussed differently than most of the other areas. We'll look at what each classification does and list the available agents that fall into that class. First, there is some general information that you need to know to give to your patients that concern all of the drugs that we'll discuss.

- These drugs are for use in the ear only; avoid contact with the eyes.
- Notify your physician if burning or itching occurs or if condition persists.

Proper use of ear drops:

- Wash hands thoroughly.
- Avoid touching the dropper to the ear or any other surface. For accuracy and to avoid contamination, have another person insert the ear drops when possible.
- Hold container in the hand for a few minutes to warm to near body temperature if it has been refrigerated.
- If the drops are in a suspension form, shake well for 10 seconds before using.
- Lie on your side or tilt the affected ear up for ease of administration.

To allow the drops to run in:

- Adults- Hold the earlobe up and back.
- Children- Hold the earlobe down and back.
- Instill the prescribed number of drops in the ear.
- Do not insert the dropper into the ear.
- Keep the ear tilted for about 2 minutes, or insert a soft cotton plug, whichever is recommended.

Products used to soften, loosen and remove earwax:

- Do not use if ear drainage, discharge, pain, irritation or rash occurs.
- If you become dizzy, consult a physician.
- Do not use if injury or perforation of the ear drum exists or after ear surgery unless directed otherwise.
- Do not use for > 4 days; if excessive earwax remains after use of this product, consult a physician.
- Any wax remaining after treatment may be removed by gently flushing with warm water using a soft rubber bulb ear syringe.

Steroid and antibiotic combinations

In these combinations hydrocortisone is the most common otic steroid found and is used for its antiallergic, antipruritic and anti-inflammatory effects. Antibiotics are used for their antibacterial actions.

Indications and dosage

These medications are indicated for the treatment of superficial bacterial infections of the external auditory canal. The usual dose is 4 drops instilled 3 to 4 times daily.

Precaution

Prolonged treatment with these agents may result in overgrowth of nonsusceptible organisms and fungi.

Otic antibiotics

Chloramphenicol is the main antibiotic used in otic preparations. Chloramphenicol is a broad-spectrum antibiotic. It is primarily bacteriostatic and acts by inhibition of protein synthesis by interfering with the transfer of activated amino acids from RNA to ribosomes. Development of resistance is minimal for staphylococci and many other types of bacteria.

Indications

Chloramphenicol is indicated for treating superficial infections involving the external auditory canal. For inner ear infections, use systemic antibiotic therapy.

Miscellaneous otic preparations

There are many miscellaneous otic preparations to perform a myriad of functions. Here is a list of some of the ingredients that can be used in otic preparations and their actions:

- Hydrocortisone and desonide are steroids used for their anti-inflammatory and antipruritic effects.
- Phenylephrine is a vasoconstrictor which may be a decongestant.
- Acetic acid, M-cresyl acetate, boric acid, benzalkonium chloride, benzethonium chloride and aluminum acetate (burow's solution) provide antibacterial or antifungal action.
- Carbamide peroxide and triethanolamine emulsify and disperse ear wax.

- Glycerin is a solvent and vehicle; it has emollient, hygroscopic and humectant properties.
- Benzocaine is a local anesthetic.
- Antipyrine is an analgesic.

Self-Test Questions

After you complete these questions, you may check your answers at the end of the unit.

625. Eye and ear disorders

1. What is conjunctivitis?
2. What is ophthalmia neonatorum?
3. What term describes an infection of the middle ear?
4. What are the two main types of hearing loss?

626. Ophthalmic and otic preparations

1. How does Dipivefrin reduce IOP?
2. Why shouldn't patients suffering from asthma use Timolol?
3. What are the effects of miotics?
4. What are the sympathomimetic affects of ophthalmic vasoconstrictors?
5. What is cycloplegia?
6. Into what three groups are otic preparations divided?
7. What is the most commonly used otic steroid?

Answers to Self-Test Questions

623

1. The sclera.
2. The watery fluid that fills most of the eyeball in front of the lens. This fluid helps to maintain the slight forward curve in the cornea.
3. To regulate the amount of light entering the eye.
4. Eardrum.
5. From the pharynx through the eustachian, or auditory tube.
6. The stapes.

624

1. Solution (liquid).
2. In the olfactory *epithelium* of the upper part of the nasal cavity.
3. Polydipsia.
4. Pain sense.

625

1. Inflammation of the membrane lining the eyelids and covering the front of the eyeball.
2. A gonococcal infection passed from a mother to her child during birth.
3. Otitis media.
4. Conduction deafness and nerve deafness.

626

1. Dipivefrin reduces IOP by reducing aqueous production and increased aqueous outflow.
2. Ophthalmic timolol may be absorbed systemically, causing the same bronchospasms in asthmatics as found with systemic beta-blockers.
3. Pupillary constriction, stimulation of ciliary muscles, and increased aqueous humor outflow.
4. Pupil dilation, increased outflow of aqueous humor, vasoconstriction, relaxation of ciliary muscles, and decreased formation of aqueous humor.
5. Paralysis of the ability to focus on close objects.
6. Steroid and antibiotic combinations, antibiotics, and miscellaneous.
7. Hydrocortisone.

Unit Review Exercises

Note to Student: Consider all choices carefully, select the *best* answer to each question, and *circle* the corresponding letter. When you have completed all unit review exercises, transfer your answers to ECI Form 34, Field Scoring Answer Sheet.

Do not return your answer sheet to ECI.

46. (623) Which section of the ear contains the receptors for hearing and equilibrium?
 - a. External.
 - b. Middle.
 - c. Internal.
 - d. Medial.
47. (624) Where are the receptors for smell located?
 - a. Olfactory epithelium.
 - b. Olfactory nerves.
 - c. Olfactory center of the brain.
 - d. Olfactory epidermis.
48. (625) What type of eye infection is referred to as granular conjunctivitis?
 - a. Choroid infections.
 - b. Trachoma.
 - c. Pink eye.
 - d. Ophthalmia neonatorum.
49. (625) Which eye disorder can be directly attributed to diabetes?
 - a. Glaucoma.
 - b. Conjunctivitis.
 - c. Retinal detachment.
 - d. Cataracts.
50. (626) How does dipivefrin decrease intraocular pressure?
 - a. Increased aqueous production and decreased outflow.
 - b. Decreased aqueous production and decreased outflow.
 - c. Increased aqueous production and increased outflow.
 - d. Decreased production and increased outflow.

Student Notes

Student Notes

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