

**CDC 4P051B**

# **Pharmacy Journeyman**

## **Volume 3. Anatomy, Physiology, and Pharmacology**



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VOLUME 3 continues the presentation of the systems of the body. As in volume 2, we'll look at a specific system's anatomy and physiology, conditions affecting that system, and drugs used to treat those conditions.

Unit 1 covers the endocrine system. We start by classifying glands and their secretions. Next, we look at hormones and their effects on the body. Endocrine conditions, such as diabetes, and adrenal cortex disorder, as well as menopause and the drug therapies to treat these conditions are covered next.

Unit 2 dives into the digestive system. We take a trip down the alimentary canal, discussing its structures and the accessory organs along the way. We then see what can go wrong—ulcers, constipation, and diarrhea. Treatment for each of these is then discussed.

Unit 3 looks at the urinary system. This is a short unit, talking about the kidneys, bladder, and excretory organs and the conditions affecting them. Only three classes of drugs are discussed here, antispasmodics, analgesics, and alkalinizers.

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This volume is valued at 12 hours and 4 points.

## Acknowledgment

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

Intense editing by Maj Thomas Bacon and Capt 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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The first of the two main parts of the book is devoted to a study of the history of the English language. The second part is devoted to a study of the English language in the United States. The book is written in a clear and concise style, and is suitable for use as a textbook or as a reference work. The author is a well-known linguist and has written several other books on the English language.

## Unit 1. The Endocrine System

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**D**O you know someone who has diabetes? Have you ever seen a giant or a dwarf? If you have, then you have witnessed visible proof of the importance of the endocrine system for normal development and health. This unit discusses the anatomy and physiology of the endocrine system, the conditions associated with the endocrine system, and the drugs used to treat those conditions.

### 1-1. Anatomy, Physiology, and Disorders of the Endocrine System

The endocrine system has the same general function as the nervous system: communication and control. The main difference is that the nervous system provides rapid, brief control by fast-traveling nerve impulses, and the endocrine system provides slower, but longer-lasting control by *hormones* (chemicals) secreted into and circulated by the blood. This section begins with the classification of secretions and glands, followed by endocrine glands and their hormones, the adrenal glands and their hormones, and finally some other hormone-producing organs. The last topic we'll discuss will be endocrine disorders.

#### 400. The classification of secretions and glands

Any organ that produces a secretion is called a **gland**. Secretions are substances manufactured from blood constituents by the specialized cells that form the gland. The various glands' secretions can be divided into two main groups, external secretions and internal secretions.

##### External secretions

These secretions are carried from the gland cells to a nearby organ or to the body's surface. They are effective in a limited area near their origin. Some of these secretions are:

- Digestive juices.
- Secretions from the sebaceous glands of the skin.
- Tears from the lacrimal glands.
- Urine (both a secretion and an excretion).

##### Internal secretions

These secretions are carried to all parts of the body by the blood or lymph. They often affect tissues a substantial distance from their point of origin. Internal secretions are called *hormones*. Hormones and

the glands that produce them are the main topic of this section. There are two categories of glands: exocrine glands and endocrine glands.

### *Exocrine glands*

These glands have tubes, known as *ducts*, to carry the secretion from the gland to another organ or part of the body.

### *Endocrine (ductless) glands*

These glands have no ducts, (fig. 1-1) and therefore are dependent upon the blood and lymph to carry their secretions to various body tissues by way of capillaries of the glandular tissue.

From time to time the lymph nodes are spoken of as glands (such as, the "neck glands," which are actually nodes); but as far as is known the lymph nodes produce no secretions.

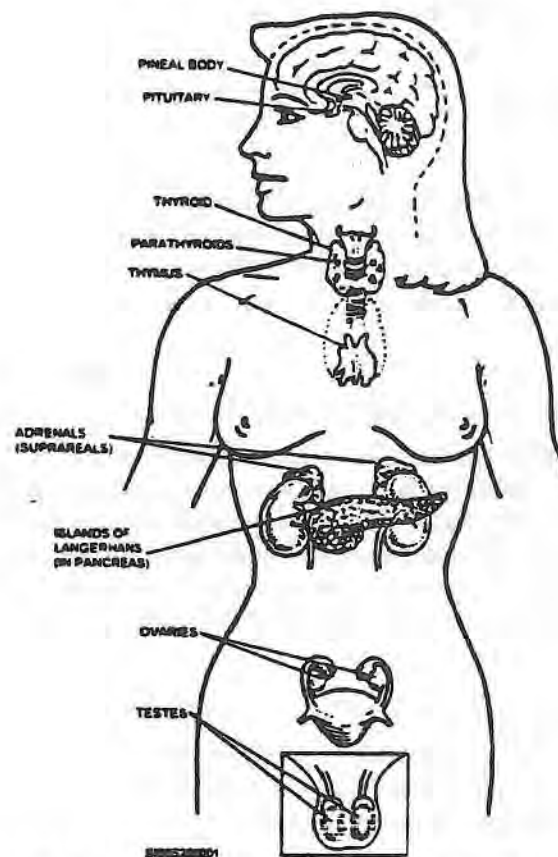


Figure 1-1. Endocrine system (male glands are shown in inset).

The endocrine glands produce only internal secretions (hormones), but there are some organs that contain both exocrine and endocrine gland tissue. Some examples are the pancreas, stomach, and small intestine. They all produce external excretions (digestive juices) and internal secretions (hormones). The following paragraphs discuss the endocrine glands, the hormones produced, and their principal function.

### *Structure of glands*

Endocrine glands differ in complexity from very simple depressions similar to tiny dimples to involved arrangements like those found in the kidneys. The stomach wall and intestinal lining house simple tube-like structures. The liver, pancreas, and salivary glands are home to complex, treelike groups of ducts. The majority of glands are made largely of epithelial tissue with a framework of connective tissue. There may be a fibrous envelope (a tough connective tissue capsule) enclosing the

organ, with extensions into the organ forming partitions. Between these partitions are groups of cells, and these units are known as *lobes*.

Like exocrine glands, most endocrine glands are made of epithelial tissue. Since they do not have ducts, they seem to make up for this lack by a most extensive blood vessel network. Surgery of endocrine glands, such as on the thyroid, requires care in the control of bleeding. The organs thought to have the richest blood supply of any in the body are the tiny adrenal, or suprarenal glands located near the upper parts of the kidneys.

#### *General functions of hormones*

Chemical substances manufactured by the endocrine glands are called *hormones*. Their overall function is to regulate the activities of various body organs. On one hand, the action of hormones can be compared with the nervous system. Hormones are sometimes called "chemical messengers." Certain hormones stimulate exocrine tissues to produce their secretions. Another category of hormone stimulates other endocrine glands to action. Some hormones have a profound effect upon growth, development, and even the personality of an individual. There are others that regulate the body chemistry; for example, the metabolism of cells. Others regulate the contraction of muscle tissues. The actions of each hormone are specific; in other words, each hormone has its specialized job to do.

#### **401. Endocrine glands and their hormones**

This lesson discusses the pituitary or "master gland," the thyroid gland, the parathyroid glands, the adrenal glands, and the sex glands.

##### **The pituitary or "master gland"**

The pituitary is a small gland about the size of a cherry. It is almost totally surrounded by bone except for its area of connection with the brain. It is located in a saddle-like depression just behind the point of optic nerve crossing, in the mid-line. The pituitary gland has two important parts, each of which produces several different hormones. They are known as the anterior and posterior lobes.

##### *The anterior lobe*

The anterior lobe of the pituitary gland produces a large number of hormones. Many of these hormones stimulate other glands; that is why the pituitary is known as the "master gland." Its main hormones are the growth hormone, thyroid-stimulating hormone, adrenocorticotrophic hormone, gonadotropic hormone, and prolactin hormone.

<i>Hormones</i>	
Types of Hormones	Functions
Growth hormone or somatotrophic hormone	<ul style="list-style-type: none"> <li>Stimulates growth of bones, muscles, and other organs.</li> <li>Is produced in varying amounts throughout life.</li> </ul> <p>A person born with a deficiency of this hormone will remain a small, though well-proportioned, individual unless treated with adequate hormones.</p>
Thyroid-stimulating or thyrotrophic hormone	Stimulates the thyroid gland.
Adrenocorticotrophic hormone (ACTH)	Stimulates the cortex of the adrenal gland.
Gonadotropic hormone	Regulates the growth, development, and functioning of the reproductive systems in both the male and female.
Prolactin or lactogenic hormone	Stimulates the production of milk in the female.

##### *The posterior lobe*

The posterior lobe of the pituitary gland stores and releases two hormones. The two hormones are produced in the hypothalamus and then trickle down nerve fibers to the posterior lobe. The two hormones are known as antidiuretic hormone and oxytocin. Antidiuretic hormone promotes the



reabsorption of water from the kidney tubules and thus decreases the excretion of water. Large amounts of this hormone cause contraction of the smooth muscle of blood vessels and raise blood pressure. Inadequate amounts of this hormone cause excessive loss of water and results in a disorder known as diabetes insipidus. This type of diabetes should not be confused with diabetes mellitus, which is an inadequate amount of insulin.

Oxytocin causes contraction of the muscle of the uterus and also causes milk ejection from the breasts. Under certain circumstances, commercial preparations of this hormone are administered during and after childbirth to cause the uterus to contract.

### **The thyroid gland**

The thyroid gland is the largest of the endocrine glands and is located in the neck. The thyroid gland has two oval parts called the *lateral lobes*, one on either side of the voice box. The *isthmus*, a narrow band, connects these two lobes. The whole gland is encased in a connective tissue capsule. The thyroid produces hormones: the main hormone is called *thyroxin*. It also produces a hormone known as *calcitonin*, which is active in calcium metabolism and will be discussed in connection with the parathyroid gland. The main function of thyroid hormones is to regulate metabolism for the production of heat and energy in the body tissues. There must be an adequate amount of iodine in the blood for these hormones to be manufactured. This iodine content is maintained by eating vegetables grown in iodine-containing soils, or by eating seafood. In certain regions of Italy and Switzerland, as well as some parts of the United States, the soil is so deficient in iodine that serious defects may result in the people who live in these areas. Iodized salt may be used to prevent difficulties.

The thyroid function tests that are most often used are blood tests that measure the uptake of radioactive iodine in a blood sample. The type of radioactive iodine used in the test determines the name of the test. If these up-take tests are abnormal, the person may have further testing where radioactive iodine is taken by mouth and the radioactivity of the thyroid gland measured.

### **The parathyroid glands**

Embedded in a capsule, behind the thyroid gland, there are four tiny epithelial bodies known as the parathyroid glands. *Parathormone* is the secretion of the parathyroid glands. Parathormone is one of three hormones involved in the regulation of calcium metabolism. The other two are *calcitonin* and *hydroxycholecalciferol*. Parathormone causes the release of calcium from storage areas in bone tissue, consequently increasing the amount of calcium circulating in the blood stream. Calcitonin is produced in the thyroid gland. It acts to lower the amount of calcium circulating in the blood.

Hydroxycholecalciferol is produced from vitamin D. After first being modified by the liver and then the kidney, it regulates the absorption of calcium by the intestine.

### **The adrenal glands and their hormones**

There are two small glands, each one situated above a kidney, known as the *adrenals*, or *suprarenals*. An adrenal gland has two separate parts, each of which has a gland. The *medulla* is the inner area, and the *cortex* is the outer portion.

#### **The medulla's hormones**

Epinephrine, which we have already discussed, is the main hormone produced by the medulla. It is also known as *adrenaline*. *Norepinephrine*, another hormone, is closely related chemically to epinephrine and is similar, but not identical, in its actions. These hormones are referred to as the "fight and flight" hormones due to their effects during emergency situations. Some of their effects are as follows:

1. Stimulation of the sympathetic nerves that supply the involuntary muscle in the walls of the arterioles. This causes these muscles to contract and the person's blood pressure to rise correspondingly.

2. Conversion of the glycogen of the liver into sugar. It is then poured into the blood and brought to the voluntary muscles, allowing them to do an amazing amount of work.
3. Rate of the heartbeat is increased.
4. Bronchiole dilation, through relaxation of the smooth muscle of their walls.

#### *The adrenal cortex's hormones*

There are three main groups of hormones secreted by the adrenal cortex: the glucocorticoids, the mineralocorticoids, and the sex hormones. Each of these groups performs certain specific functions.

#### *Glucocorticoids*

This group of hormones maintains the carbohydrate reserve of the body. They do this by controlling the conversion of amino acids into sugar instead of protein. Glucocorticoids are produced in larger amounts in times of stress, thereby aiding the body in responding to unfavorable conditions. These hormones have the ability to suppress the inflammatory response. They are often administered as medications for this purpose. The major hormone of this group is *cortisol*.

#### *Mineralocorticoids*

This group of hormones is important in the regulation of electrolyte balance. They do this by controlling the reabsorption of sodium and the secretion of potassium by the kidney tubules. *Aldosterone* is the major hormone of this group.

#### *Sex hormones*

This group of hormones is normally secreted in small amounts so that their effect in the body is slight.

**NOTE:** Once again, it should be mentioned that production of these hormones by the adrenal cortex is stimulated by ACTH from the "master gland" (pituitary). The pituitary gland is stimulated by impulses from the hypothalamus. The endocrine glands are not only interrelated so they affect each other, but research has shown complex nervous and hormone connections.

#### *The pancreas and insulin*

There are small groups of specialized cells called *islets* scattered throughout the pancreas. They are also known as the *islands of Langerhans*. These islets function independently, and are *not* connected with the ducts that supply the exocrine part of the pancreas. *Insulin* is the most important hormone secreted by these islets.

Insulin is active in glucose transport across the cell membrane. Once glucose is inside the cell, it can be used for energy metabolism. When insulin is present, excessive amounts of carbohydrates enter fat cells, where they are converted and stored as fat. Furthermore, insulin increases the transport of amino acids into the cells and improves their use in protein manufacturing. When there is a lack of insulin, there is not enough glucose for cell metabolism; consequently, this causes an abnormal breakdown of proteins and fats.

#### *Sex glands*

Sex glands, including the ovaries of the female and the testes of the male, are important endocrine structures. The hormones that these organs produce play an important role in the development of sexual characteristics. These sexual characteristics usually first appear in the early teens. They also play an important role in the maintenance of the reproductive apparatus once full development has been attained. *Testosterone* is the hormone produced by the male sex glands. It is responsible for the functioning of certain organs of reproduction. The structures directly concerned with reproduction are considered to be *primary* sexual characteristics. Additionally, testosterone is responsible for such *secondary* sexual characteristics as the deep voice, and facial hair growth.

The hormones most nearly paralleling testosterone in their actions, in the female, are *estrogens*. Estrogens contribute to the development of the female sexual characteristics. They stimulate the development of the mammary glands, the onset of menstruation, and the development and functioning of the reproductive organs.

One other hormone produced by the female sex glands is called *progesterone*. This hormone aids in the normal development of pregnancy.

#### **402. Other hormone producing organs**

##### **Kidney**

The kidney (juxtaglomerular apparatus) produces the hormones renin, hydroxycholecalciferol, and erythropoietin. Renin acts on the vascular system. Hydroxycholecalciferol is active in calcium metabolism. Erythropoietin stimulates red blood cell production.

##### **Placenta**

The *placenta* produces various hormones during pregnancy. These hormones cause changes in the uterine lining. Later in pregnancy, they help prepare the breasts for lactation. Tests for pregnancy are based on the presence of placental secretions.

##### **Thymus**

The *thymus* is the primary central organ of the lymphatic system. It is a single unpaired organ consisting of two pyramid-shaped lobes. It is located in the mediastinum, extending up into the neck as far as the lower edge of the thyroid gland. The *thymus* produces hormones that stimulate the production of small lymphocytes. Lymphocytes function in the body's defense against infection. The thymus secretes a substance that is called *thymosin* (also known as thymic hormone). Thymosin promotes the growth of peripheral lymphoid tissue. The thymus is most active during prenatal life and in infancy.

##### **Pineal body**

There is a small, flattened, cone-shaped structure located between the two parts of the thalamus, called the *pineal body*. It produces the hormone *melatonin* in a number of animals and possibly in humans. Melatonin, or some other hormone from the pineal, is thought to regulate the release of certain substances from the hypothalamus. These substances may in turn, regulate the secretion of gonadotropins from the pituitary. The pineal body of humans can be invaded by tumor tissue that can either increase the production of pineal hormone or can destroy the gland. The symptoms of these conditions indicate the possible role of the pineal body in gonadal activity.

##### **Hypothalamus**

The *hypothalamus* is located immediately above the pituitary gland, and produces substances called *neurohormones*. They are carried through special blood vessel pathways directly from the hypothalamus to the anterior pituitary where they regulate the secretory activity of that gland.

##### **Prostaglandins**

*Prostaglandins* are hormone-like structures and are the objective of many studies. They are found widely distributed in cells throughout the body. Organs that have been named as manufacturers of prostaglandins include the following:

1. Seminal vesicles (male reproductive system).
2. Thymus.
3. Brain.
4. Kidney medulla.



A wide array of functions has been attributed to them: which include constriction of blood vessels, constriction of bronchial tubes, and constriction of the intestine. Others cause dilation of these same structures. Some prostaglandins are used to induce labor or abortion, and have been recommended as possible contraceptive agents. There has been a vast amount of information written about these substances and extensive research continues.

### 403. Endocrine system disorders

The thyroid, parathyroid, and adrenal cortex are susceptible to many disorders, some of which we will discuss. This lesson covers goiters, hypothyroidism, hyperthyroidism, tetany, kidney stone production, Addison's disease, Cushing's syndrome, adrenal gland tumors, diabetes mellitus, and menopause.

#### Thyroid

##### *Goiters*

A goiter is a swelling of the neck due to an enlarged thyroid. The enlargement may form as the result of iodine deficiency of the blood. As you will see, there are other causes of a goiter as well. However, in this first-mentioned case, known as *simple goiter*, the thyroid becomes enlarged as the size and number of glandular cells increase in an attempt to produce enough thyroid hormones.

The *adenomatous* or *nodular goiter* is another form of goiter. This type of goiter has an accompanying tumor formation that comes about through the overgrowth of the cells of the thyroid tissue. In this type of goiter, the tumor formation may be single or multiple. Single tumor formation seems to be more likely to become malignant.

##### *Hypothyroidism*

There are numerous reasons why the thyroid gland may become either under-active or overactive. Under-activity of the thyroid is known as *hypothyroidism* and appears as two characteristic states—*cretinism* and *myxedema*.

##### *Cretinism*

This is a condition where there is a serious lack of thyroid activity from the beginning of the individual's life. Blood testing of newborns for thyroid hormone is routine in most hospitals. Now and then this condition is the result of the complete absence of thyroid tissue. These infants become dwarfed, as well as mentally deficient, due to the failure of physical and mental development. The only hope of altering the outlook is if continuous thyroid replacement therapy is started. Fortunately, this disorder is rather rare in the United States, though endemic in certain regions where iodine is lacking.

##### *Myxedema*

This condition is the result of atrophy of the thyroid in the adult. These patients become both mentally and physically sluggish. Their skin and hair become dry, and they develop a peculiar swelling of the tissues of the face. Because thyroid extract or the hormone itself may be administered by mouth, the victims of myxedema can be restored to health very easily, though treatment must be maintained throughout the remainder of their lives.

##### *Hyperthyroidism*

This condition, which is an over-activity of the thyroid gland, is the opposite of hypothyroidism. The development of a simple goiter may suggest hyperthyroidism; however, there is a difference. Patients with simple goiter usually have a normal thyroid, but it is enlarged due to the increase in work that it must do. This is similar to the heart enlarging when something causes its workload to increase. However, hyperthyroidism is an abnormal activity of the thyroid without an accompanying need for it by any other part of the body.

### *Exophthalmic goiter or Graves disease*

This disease is a common form of hyperthyroidism in which there is a goiter, eye bulging, a strained facial appearance, intense nervousness, loss of weight, a rapid pulse, sweating, and a tremor. The patient's metabolism is stepped up to a super rate. In numerous cases, drug administration or surgery to remove a part of the thyroid will cure the condition.

### *Thyroid storm*

Thyroid storm is an exaggerated form of hyperthyroidism with a sudden onset. If this condition is left untreated, it is usually fatal. But with appropriate care the majority of patients with this condition can be saved.

### **Parathyroids**

When the parathyroid glands are removed there follows a series of muscle contractions, mainly involving the hand and face muscles. These spasms are caused by a low concentration of calcium in the blood. This condition is called *tetany*. Be careful not to confuse this disorder with the infection called tetanus (lockjaw).

Calcium, normally stored in the bones for use by the tissues as needed, is removed from its storage place and is poured into the bloodstream if the parathyroid glands have an excess secretion production such as parathyroid tumors. It is finally excreted by the kidneys. These patients will have stone formation in the kidneys and easily fractured bones.

### **Adrenal cortex**

#### *Addison's disease*

Addison's disease is the result of hypo-function of the adrenal cortex. This disease is characterized mainly by atrophy (loss of muscle tissue), weakness, skin pigmentation, and disturbances in salt and water balance.

#### *Cushing's syndrome*

Hyper-function of the adrenal cortex results in a condition known as Cushing's syndrome. The symptoms include:

- Obesity with a round face.
- Thin skin that bruises easily.
- Muscle weakness.
- Bone loss.
- Elevated blood sugar.

Use of steroid drugs may also produce these symptoms.

### **Adrenal gland tumors**

Tumors of the adrenal gland give rise to a wide range of symptoms resulting from an excess or a deficiency of hormones secreted.

### **Diabetes mellitus**

If for some reason the pancreatic islets do not produce enough insulin, sugar is not oxidized (burned in the tissues) for transformation into energy. Instead, sugar is excreted along with the urine. This condition is called *diabetes mellitus*. For a diabetic patient to lead a normal life, proper utilization of the body's fuel must be restored and maintained. This can be achieved in mild cases of diabetes by a modification of diet, and at times with the addition of oral medications that increase the output of insulin by the pancreas. On the other hand, in severe cases of diabetes patients must also receive insulin from an outside source in periodic doses. Insulin is destroyed by the action of digestive juices and, therefore, must be given by injection. Normally, it is desirable for these patients to learn to

administer their injections. They must adjust their diets, exercise, and other activities in order to maintain the proper balance between the intake of insulin and sugar needs. These patients should carry special identification cards that let people know that they are diabetic patients taking insulin, and that a dazed condition may indicate a need for sugar.

Some patients may use a mechanical pump that provides a round-the-clock supply of insulin. Insulin is placed in this device, which then injects it into the subcutaneous tissues of the abdomen. This allows for a more consistent blood sugar level, resulting in a more nearly normal metabolism.

Some of the long-term complications of diabetes are:

- Infection resistance is lowered.
- Arteries, including those of the retina, kidneys, and heart, may be seriously damaged.
- Peripheral nerves are affected also, with accompanying pain and loss of sensation.

### **Menopause and amenorrhea**

#### ***Menopause***

Menopause is becoming a more prevalent condition as we see our population getting older. Menopause, strictly defined, is the last menstrual period and the cessation of hormone excretion from the ovaries. Ovarian function does not cease abruptly though. It will decline slowly over a period of two to eight years. From the time ovarian function begins to stop, to one year after complete failure is when women experience the hot flashes, vaginal dryness, and drastic changes in menstrual cycle. Only after one year of not having a menstrual cycle is a woman considered postmenopausal.

The lack of estrogen plays a much more important role in women's health than the well-known irritability. Vasomotor instability (flushing) and urogenital atrophy, along with more serious conditions such as osteoporosis and heart disease, may occur from the lack of estrogen.

#### ***Amenorrhea***

Amenorrhea is the lack of a menstrual cycle. It happens normally with menopause. Sometimes though, younger women may suffer from an unusual cessation of menstruation. Women who exercise at high levels for long periods of time may suffer from amenorrhea. Also, lactating women may experience amenorrhea because infant suckling disrupts the hormonal flow. The progesterone hormone softens the endometrium into a secretory state. If a woman suffers from amenorrhea, this softening action may allow normal muscle contractions to expel the lining of the uterus.

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## **Self-Test Questions**

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

### **400. The classification of secretions and glands**

1. Define gland.
  
2. What types of secretions are carried from the gland cells to a nearby organ or to the body's surface?
  
3. What is another name for internal secretions?

4. What is the function of hormones?

**401. Endocrine glands and their hormones**

1. What are the main hormones of the anterior lobe of the pituitary gland?
2. What two hormones are produced in the posterior lobe of the pituitary gland?
3. What is the largest endocrine gland?
4. What is the main hormone produced by the medulla of the adrenal gland?
5. What are the three main groups of hormones secreted by the adrenal cortex?

**402. Other hormone producing organs**

1. List the hormones produced by the kidney?
2. What is the function of the thymosin?
3. Which organs manufacture prostaglandins?

**403. Endocrine system disorders**

1. What is a goiter?
2. What condition results from atrophy of the thyroid in adults?
3. List five symptoms of an exophthalmic goiter?
4. What term is used to describe spasms caused by a low concentration of calcium in the blood?

5. What causes Addison's disease?
6. What causes diabetes mellitus?
7. What treatment is given to patients with mild cases of diabetes?
8. Why is insulin given by injection?
9. List some long-term complications of diabetes mellitus.
10. Define menopause.
11. How does lactation cause amenorrhea?

## **1-2. Drugs Used to Treat Conditions Associated with the Endocrine System**

There are a wide variety of drugs used to treat ailments associated with the endocrine system. This section covers estrogens, progestin, oral contraceptives, antidiabetic agents, and thyroid replacement products.

### **404. Estrogens**

Estrogens are female hormones. They are produced by the body and are essential for the normal sexual development of the female and for the regulation of the menstrual cycle during childbearing years.

Estrogens are prescribed for several reasons:

1. To provide additional hormone when the body doesn't produce enough of its own.
2. In the treatment of selected cases of breast cancer in men and women.
3. In the treatment of men with certain types of prostate cancer.
4. To help prevent osteoporosis in women past menopause.

Risks associated with estrogen therapy include endometrial hyperplasia and possibly a slight increase in the incidence of breast cancer.

### **Indications**

Estrogens are most commonly used as a component of combination contraceptives or as hormone replacement therapy in postmenopausal women. Benefits in postmenopausal women include relief of moderate-to-severe vasomotor symptoms, decreased risk of osteoporosis and cardiovascular disease. Hormone replacement therapy may also be used in female hypogonadism or primary ovarian failure.



Less commonly, select breast or prostate cancer patients with advanced disease may receive estrogens as relief therapy. Estrogens are available in various dosage forms and a multitude of strengths. There are too many to list them all here so we'll just talk about the class in general.

### Contraindications

Females should *not* take estrogen if they have breast cancer, except in appropriately selected patients being treated for metastatic disease, known or suspected pregnancy, or hypersensitivity to any product component.

### Warning

Estrogens have been reported to increase the risk of endometrial carcinoma in postmenopausal women. Studies have shown an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for prolonged periods. The risk of endometrial cancer in estrogen users was 4.5 to 13.9 times greater than in nonusers and appears to depend on duration of treatment and dose. Therefore, when estrogens are used for the treatment of menopausal symptoms, use the lowest dose and discontinue medication as soon as possible. When prolonged treatment is indicated, reassess the patient at least semi-annually by endometrial sampling to determine the need for continued therapy. Cyclic administration of low doses of estrogen may carry less risk than continuous administration.

There is no pregnancy category officially assigned. Do not use estrogens during pregnancy. Estrogen therapy during pregnancy is associated with an increased risk of congenital defects in the reproductive organs of the fetus and possibly other birth defects.

### Drug interactions

Estrogens presumably have similar drug interactions to those observed with oral contraceptives.

<b>Estrogen Drug Interactions</b>		
Precipitant Drug	Object Drug	Description
Estrogens	Anticoagulants, oral	Estrogens may reduce the hypoprothrombinemic effect of anticoagulants.
Estrogens	Antidepressants, tricyclic	Effects may be altered by estrogens; they are estrogen dose dependent.
Barbiturates, Rifampin	Estrogens	May produce lower estrogen levels.
Hydantoins	Estrogens	Breakthrough bleeding, spotting, and pregnancy have resulted when these medications were used concurrently. A loss of seizure control has also been suggested.
Estrogens	Corticosteroids	An increase in the pharmacologic and toxicologic effects of corticosteroids may occur.

### Patient information

Patient package insert is available with products.

Notify physician if any of the following occur:

1. Pain in the groin or calves.
2. Sharp chest pain or sudden shortness of breath.
3. Abnormal vaginal bleeding.
4. Missed menstrual period or suspected pregnancy.
5. Lumps in the breast.
6. Sudden severe headache.
7. Dizziness or fainting.
8. Vision or speech disturbance.

9. Weakness or numbness in an arm or leg.
10. Severe abdominal pain, yellowing of the skin or eyes.
11. Severe depression.

#### **405. Progestins**

Progestin hormones are a group of synthetic drugs that have a progesterone-like effect on the uterus. Progesterone is a hormone that prepares the endometrium for implantation of the fertilized egg. Once an egg is implanted, progesterone acts to maintain the pregnancy. It does this by inhibiting the secretion of gonadotropins, preventing ovulation. Progesterone also inhibits spontaneous uterine contractions. It also aids in the treatment of amenorrhea by softening the endometrium, almost to a liquid state so the normal muscle contractions can do their work to expel the menstrual materials. We will discuss only one progestin hormone in this lesson: medroxyprogesterone.

#### **Medroxyprogesterone**

##### ***Indications***

Medroxyprogesterone is indicated in the treatment of the following conditions:

- Amenorrhea.
- Abnormal uterine bleeding.

##### ***Contraindications***

Medroxyprogesterone is contraindicated in patients with the following conditions:

- Breast carcinoma.
- Breast feeding.
- Ectopic pregnancy.
- Hepatic disease.
- Incomplete abortion, pregnancy, and vaginal bleeding.

Medroxyprogesterone is available in 2.5-, 5-, and 10-mg tablets. Normal dosing for amenorrhea is 5 to 10 mg daily for five to 10 days. Start therapy any time. Withdrawal bleeding usually occurs three to seven days after therapy ends. The dose for abnormal uterine bleeding due to hormonal imbalance is 5 to 10 mg daily for five to 10 days, beginning on the 16th or 21st day of the menstrual cycle. Withdrawal bleeding usually occurs three to seven days after discontinuing therapy. Patients with recurrent episodes of abnormal uterine bleeding may benefit from planned menstrual cycling with medroxyprogesterone.

##### ***Warnings***

There is no pregnancy category assigned to medroxyprogesterone. As stated earlier, progestins may play a part in preventing abortions. Care must be used when dispensing any progestin to a pregnant patient.

Detectable amounts of progestins enter the milk of lactating mothers receiving these agents. The effect on the nursing infant has not been determined. Medroxyprogesterone does not adversely affect lactation and may increase milk production and duration of lactation.

##### ***Drug interactions***

Medroxyprogesterone can cause amenorrhea or galactorrhea, which would counteract the desired effect of bromocriptine. These drugs *should not* be used together.

**Patient information**

Patients taking this medication should have a complete physical examination and continued annual check-ups to ensure continued safety and effectiveness. They should also have the following information:

- Medroxyprogesterone can have a prolonged effect on fertility. Most (about two-thirds) of women who wish to become pregnant are able to do so within the first year following use of this medication. Other women can require up to two years for return of fertility following the use of this medication.
- Progestins can cause swelling, tenderness, or bleeding of the gums; be careful when brushing and flossing teeth. Schedule regular dentist appointments for evaluation and routine dental care.
- If they become pregnant, they must stop taking this medication and *immediately* contact a health care provider.

**Tablets**

- Take exactly as directed. Do not exceed the prescribed dose.
- Do not stop taking except on their health care provider's advice.

**Injection**

Medroxyprogesterone is not for self-medication. For contraception, this medication is injected into a muscle every three months during the first five days of the menstrual cycle. In order for this contraceptive to be effective, they must receive the injections at regular, 3-month intervals. Do not forget to schedule and keep their clinic visit to receive their next medroxyprogesterone injection. If it has been more than 14 weeks since their last injection, they will need to have a pregnancy test to confirm that they are not pregnant before receiving another medroxyprogesterone injection.

**406. Oral contraceptives—estrogen-progestin products****Pharmacology**

Oral contraceptives (OC) include estrogen-progestin combos and progestin-only products.

**Progestin-only**

The mechanism by which progestin-only contraceptives prevent conception is not completely known, but they alter the cervical mucus and exert a progestational effect on the endometrium. This action seems to make the endometrium hostile to implantation by a fertilized ovum (egg) and, in some patients, suppresses ovulation.

**Estrogen-progestin combos**

Combination OCs inhibit ovulation by suppressing the gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). All of this alters the genital tract, changing the cervical mucus, inhibiting sperm penetration of the endometrium (as above).

These products differ in the type and relative potency of the components and in their relative activity. Ultimate effects are related to combined estrogenic, progestational, androgenic, and antiestrogenic effects.

Progestins may modify the effects of estrogens; these effects depend on the type or amount of progestin present and the ratio of progestin to estrogen. The total estrogenic potency of an OC is based on the combined effects of the estrogen and the effect of the progestin.



### Contraceptive efficacy

Efficacy in most cases depends greatly upon the degree of compliance and user reliability. No other contraceptive drug or device except levonorgestrel implant and medroxyprogesterone injection approaches the efficacy of the combined oral contraceptives.

The most common oral contraceptive used is a combination of progesterone with an estrogen. Combination products offer better contraceptive protection than either agent administered as a single entity. Estrogen-progestin combinations can be used as a post-coital contraceptive. These products are also used to regulate menstruation in patients with coagulation problems or heavy menstrual bleeding. In general, the estrogen-progestin products are available in three types:

1. Monophasic: Fixed dosage of estrogen to progestin throughout the cycle.
2. Biphasic: Amount of estrogen remains the same for the first 21 days of the cycle. Decreased progestin-estrogen ratio in first half of cycle allows endometrial proliferation. Increased ratio in second half provides adequate secretory development.
3. Triphasic: Estrogen amount remains the same or varies throughout cycle. Progestin amount varies.

### Indications

Estrogen-progestin products are indicated in the treatment of contraception and post-coital contraception.

### Contraindications

Estrogen-progestins products are contraindicated in patients with the following conditions:

- Thrombophlebitis.
- Coronary artery disease.
- Known or suspected breast carcinoma or estrogen-dependent neoplasia.
- Carcinoma of endometrium.
- Undiagnosed abnormal genital bleeding.
- Known or suspected pregnancy.

### Drug interactions

Oral contraceptives may *decrease* the actions of the following drugs:

- Acetaminophen.
- Benzodiazepines.
- Salicylates.

Oral contraceptives may *increase* the effects of the following drugs:

- Tricyclic antidepressants.
- Beta-blockers.
- Corticosteroids.
- Theophyllines.

The effectiveness of oral contraceptives may be decreased by antibiotics, barbiturates, or hydantoin. *The antibiotic interaction is extremely important!* Counsel every patient to use an alternate method of contraception for the period of time she is taking the antibiotic and continue that until her next menstrual cycle.

**Patient information**

Be sure to read patient package insert available with product. To achieve maximum contraceptive effectiveness, take OCs *exactly* as directed at intervals *not* exceeding 24 hours, preferably at the same time each day. Take tablets regularly with a meal or at bedtime. Efficacy depends on strict adherence to the dosage schedule.

Patients must be aware of the following when taking OCs:

- May cause spotting or breakthrough bleeding during the first few months of therapy; if bleeding occurs in > 1 cycle or last more than a few days, notify physician.
- Must use an additional method of birth control until after the first week of administration in the initial cycle, or for the entire cycle if vomiting or diarrhea occurs.
- Do not protect against human immunodeficiency virus (HIV) infection and other sexually transmitted diseases (STDs).
- May cause visual changes in contact lens wearers. If they notice visual changes or if the lenses begin to feel uncomfortable, they should consult their eye health care provider.
- Increases the risk of developing blood-clotting disorders and strokes in tobacco smokers. Before using estrogen-containing products, they should avoid smoking or talk with their health care provider, pharmacy, or other health care provider about methods to help them stop smoking.

**Missed doses**

There is little likelihood of ovulation occurring if only one tablet is missed, but the possibility of spotting or bleeding is increased. The possibility of ovulation occurring increases with each successive day that scheduled tablets are missed. This is particularly likely to occur if two consecutive tablets are missed. Any time a tablet has been missed, use another method of contraception for the balance of the cycle until tablets have been taken for seven consecutive days. If a patient forgets to take one or more tablets, the following is suggested:

1. One tablet - Take it as soon as remembered, or take two tablets the next day; alternatively take one tablet, discard the other missed tablet, continue as scheduled and use another form of contraception until menses.
2. Two consecutive tablets - Take two tablets as soon as remembered with the next pill at the usual time, or take two tablets daily for the next two days, then resume the regular schedule. Use an additional form of contraception for the seven days after pills are missed, preferably for the remainder of the cycle.
3. Three consecutive tablets - Begin a new compact of tablets, starting on day one of the cycle after the last pill was taken or starting seven days after the last tablet was taken. Use an additional form of birth control until pills have been taken for seven consecutive days, preferably for the remainder of the cycle.

**407. Oral antidiabetic agents**

This lesson covers the hypoglycemic agents and two antidiabetic agents that fall into their own category. These oral antidiabetic agents both have the capability to help diabetic patients lead a normal life. The drugs that we'll cover in this lesson are the sulfonylureas, metformin, and rosiglitazone. We'll start with the hypoglycemic agents – sulfonylureas.

**Sulfonylureas**

The sulfonylurea hypoglycemic agents are sulfonamide derivatives without any of the antibacterial activity. These agents are divided into two groups: First generation (acetohexamide, chlorpropamide, tolazamide, tolbutamide) and second generation (glipizide, glyburide). They are used with diet and exercise in the treatment of non-insulin-dependent diabetes mellitus (NIDDM). NIDDM has also been

referred to as adult-onset diabetes, ketosis-resistant diabetes, and Type II diabetes. NIDDM is characterized by insulin resistance and defects in insulin secretion.

Guidelines for oral hypoglycemic therapy in NIDDM patients include:

- Onset of diabetes at  $\geq 40$  years of age.
- Obese or normal body weight.
- Duration of diabetes  $< 5$  years.
- Fasting serum glucose  $\leq 200$  mg/dl.
- Insulin requirement  $< 40$  units/day.
- Absence of renal or hepatic dysfunction.

The sulfonylurea hypoglycemic agents lower blood glucose by stimulating insulin release from beta cells in the pancreatic islets. These agents are only effective in patients with some capacity for natural insulin production. They may improve the binding between insulin and insulin receptors or increase the number of insulin receptors. Hypoglycemic effects seem to be due to improved beta cell sensitivity. This lesson discusses two oral antidiabetic agents: glyburide, and glipizide. All indications, contraindications, and patient information are identical for both drugs *except* the pregnancy category. Glyburide is pregnancy category B and glipizide (as well as all other sulfonylureas) is category C.

<b>Sulfonylurea Comparison</b>				
Drug	Equivalent doses (mg)	Doses/ day	Onset (hrs)	Duration (hrs)
Glipizide	10	1-2	1-1.5	10-16
Glyburide Nonmicronized	5	1-2	2-4	24
Glyburide Micronized	3	1-2	1	24

### **Indications**

As an adjunct to diet to lower the blood glucose in patients with non-insulin-dependent diabetes mellitus (Type II) whose hyperglycemia cannot be controlled by diet alone.

### **Contraindications**

Hypersensitivity to sulfonylureas; diabetes complicated by ketoacidosis, with or without coma; sole therapy of insulin-dependent (Type I) diabetes mellitus; diabetes when complicated by pregnancy.

Glyburide should not be used as sole therapy in patients with Type I diabetes, diabetic ketoacidosis, diabetic coma, major surgery, severe infection, or severe trauma. The drug is also contraindicated in patients with severe hepatic disease, severe renal disease, or thyroid disease.

**Drug Interactions**

<b>Sulfonylurea Interactions</b>	
<b>Precipitant Drug</b>	<b>Reaction</b>
Anticoagulants, H <sub>2</sub> antagonists, Fenfluramine, Fluconazole, Gemfibrozil, Magnesium salts, Methyldopa, MAO Inhibitors, Probenecid, Salicylates, Sulfonamides, Tricyclic Antidepressants, Urinary Acidifiers	The hypoglycemic effects of sulfonylureas may be enhanced.
Beta blockers, Cholestyramine, Diazoxide, Hydantoins, Rifampin, Thiazide diuretics, Urinary alkalizers	The hypoglycemic effects of sulfonylureas may be decreased.
Ethanol	May prolong reductions in blood glucose. May result in Disulfiram-like reaction.
Digitalis glycosides	Sulfonylureas may increase digitalis serum levels.

**Patient information**

Patients must receive full and complete instructions about the nature of diabetes. Strict adherence to prescribed diet, an exercise program, personal hygiene, and avoidance of infection are essential. It is important to teach patients to self-monitor blood glucose.

Patients taking diabetic medication must know the following:

- Do not discontinue medication except on the advice of a physician.
- May cause gastrointestinal (GI) upset; may be taken with food.
- Take glipizide >30 minutes before a meal to increase effectiveness.
- Avoid alcohol and salicylates except on professional advice.
- Monitor urine for glucose and ketones as prescribed; monitor blood glucose as prescribed.

Notify physician if any of the following occurs:

- Hypoglycemia: Fatigue, excessive hunger, profuse sweating, numbness of extremities.
- Hyperglycemia: Excessive thirst or urination, urinary glucose or ketones.
- Other: Fever, sore throat, rash, unusual bruising or bleeding.

**Antidiabetic agents**

As promised, here are the antidiabetic agents. Neither of these drugs is currently listed in the Department of Defense (DOD) Basic Core Formulary, but they are both important enough to be covered in this course. This section will cover metformin and rosiglitazone. Because of their differences, these drugs will be covered separately.

**Metformin**

Metformin is an oral antihyperglycemic drug used in the management of NIDDM. It is not chemically or pharmacologically related to the oral sulfonylureas. Metformin improves glucose tolerance in NIDDM subjects, lowering plasma glucose. Its pharmacologic mechanisms of action are different from those of sulfonylureas. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose and improves insulin sensitivity. Unlike sulfonylureas, metformin does not produce hypoglycemia in either diabetic or nondiabetic subjects and does not cause hyperinsulinemia. With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.



### *Indications*

Metformin is indicated to be used alone or as an adjunct to diet to lower blood glucose in patients with NIDDM whose hyperglycemia cannot be satisfactorily managed on diet alone. Metformin may be used concomitantly with a sulfonylurea when diet and metformin or a sulfonylurea alone do not result in adequate glycemic control. Normal dosing for metformin is 1,500 – 2,550 mg daily in 2 or 3 doses, given with meals. A starting dose of 500 mg twice daily with the morning and evening meal may be used if the patient has GI problems. As the dosage is increased, the three times daily dosing will be better tolerated. Metformin is available in 500 and 850 mg tablets.

### *Contraindications*

Metformin is contraindicated in patients with kidney disease, a hypersensitivity to metformin, or metabolic disorders.

### *Warnings*

**Lactic acidosis:** Lactic acidosis is a rare, but serious, metabolic complication that can occur due to metformin accumulation during treatment. When it occurs, it is fatal in approximately 50 percent of cases. Lactic acidosis is characterized by elevated blood lactate levels, decreased blood pH, and electrolyte disturbances.

**Pregnancy:** Metformin is fairly new. Safety has not been established, so metformin gets a pregnancy category B. Metformin is excreted into breast milk. A decision should be made to discontinue therapy during breastfeeding or not to breastfeed.

### *Drug interactions*

Metformin's actions are increased by alcohol, cimetidine, furosemide, and nifedipine. While furosemide increases metformin's actions, metformin has a decreasing effect on furosemide.

### *Patient information*

Inform patients of the potential risks and advantages of metformin and of alternative modes of therapy. Also inform them about the importance of adherence to dietary instructions, of a regular exercise program and of regular testing of blood glucose, glycosylated hemoglobin, renal function, and hematologic parameters.

Counsel patients against excessive alcohol intake while receiving metformin.

### *Rosiglitazone*

Rosiglitazone is different from other diabetic agents. Rosiglitazone is an antidiabetic agent that lowers blood glucose by improving target cell response to insulin, without increasing pancreatic insulin secretion. It decreases insulin resistance. Its unique action mechanism depends on the presence of insulin for activity. Addition of rosiglitazone to a sulfonylurea has a synergistic effect because both agents act to improve glucose tolerance by different but complementary mechanisms. Unlike sulfonylureas, rosiglitazone is not an insulin secretagogue.

### *Indications*

Rosiglitazone is indicated for Type II diabetes. It is used concomitantly with a sulfonylurea or insulin to improve glycemic control. It can also be used as monotherapy as an adjunct to diet and exercise to lower blood glucose. Here is the dosing schedule for both combination and monotherapies:

<b>Dosing Schedule</b>	
<b>Types of Therapy</b>	<b>Dosage</b>
<b>Combination</b> <ul style="list-style-type: none"> <li>With insulin</li> <li>With sulfonylureas</li> </ul>	<p>Start with 2 mg once daily and continue the current insulin dose. For patients not responding adequately, increase the rosiglitazone dose after two to four weeks. The usual dose is 400 mg/day. The maximum recommended dose is 600 mg/day. Individualize insulin adjustments are based on glucose-lowering response.</p> <p>Start with 2 mg once daily and continue the current sulfonylurea dose. For patients not responding adequately, increase the rosiglitazone dose at two to four weeks, not to exceed 6 mg once daily. The sulfonylurea dose may require lowering to optimize therapy.</p>
<b>Monotherapy</b>	Initiate at 4 or 6 mg once daily for patients not adequately controlled with diet alone. For patients not responding to 4 mg once daily, increase the dose to 6 mg after one month. For patients not responding adequately to 6 mg after one month, consider alternative therapeutic options.
Rosiglitazone is available in 2, 4, and 8 mg tablets.	

### **Contraindications**

The only labeled contraindication for rosiglitazone is hypersensitivity to any of the components of the medication.

### **Warnings**

Rare cases of severe idiosyncratic hepatocellular injury have occurred. The hepatic injury is usually reversible, but very rare cases of hepatic failure, leading to death or liver transplant, have occurred. Injury has occurred after both short- and long-term rosiglitazone treatment.

**Pregnancy:** Category B. There are no adequate and well-controlled studies in pregnant women. *Do not use rosiglitazone during pregnancy unless the potential benefit justifies the potential risk to the fetus.*

**Lactation:** It is not known whether rosiglitazone is secreted in breast milk. Rosiglitazone is secreted in the milk of lactating rats. Do not administer to breastfeeding women.

### **Drug interactions**

Cholestyramine reduces the absorption of rosiglitazone by 70 percent and should not be used in patients taking rosiglitazone.

Administration of rosiglitazone with an oral contraceptive containing ethinyl estradiol and norethindrone reduced the plasma concentrations of both components by 30 percent. These changes could result in loss of contraception. Use either a higher dose of oral contraceptive or an alternative method of contraception.

### **Patient information**

Take rosiglitazone with meals. If the dose is missed at the usual meal, take it at the next meal. If the dose is missed on one day, *do not double the dose the following day.*

It is important to adhere to dietary instructions and to have blood glucose and glycosylated hemoglobin tested regularly. During periods of stress such as fever, trauma, infection, or surgery, insulin requirements may change and patients should seek the advice of their physician.

When using combination therapy with insulin or an oral hypoglycemic, explain the risks of hypoglycemia, its symptoms, treatment, and predisposing conditions to patients and their family members.

Instruct patients to immediately report any signs or symptoms of hepatic dysfunction (e.g., nausea, vomiting, abdominal pain, fatigue, anorexia, dark urine, or jaundice) to their physician.

Use of rosiglitazone can cause resumption of ovulation in women taking oral contraceptives and in patients with polycystic ovary disease. Therefore, advise patients to consider an alternative method of contraception or refer them to their physician for consideration of a dose increase in their oral contraceptive.

#### 408. Insulin

Insulin is a pancreatic hormone. It is secreted by the pancreatic cells of the islets of Langerhans and is essential for the metabolism of glucose and for the homeostasis of blood glucose. FDA approval of insulin products began in 1939. The precise amino acid sequence of insulin was established in 1960, leading to complete synthesis of the hormone by 1963. Bovine, porcine, and recombinant human insulin preparations are currently available for use in diabetic patients. Regular (rapid, short-acting) and NPH (slower onset, longer duration) human insulin are the most commonly used preparations. The first biosynthetic human insulin was given FDA approval in 1982.

#### Indications

Insulin is indicated in the treatment of diabetes mellitus, diabetic ketoacidosis, and hyperkalemia. Insulin distributes widely throughout the body. Peripheral tissues inactivate a small portion, but the majority is metabolized by the liver and kidneys. Insulin is filtered and reabsorbed by the kidneys, with the plasma half-life of insulin following IV injection being approximately nine minutes. Regular insulin is the only insulin that should be administered by an IV. All other types of insulin are injected subcutaneously. The following table illustrates the different types of insulins and their properties.

<i>Insulins</i>					
Insulin Preparations		Onset (hrs)	Peak (hrs)	Duration (hrs)	Compatible mixed with
Rapid-acting	Regular	0.5 - 1	1 - 3	8 - 12	All
	Semi-lente	1 - 1.5	5 - 10	12 - 16	Lente
	Lispro Solution	0.25	0.5 - 1.5	6 - 8	Ultralente, NPH
Intermediate-acting	NPH	1 - 1.5	4 - 12	24	Regular
	Lente	1 - 2.5	7 - 15	24	Regular, semilente
Long-acting	Protamine Zinc	4 - 8	14 - 24	36	Regular
	Ultralente	4 - 8	10 - 30	> 36	Regular, semilente

#### Drug interactions

<i>Drugs that Decrease the Hypoglycemic Effects of Insulin</i>	
Diuretics	Diltiazem
Epinephrine	Morphine
Estrogens	Niacin
Isoniazid	Phenytoin
Lithium	Nicotine
Calcitonin	Thiazide diuretics
Contraceptives, oral	Thyroid
Corticosteroids	

<i>Drugs that Increase the Hypoglycemic Effects of Insulin</i>	
ACE inhibitors	Mebendazole
Alcohol	Salicylates
Beta blockers	Sulfonamides
Calcium	Tetracyclines
Chloroquine	
Lithium	
MAO inhibitors	

### **Contraindications**

Insulin is contraindicated in patients with bovine hypersensitivity and porcine hypersensitivity. Beef insulin should not be used in patients with a history of bovine hypersensitivity unless these patients have been adequately desensitized. Pork insulin should not be used in patients with a history of porcine hypersensitivity unless these patients have been adequately desensitized.

Regular insulin is the only formulation appropriate for IV administration. Only regular insulin should be used in patients with poor tissue perfusion, shock, or cardiovascular collapse; in patients with diabetic ketoacidosis; or in patients requiring insulin for the treatment of hyperkalemia. All other preparations of insulin are contraindicated for these conditions.

### **Patient information**

Make sure patient understands the following information:

- Use same type and brand syringe to avoid dosage errors. Rotate sites to prevent lipodystrophy (atrophy of subcutaneous fat). If using "pen-filled" device, follow information for proper use.
- Do not change the order of mixing insulins (if applicable) or change the brand, strength, type, species, or dose without your physician's knowledge.
- Consult a physician if you have vomiting or fever. Illness may change insulin requirements.
- See your dentist twice yearly; see an ophthalmologist regularly.
- Read and understand all aspects of insulin use available in the patient information inserts. Strict adherence to prescribed diet, exercise program, and personal hygiene are essential.
- Wear a diabetic identification (Medic-Alert) so appropriate treatment can be given if complications occur away from home.
- Monitor blood glucose and urine for glucose and ketones as prescribed; monitor blood pressure regularly.
- Allow refrigerator-stored insulin to come to room temperature prior to injecting it. Insulin stored at room temperature will be less painful to inject compared with that stored in the refrigerator.
- Store the insulin in the refrigerator, except the bottle currently being used. Store that bottle at a room temperature of less than 72 degrees.

### **409. Thyroid agents**

Thyroid hormones include both natural and synthetic derivatives. The natural products, desiccated thyroid and thyroglobulin, are derived from beef or pork. Although these preparations are most economical, standardization is inexact; synthetic derivatives are generally preferred because of more uniform standardization of potency.



Synthetic derivatives include levothyroxine, liothyronine, and liotrix. The principal effect of thyroid hormones is to increase metabolic rate of body tissues noted by increases in oxygen consumption, respiratory rate, body temperature, cardiac output, heart rate, blood volume, rate of fat, protein and carbohydrate metabolism, enzyme system activity, and growth and maturation. Thyroid hormones exert a profound influence on every organ system and are particularly important in central nervous system (CNS) development.

Thyroid hormones are also concerned with growth and differentiation of tissues. In deficiency states in the young, there is growth retardation and failure of maturation of the skeletal and other body systems, especially in failure of the formation of bone in the epiphyses and in brain growth and development. The following text covers both thyroid hormones and levothyroxine.

### Indications

Specific indications include: Cretinism, myxedema, non-toxic goiter and ordinary hypothyroidism; primary hypothyroidism resulting from functional deficiency, primary atrophy, partial or total absence of thyroid gland, or the effects of surgery, radiation, or drugs, with or without the presence of goiter; secondary (pituitary) or tertiary (hypothalamic) hypothyroidism.

### Warnings

#### Pregnancy

Category A thyroid hormones do not readily cross the placenta. Clinical experience does not indicate any adverse effect on the fetus when thyroid hormones are administered to a pregnant woman. Do not discontinue thyroid replacement therapy in hypothyroid women during pregnancy.

#### Lactation

Minimal amounts of thyroid hormones are excreted in breast milk. Thyroid is not associated with serious adverse reactions. However, exercise caution when thyroid is administered to a nursing woman.

<b>Drug Interactions</b>		
Precipitant Drug	Object Drug	Description
Cholestyramine and colestipol	Thyroid hormones	Loss of thyroid efficacy, administer four–six hrs apart
Estrogens	Thyroid hormones	Patient response to thyroid therapy may be decreased
Thyroid hormones	Anticoagulants	The anticoagulant activity is increased
Thyroid hormones	Beta blockers	Beta blocker action may be impaired
Thyroid hormones	Digitalis glycosides	Therapeutic effects of digitalis glycosides may be decreased
Thyroid hormones	Theophyllines	Decreased theophylline clearance

### Patient information

Replacement therapy is to be taken for life, except in cases of transient hypothyroidism, usually associated with thyroiditis, and in those receiving a trial of the drug.

- Take thyroid hormones as a single daily dose, preferably before breakfast.
- Do not change from one brand of hormones to another without consulting your pharmacist or physician. Products manufactured by different companies may not be equally effective.
- Do not discontinue medication except on advice of a physician.

- Notify physician if headache, nervousness, diarrhea, excessive sweating, heat intolerance, chest pain, increased pulse rate, palpitations (symptoms of hyperthyroidism) or any unusual event occurs.
- Children can experience partial hair loss in the first few months of therapy, but this is usually a transient phenomenon that results in later recovery.
- Absorption is increased if levothyroxine is taken on an empty stomach.
- Take missed doses as soon as they remember, unless it is almost time for their next dose; then, skip the missed dose and wait for their next regularly scheduled dose. Do not take double doses. Contact their health care provider or pharmacy if they need help adjusting their dosing schedule.

#### **410. Corticosteroids**

In volume 2, we talked about topical corticosteroids. In this lesson, we'll look at some systemic corticosteroids. We'll also cover additional steroid uses later in the respiratory system.

Corticosteroids are found both naturally occurring and synthetically produced. Corticosteroids are also differentiated by their properties. Corticosteroids are classified as either mineralocorticoid or glucocorticoid. Mineralocorticoid steroids alter electrolyte balance and sodium retention.

Glucocorticoids are known more for their anti-inflammatory effects. Hydrocortisone and cortisone are both naturally occurring cortical steroids with both mineralo and glucocorticoid activity. Additionally, triamcinolone, dexamethasone, methylprednisolone, and betamethasone are synthetic steroids with high glucocorticoid activity and almost no salt-retaining activity. Our discussion of steroids in this section will be limited to prednisolone and prednisone, dexamethasone, and methylprednisolone.

Before we jump into the drugs though, no discussion of corticosteroids would be complete without some words on the hypothalamic-anterior pituitary-adrenal axis (HPA). Cortisol, the major endogenous glucocorticoid produced in the body is produced and secreted through the HPA. There is a negative feedback system that tells the body how much cortisol to produce. If systemic steroid medications are taken when the body is at a natural "low" on these hormones, the feedback system will sense the presence of medication and not produce any for itself, maintaining a steady, lower level of steroid and defeating the purpose of taking the medication. However, if the medication is taken after the feedback system has acted, the steroid medication will act to effectively increase steroid level and treat the disorder. The feedback system works and produces most of its steroids between 2:00 and 8:00 in the morning. Therefore, early morning is the best time to take these medications. After saying all that, on to our discussion of corticosteroids.

##### **Prednisolone and Prednisone**

Prednisolone and Prednisone are synthetic steroid compounds that exhibit both mineralocorticoid (salt retaining) and glucocorticoid (anti-inflammatory) effects. Both of these drugs, however, are used for their glucocorticoid effects. Prednisone is an inactive drug and must be metabolized into prednisolone before becoming active. The equivalent doses of the two are approximately the same on a mg to mg basis with prednisolone having a faster onset of action and a two to three times longer half-life.

##### **Dexamethasone and Methylprednisolone**

These two are synthetic compounds with marked glucocorticoid properties and show no significant mineralocorticoid actions.

The following table lists the steroids that we are discussing and relates them to each other (oral dosage forms only). All of the corticosteroids listed, except prednisone, also come in injectable forms.

<b>Corticosteroid Dosage</b>				
<b>Corticosteroid</b>	<b>Approximate Equivalent Dose</b>	<b>Relative Anti-inflammatory Potency</b>	<b>Dosage mg/day</b>	<b>Dosage Forms</b>
Prednisone	5 mg	4	5 – 60	1, 2.5, 5, 10, 20, 50 mg tablets and 5mg/5ml liquid
Prednisolone	5 mg	4	5 – 60	5 mg tablets and 5mg/5ml, 15mg/5ml liquid
Dexamethasone	0.75 mg	20	0.75 – 9	0.25, 0.5, 0.75, 1, 2, 4, 6, Therapeutic pack, 0.5mg/0.5ml and 0.5mg/5ml liquid
Methylprednisolone	4 mg	5	4 – 48	2, 4, 8, 16, 24, 32 mg tablets

### **Indications**

Corticosteroids are indicated in numerous disorders. Some of the recognizable ones are rheumatic disorders like bursitis and arthritis; dermatological disorders such as psoriasis and dermatitis; allergic rashes and itching problems; respiratory disorders including asthma and tuberculosis; and gastrointestinal disorders such as colitis and enteritis. The dosage on these disorders is individualized. If therapy lasts more than one week, tapering on and off the medication is needed. Over a two-to-three day period, the amount of medication is increased, building to a therapeutic level. After a few days at the therapeutic level, the dosage is decreased in the same manner as it was increased. Tapered dosing provides minimal interruption of the HPA feedback system. "Short-burst" therapy, where higher doses are given over two to three days, may work for some patients just as well as longer therapy. Tapering is not needed using this dosing regime.

### **Contraindications**

Systemic steroids are contraindicated in people who are sensitive to the drug or its components. They are also contraindicated in people suffering from systemic fungal infections.

### **Warnings**

Corticosteroids may mask the signs of infection and new infections may occur during their use. There may be a decreased resistance and the inability to prevent the spread of infection. Corticosteroids will make fungal infections worse.

### **Pregnancy**

Corticosteroids are in pregnancy category C. Chronic ingestion during the first trimester has ended with an increase in cleft palates. Corticosteroids are excreted into breast milk. Mothers taking corticosteroids should not breast feed.

### **Children**

Prolonged corticosteroid use may stunt growth.

### **Interactions**

The use of

- Barbiturates, ephedrine, or hydantoins may decrease the effectiveness of corticosteroids.
- Estrogens and oral contraceptives, macrolide antibiotics, and ketoconazole decrease the clearance of corticosteroids, increasing their effects.

- Corticosteroids increase the chances of toxicity when taken with digitalis glycosides or diuretics, mainly due to hypokalemia.
- Corticosteroids reduce serum levels and effectiveness of salicylates.

**Patient information**

These compounds can 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 your physician if you experience 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.

Signs of adrenal insufficiency include fatigue, anorexia, nausea, vomiting, diarrhea, weight loss, weakness, dizziness, and low blood sugar. Notify your physician promptly if these symptoms occur following dosage reduction or withdrawal of therapy.

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**Self-Test Questions**

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

**404. Estrogens**

1. What is the function of estrogen?
2. What effect can estrogen have on endometrial carcinoma in post-menopausal women?

**405. Progestins**

1. What is progestin?
2. List the indications for medroxyprogesterone.
3. What possible drug interaction can occur between medroxyprogesterone and bromocriptine?

**406. Oral contraceptives—estrogen-progestin products**

1. What are the three types of estrogen-progestin combination products?
2. What information should be given to patients in regard to additional contraception when first beginning oral contraceptives?

**407. Oral antidiabetic agents**

1. What are the guidelines for oral hypoglycemic therapy?
2. How does metformin produce its action?
3. What is the synergistic effect of rosiglitazone?

**408. Insulin**

1. Insulin is used to treat what conditions?
2. What type of insulin is rapid-acting: with an onset of action beginning approximately 30 minutes after SQ administration and lasting roughly eight to 12 hours?
3. What type of insulin is the only insulin that can be administered in an IV?
4. What type of insulin is an intermediate-acting insulin routinely used in the management of diabetes mellitus, with an onset of action of about one hour following SQ administration, and a 24-hour duration of effect?

**409. Thyroid agents**

1. Thyroid hormone is used to treat what conditions?
2. What possible drug interaction can occur between estrogens and thyroid hormone?

**410. Corticosteroids**

1. What are the two categories of corticosteroids?
2. What warning is given for corticosteroid use in children?



## Answers to Self-Test Questions

400

1. Any organ that produces a certain secretion.
2. External secretions.
3. Hormones.
4. To regulate the activities of various body organs.

401

1. Growth hormone, thyroid stimulating hormone, adrenocorticotrophic hormone, gonadotropic hormone, and prolactin hormone.
2. The antidiuretic hormone and oxytocin.
3. The thyroid gland.
4. Epinephrine.
5. The glucocorticoids, the mineralocorticoids, and the sex hormones.

402

1. Renin, hydroxycholecalciferol, erythropoietin.
2. It promotes the growth of peripheral lymphoid tissue.
3. The seminal vesicles, thymus, brain, and kidney medulla.

403

1. Swelling of the neck due to an enlarged thyroid.
2. Myxedema.
3. The patient will have a goiter, eye bulging, a strained facial appearance, intense nervousness, loss of weight, a rapid pulse, sweating, and a tremor. The patient's metabolism is stepped up to a super rate.
4. Tetany.
5. Hypofunction of the adrenal cortex.
6. The pancreatic islets do not produce enough insulin, sugar is not oxidized (burned in the tissues) for transformation into energy. Instead, sugar is excreted along with the urine. —
7. The patient must modify his or her diet, and at times must take oral medications that increase the output of insulin by the pancreas.
8. Because it cannot be taken orally because digestive juices destroy insulin.
9. Infection resistance is lowered, arteries may be seriously damaged, peripheral nerves are affected also, with accompanying pain and loss of sensation.
10. Menopause is the last menstrual period and the cessation of hormone excretion from the ovaries.
11. Infant suckling disrupts the hormonal flow.

404

1. They are essential for the normal sexual development of the female and for the regulation of the menstrual cycle during childbearing years.
2. Estrogens can increase the risk of endometrial carcinoma.

405

1. Progesterin is a corpus luteum hormone that prepares the endometrium for implantation of the fertilized egg.
2. Amenorrhea and abnormal uterine bleeding.
3. Medroxyprogesterone can cause amenorrhea and galactorrhea, which would counteract the desired effect of bromocriptine.

**406**

1. Monophasic, Bipasic, and Triphasic.
2. Use an additional form of contraception during the first week of the first cycle (first pack) of this contraceptive.

**407**

1. Onset of diabetes at  $\geq 40$  years of age, obese or normal body weight, duration of diabetes  $< 5$  years, fasting serum glucose  $\leq 200$  mg/dl, insulin requirement  $< 40$  units/day, absence of renal or hepatic dysfunction.
2. Metformin decreases hepatic glucose production, intestinal absorption, and improves insulin sensitivity.
3. It uses a different mechanism than sulfonylureas to produce the same effects so the two add together.

**408**

1. Diabetes mellitus, diabetic ketoacidosis, and hyperkalemia.
2. Regular insulin.
3. Regular insulin.
4. NPH insulin (isophane insulin).

**409**

1. Hypothyroidism, cretinism, myxedema, and goiter.
2. Patient response to thyroid therapy may be decreased.

**410**

1. Mineralocorticoids and glucocorticoids.
2. Prolonged corticosteroid use may stunt growth.

**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. 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. (400) Into what category of secretions do digestive juices and tears fall?
  - a. Hormones.
  - b. Internal.
  - c. External.
  - d. Endocrine.
2. (400) The gland that has the richest blood supply is the
  - a. pancreas.
  - b. stomach.
  - c. salivary.
  - d. adrenal.
3. (401) Which hormone stimulates the growth of bones, muscles, and other organs?
  - a. Thyrotropic.
  - b. Somatotropic.
  - c. Gonadotropic.
  - d. Adrenocorticotropic.
4. (401) Which hormone is produced by the parathyroid?
  - a. Thyroxin.
  - b. Calcitonin.
  - c. Parathormone.
  - d. Hydroxycholecalciferol.
5. (401) Which hormone is active in glucose transport across the cell membrane?
  - a. Epinephrine.
  - b. Aldosterone.
  - c. Cortisol.
  - d. Insulin.
6. (402) Which hormone is *not* produced by the kidney?
  - a. Renin.
  - b. Testosterone.
  - c. Erythropoietin.
  - d. Hydroxycholecalciferol.
7. (402) The organ that produces hormones that stimulate lymphocyte production is the
  - a. kidney.
  - b. placenta.
  - c. thymus.
  - d. pancreas.



- 
8. (403) After the parathyroid glands are removed, a low concentration of calcium in the blood results causing
    - a. tetanus.
    - b. tetany.
    - c. Addison's disease.
    - d. A thyroid storm.
  9. (403) Hyper-function of the adrenal cortex, characterized by thin, easily bruised skin, muscle weakness, and bone loss describes what condition?
    - a. Diabetes mellitus.
    - b. Hyperthyroidism.
    - c. Addison's disease.
    - d. Cushing's syndrome.
  10. (403) Which of the following is NOT a long-term complication of diabetes?
    - a. Decreased sucrose levels.
    - b. Lowered infection resistance.
    - c. Arterial damage.
    - d. Peripheral nerve damage.
  11. (403) When is a woman considered postmenopausal?
    - a. After the completion of her last menstrual cycle.
    - b. After 6 months of not having a menstrual cycle.
    - c. After one year of not having a menstrual cycle.
    - d. At the beginning of her last menstrual cycle.
  12. (404) What interaction occurs between estrogens and corticosteroids?
    - a. A decrease in the pharmacologic effects of corticosteroids.
    - b. An increase in the pharmacologic effects of corticosteroids.
    - c. A decrease in the pharmacologic effects of estrogen.
    - d. An increase in the pharmacologic effects of estrogen.
  13. (405) Progesterone aids in the treatment of amenorrhea by
    - a. softening the endometrium.
    - b. hardening the endometrium.
    - c. keeping the endometrium from forming.
    - d. enhancing the muscle contractions to expel the endometrium.
  14. (405) What should a patient using medroxyprogesterone be told concerning fertility?
    - a. There is no affect on fertility.
    - b. Fertility is enhanced.
    - c. Fertility may never return.
    - d. Fertility will return within two years.
  15. (405) How often must medroxyprogesterone be injected to provide effective contraception?
    - a. Monthly.
    - b. Every three months.
    - c. Every six months.
    - d. Yearly.

16. (406) Which type of oral contraceptive contains fixed dosages of estrogen to progestin throughout the cycle?
- Monophasic.
  - Biphasic.
  - Triphasic.
  - Quadruphasic.
17. (407) How do sulfonylurea hypoglycemic agents lower blood glucose?
- Inhibits insulin release.
  - Stimulates insulin release.
  - Increases sensitivity to insulin.
  - Decreases sensitivity to insulin.
18. (407) What is the equivalent dose of glipizide to 5 mg of nonmicronized glyburide?
- 2 mg.
  - 5 mg.
  - 10 mg.
  - 20 mg.
19. (407) Which drugs can enhance the hypoglycemic effects of sulfonylureas?
- Beta blockers.
  - Hydantoins.
  - Digitalis glycosides.
  - H<sub>2</sub> antagonists.
20. (407) Which antidiabetic agent may cause lactic acidosis?
- Metformin.
  - Glyburide.
  - Troglitazone.
  - Insulin.
21. (408) Which type of insulin can be given intravenously?
- NPH.
  - Lente.
  - Ultralente.
  - Regular.
22. (408) Which drugs decrease the hypoglycemic effects of insulin?
- Tetracyclines.
  - Beta blockers.
  - Thiazide diuretics.
  - ACE inhibitors.
23. (408) Tell the patient to store *all* insulin
- in the refrigerator. *except* the bottle currently being used.
  - in the freezer until ready for use.
  - at room temperature.
  - in the refrigerator.
24. (409) Why are synthetic thyroid agents preferred over natural products?
- Synthetic agents cost less.
  - Synthetic agents have more uniform standardized potency.
  - Natural products are harder to obtain.
  - Natural products have more interactions.

- 
25. (409) How do thyroid hormones and beta blockers interact?
- a. Beta blocker action may be enhanced.
  - b. Beta blocker action may be impaired.
  - c. Thyroid hormone action may be enhanced.
  - d. Thyroid hormone action may be impaired.
26. (410) Which category of corticosteroid is known for its anti-inflammatory effects?
- a. Mineralocorticoids.
  - b. Natural corticoids.
  - c. Glucocorticoids.
  - d. Synthetic corticoids.
27. (410) Which drug must prednisone be metabolized into before becoming active?
- a. Prednisolone.
  - b. Dexamethasone.
  - c. Methylprednisolone.
  - d. Triamcinolone.
28. (410) How can prolonged corticosteroid use affect children?
- a. Accelerate their growth.
  - b. Stunt their growth.
  - c. Increase muscle mass.
  - d. Decrease muscle mass.

**Please read the unit menu for unit 2 and continue →**

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## Student Notes

## Unit 2. The Digestive System

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**T**HIS unit deals with the digestive system. The digestive system performs a vital function—preparing food for absorption and use by the millions of body cells. The majority of food when eaten is in a form that cannot reach the cells because it cannot pass through the intestinal mucosa into the blood stream; nor can it be used by the cells even if it could reach them.

In the following information, we will discuss anatomy and physiology of the digestive system, some conditions associated with this system, and drugs used to treat those conditions.

### 2-1. Anatomy and Physiology of the Digestive System

In this section, we will study the system that converts food into nourishment for all our body cells. This process is not so simple as it might seem. A solitary cell would be baffled if a fragment of food, in the state that is familiar to us, appeared across the lake of tissue fluid and sought admission. Food must be converted to a state in which the cells can absorb the nutrients. This conversion process is known as *digestion*. Once the food is digested, it must be transferred to the blood or lymphatic vessels. This transfer process is known as *absorption*. Digestion and absorption are the two chief functions of the digestive system.

For purposes of study, the digestive system (fig. 2-1) may be divided into two groups of organs, the alimentary canal and accessory organs. *Alimentary canal* is a continuous passageway that begins at the mouth, where food is taken in, and terminates at the anus, where the solid waste products of digestion are expelled. *Accessory organs*, while vitally necessary for the digestive process, are not part of the alimentary canal.

#### 411. Alimentary canal

The *alimentary canal* is a muscular digestive tube extending through the body. It is composed of several parts: the *mouth*, *pharynx*, *esophagus*, the *stomach*, *small intestine*, and *large intestine*. In this lesson there will be a separate section devoted to the accessory organs. After finishing our study of the alimentary canal, we will be familiar with the main functions of these body parts.

The word *aliment* comes from a Latin word that means "food" or "nutrients." Those foods that undergo changes and are absorbed into the blood leave the tube from the region of the small intestine. Indigestible substances, such as the cellulose in food, pass through the alimentary canal and are expelled from the body.



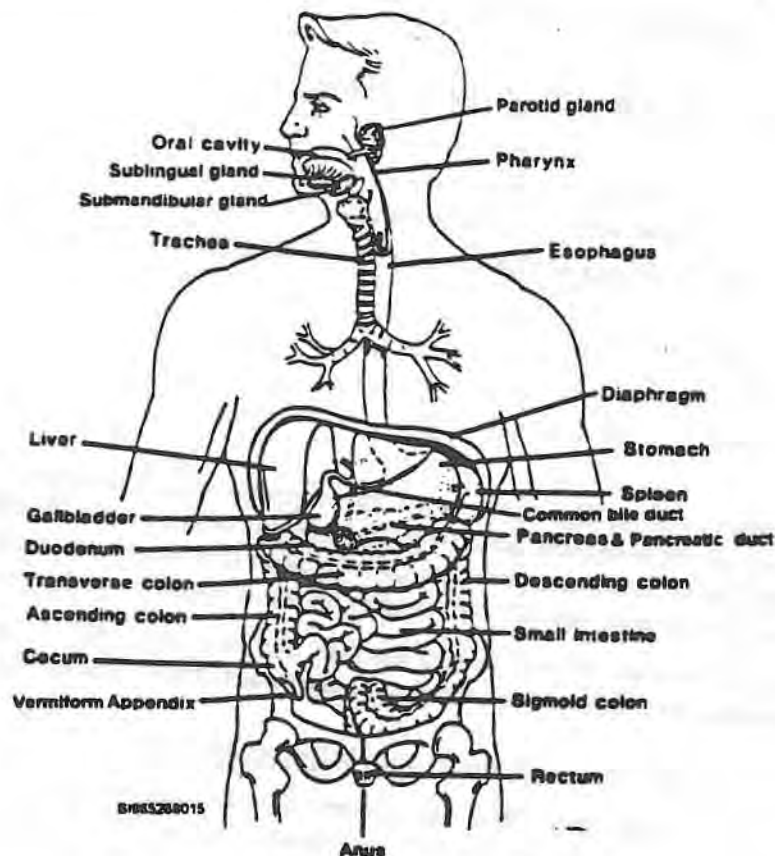


Figure 2-1. The digestive system.

### Mouth (oral cavity)

A digestible substance begins the tour of the alimentary canal in this cavern. The oral cavity has three purposes:

1. Receives food.
2. Prepares food initially for the digestive process.
3. Aids in the accomplishment of speech.

The tongue, a muscular accessory organ for digestion, projects into the mouth. The tongue aids in chewing and swallowing and is one of the principal organs of speech. It has a number of special organs on its surface called *taste buds*, which differentiate taste sensations (bitter, sweet, sour, or salty). This cavity also contains teeth. There are 20 teeth in a child between two and six years of age. The adult, with a complete set, has 32 teeth. The cutting teeth, or *incisors*, occupy the front part of the oral cavity, while the larger grinding teeth, the *molars*, are in the back portion.

### Deciduous (baby teeth)

The first eight *deciduous teeth* to make their appearance through the gums are the incisors. Later, the *canines* (eyeteeth) and molars appear. Usually, the 20 baby teeth make their appearance by the time the infants pass their second birthday. During this time, the permanent teeth continue developing within the jawbones. The first permanent teeth to appear are the very important six-year molars. The molars come in before the baby incisors are lost and a parent may not realize that key permanent teeth have appeared. Decay and infection of the adjacent deciduous molars may spread to and involve the new permanent molar tooth. Deciduous teeth need proper care in order to help preserve the six-year molars and other permanent teeth.

### Permanent teeth

Although the buds for the second set of teeth are present at birth, the first permanent tooth does not usually appear until the child is about six years old. At that time, the first molar, the keystone for the future grinding surfaces, appears in the space behind the baby molars. As the child grows, the jawbones also grow; therefore, there is space for more teeth than are in the first set. After the first permanent molars appear, the baby incisors loosen and are replaced by *permanent incisors*. Then the baby canines (cuspids) are replaced by *permanent canines*, and the baby molars are replaced by the permanent bicuspid (premolars). Now the larger jawbones are ready for the 12-year or second permanent molar teeth. Somewhat later, the third molars, the *wisdom teeth*, appear. If the jaw is not large enough or if there are other abnormalities, these teeth may have to be removed early in life.

### Salivary glands

Another function of the oral cavity is the production of *saliva*. The purpose of saliva is to dissolve the food and to facilitate the processes of *mastication* (chewing) and *deglutition* (swallowing). Saliva also coats the food with mucus so it can be easily swallowed. The chemical function of saliva will be discussed later in this lesson.

Saliva is manufactured by three pairs of glands, which are also accessory organs:

1. Parotid glands—The largest of the group, they are located near the ear.
2. Submandibular or submaxillary glands—Located near the body of the lower jaw.
3. Sublingual glands—Located under the tongue.

The parotid salivary glands are infected in the contagious disease commonly called mumps. The infecting agent is a virus. *Parotitis*, inflammation of the parotid glands, may lead to inflammation of the testicles by the same virus. Males affected after puberty are at risk for permanent damage to these sex organs and can become sterile. Another complication that may occur in 10 percent of all cases is meningitis. As is true of many contagious diseases, mumps is now preventable by routinely giving a vaccine to children early in life.

### Layers of the alimentary canal

Beyond the oral cavity and throat, the walls of the alimentary canal from the esophagus to the anus are similar in structure, but modified to perform particular functions. Beneath the mucosa is a layer of connective tissue containing blood vessels and nerves. Next come layers of involuntary muscle tissue with a most interesting function. When food reaches the first part of the canal (the esophagus); it stimulates the muscle tissue to produce a rhythmic, wavelike motion known as *peristalsis*. Peristalsis transports food the entire length of the alimentary canal and mixes with digestive juices *en route*.

The involuntary muscle layers include an outer longitudinal one whose fibers run lengthwise, and an inner circular layer that reduces the size of the lumen during contraction. In some areas, the circular layer is markedly thickened to form valves that close openings. These muscular valves are called *sphincters*.

The final layer of the alimentary canal is fibrous connective tissue except for those parts that extend into the abdominal cavity, which have an additional layer called peritoneum.

### Pharynx and esophagus

The *pharynx* is often referred to as the *throat*. The tongue pushes food into the pharynx. Walls of the pharynx and tongue are voluntary muscles lined with a mucosa. The tonsils can be seen at either side of the pharynx. The *soft palate* is muscular tissue that forms the back of the roof in the oral cavity. The soft palate guards the opening to the nasal cavity from the upper pharynx and prevents foods and liquids from entering the nasal cavities. When swallowing, the pharynx muscles contract constricting the space. At this time, the openings into the air spaces, both above and below the mouth, are closed by the soft palate above and by the *epiglottis* (a leaf-shaped lid).

The *esophagus* or *gullet* receives the contents of the contracting pharynx and forces them on by peristalsis. The esophagus—about 22.5-cm long—extends through the neck and the thorax. After passing through the diaphragm, the esophagus reaches the abdominal cavity. There it empties into a saclike structure, the stomach.

### Stomach

The stomach is actually an enlarged (dilated) section of the alimentary tube shaped like a gourd (fig. 2-2). Both ends of the stomach are guarded by sphincters that permit substances to pass in only one direction. The first of these is the *lower esophageal sphincter*, located between the esophagus and stomach. We are frequently aware of the existence of this sphincter: sometimes it does not relax as it should, and there is a feeling of having a place one can't swallow past. At the distal or far end of the stomach, connecting it with the small intestine, is the other valve called the *pyloric sphincter*. This valve is especially important in that it plays a role in determining how long food remains in the stomach.

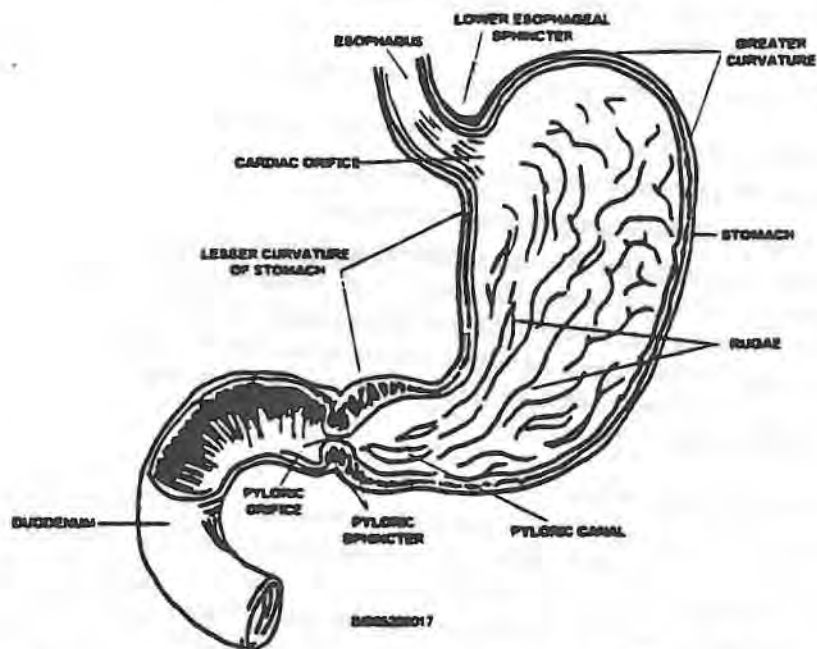


Figure 2-2. Longitudinal section of stomach and a portion of the duodenum, showing interior.

The stomach is a combination storage pouch and churn. There are many folds in the lining of an empty stomach. These folds are called *rugae*, and they disappear as the stomach dilates (it may be stretched so that it holds a half gallon of food and liquid). When the stomach is filled, the pyloric sphincter closes and retains the contents until the food has been mixed with digestive juices collectively called *gastric juices*. These juices are secreted by many glands in the stomach wall. The mixture of gastric juices and food is known as *chyme*.

The gastric juice itself has two main components, *hydrochloric acid* and *enzymes*. The hydrochloric acid in the stomach juice has three important functions:

1. Softens the connective tissues in meat.
2. Kills bacteria and thus destroys many potential disease-producing agents.
3. Activates at least one of the stomach enzymes, which are chemicals that begin the digestion of food.

An abnormally low production of stomach acid may cause digestive disturbances that are greatly aggravated by soda or other alkaline substances contained in many patent medicines used to relieve

indigestion. Such self-medicating substances neutralize the valuable normal functions of the stomach acid, and in many cases cause grave harm. Occasionally, hydrochloric acid is produced in excess, and its presence can be determined by an analysis of the stomach contents. This condition is called hyperacidity and may be associated with ulcer disease.

### **Pyloric sphincter**

The pyloric sphincter is a ringlike muscle surrounding the end of the stomach. Normally, the stomach contents escape through this muscular ring in about two to six hours after eating. This action may be delayed by a spasm of the muscle (pylorospasm). In some infants, more often males, there may be a congenital obstruction called *pyloric stenosis*. Usually, surgery is required to modify the muscle so food can pass from the stomach into the duodenum.

### **The small intestine**

The small intestine is the longest part of the alimentary canal. It is known as the small intestine because its diameter is smaller than that of the large intestine. The small intestine is about 6 m (20 feet) long compared with 1.2 m to 1.5 m (4 or 5 feet) for the large intestine. In addition, the mucosal surface of the small intestine has a greatly increased surface area due to the presence of tiny, finger-like projections called *villi*. The first 25 cm to 27 cm (10 to 12 inches) of the small intestine is called the *duodenum*. The *pancreas* and *liver*, two accessory organs, carry digestive juices through two ducts into the duodenum. Pancreatic juice arrives in the duodenum by way of the pancreatic duct, while bile from the liver and gallbladder is carried by the *common bile duct*. Bile contains no enzymes, but it is important in the digestion of fats. The small intestine secretes its own intestinal juice. As the chyme passes into the duodenum, it is exposed to several digestive juices.

Two more divisions of the small intestine are:

1. *Jejunum*—Forms the next two-fifths of the small intestine.
2. *Ileum*—Constitutes the remaining portion of the small intestine and joins the large intestine through a muscular ring called the *ileocecal valve*.

The food in the stomach is partially digested by the gastric juices, but the small intestine is the organ where most of the digestive and absorptive processes occur. We shall have a closer look at these two processes.

### **Digestion**

The lesson on blood pointed out that blood plasma contains water, food substances, and mineral salts that together are necessary for the life and growth of the cells. Ingested foods must be converted to simple substances before they can nourish the cells. This conversion process is called digestion.

Let us review the basic materials found in food needed for cell nourishment:

1. Carbohydrates include starches and sugars and contain the elements carbon, hydrogen, and oxygen.
2. Fats are more concentrated in fuel value than carbohydrates and are important for the absorption of certain vitamins.
3. Proteins and water are important for protoplasm formation.
4. Mineral salts include a large variety of somewhat simpler compounds than those mentioned previously. Salts maintain the proper conditions for osmosis in the cells, form a part of the body structure (as in bone), and play an important part in such life processes as muscle contraction, nerve responses, and blood clotting (see following table).



<b>Mineral Salts</b>			
<b>Minerals</b>	<b>Functions</b>	<b>Sources</b>	<b>Deficiencies</b>
Potassium (K)	Nerve and muscle activity	Fruits and other foods	Muscular and neurologic disorders
Sodium (Na)	Body fluid balance	Most foods and table salt	Weakness, cramps, diarrhea, dehydration
Calcium (Ca)	Formation of bones and teeth, blood clotting, nerve conduction	Dairy products, eggs	Rickets, tetany, bone demineralization
Phosphorus (P)	Formation of bones and teeth required for processes that need energy	Beef, egg yolk, dairy products	Bone demineralization, abnormal metabolism
Iron (Fe)	Oxygen carrier (hemoglobin)	Meat, eggs, spinach, prunes	Anemia, dry skin, indigestion
Iodine (I)	Thyroid hormones	Seafood, iodized salt	Hypothyroidism, goiter
Magnesium (Mg)	Catalyst for enzyme reactions, carbohydrate metabolism	Green vegetables	Spasticity, arrhythmia, vasodilation
Manganese (Mn)	Catalyst in the actions of calcium and phosphorus	Legumes, nuts, cereals, green leafy vegetables	Possible reproductive disorders
Copper (Cu)	Necessary for absorption and oxidation of vitamin C and iron and in formation of hemoglobi.	Liver, fish, oysters, legumes, nuts	Anemia
Cobalt (Co)	Part of vitamin B <sub>12</sub> , involved in blood cell production and in synthesis of insulin.	Animal products	Pernicious anemia
Zinc (Zn)	Promotes carbon dioxide metabolism, aids in the breakdown of proteins.	Many foods	Alopecia (baldness), possibly related to diabetes
Fluorine (F)	Prevents tooth decay	Water and many foods	Dental caries

5. Vitamins help regulate cell metabolism and are essential food substances for good health (see following table).

<b>Vitamins</b>			
<b>Vitamins</b>	<b>Functions</b>	<b>Sources</b>	<b>Deficiencies</b>
Retinol (A)	Required for healthy epithelial tissues and for eye pigments	Yellow vegetables, fish-liver oils	Night blindness, dry scaly skin
Thiamin (B <sub>1</sub> )	Required for some enzyme systems involved in converting food into energy	Pork, cereal grains	Beriberi, a disease of nerves (neuritis)
Riboflavin (B <sub>2</sub> )	Needed for enzyme systems that aid oxidation of sugars and amino acids (proteins)	Milk, eggs, kidney, liver	Skin and tongue disorders
Niacin (nicotinic acid)	Involved in oxidation of carbohydrates	Yeast, lean meat, liver	Pellagra with dermatitis, diarrhea, mental disorders
Pyridoxine (B <sub>6</sub> )	Involved in metabolism of various food substances.	Liver, rice, milk, cereals	Skin disorders, anemia, lack of growth



Vitamins			
Vitamins	Functions	Sources	Deficiencies
	transport of amino acids		
Pantothenic acid	Essential for normal growth	Yeast, liver, eggs	Skin lesions, gray hair
Cyanocobalamin (B <sub>12</sub> )	Production of blood cells (hemopoiesis)	Meat, liver, milk, eggs	Pernicious anemia
Biotin	Involved in carbon dioxide and fat metabolism	Peanuts, liver, tomatoes, eggs	Lack of coordination, dermatitis
Folic acid and folates	Required for synthesis of amino acids in DNA	Vegetables, liver	Anemia, digestive disorders
Ascorbic acid (C)	Maintains healthy skin and mucous membranes synthesis of collagen	Citrus fruits, green vegetables	Scurvy, poor bone and wound healing
Calciferol (D)	Aids in absorption of calcium from intestinal tract, and prevents rickets	Fish liver oils, sun on skin oils	Rickets, bone deformities

6. Water is one of our biggest needs. Water constitutes about 66 percent of an adult's body composition. Our diet provides a large amount of our water needs. Fruits and vegetables contain about 80 percent water and meats and fish are 50-75 percent water.

**NOTE:** Vitamin E has been omitted because its role in normal nutrition is not established. It is widely distributed in common foods.

The chemical action of digestive juices extracts vitamins and minerals so they can be absorbed. Most of the digestive juices contain chemicals known as *enzymes* which speed up the chemical reactions that help breakdown food. Although enzymes enable the chemical reaction to take place, the enzymes themselves do not enter into the reaction. For example, an enzyme may help separate a basic protein from the rest of the food, but the enzyme itself does not become a part of the protein. There are several different enzymes, and each acts on a specific food compound and no other. For example, some enzymes act only on fats, others act only on starches, and so forth. But let us see what happens to a mass of food from the time it is taken into the mouth to the moment that it is ready to be absorbed.

When food is chewed, saliva (the first digestive juice) softens the food so it can be easily swallowed. Saliva contains the enzyme *salivary amylase*, which initiates the process of digestion by changing some of the starches into sugars. Carbohydrates are found in the blood plasma in the form of simple sugar (glucose), and we should begin to understand where this blood sugar originates. When the food reaches the stomach, it is acted upon by the gastric juice, which contains hydrochloric acid and certain enzymes. Gastric juice functions similarly to hydrochloric acid on liquefying food. The most important functions of the gastric juice are those related to the actions of the hydrochloric acid and the liquefying of the food. In addition, the enzyme *pepsin* has some action, particularly on proteins. Although secreted by the gastric lining cells in an inactive form, pepsin is activated by the presence of *hydrochloric acid* in the stomach, aiding in protein digestion. Nearly every type of protein in the diet begins digestion with the action of pepsin. The stomach's churning action mixes food, gastric juice, and mucus (secreted by cells from the stomach wall) until the semi-liquid substance, *chyme*, is formed. From the stomach *chyme* proceeds to the small intestine for more chemical treatment.

Greenish yellow bile from the liver and gallbladder go through the common bile duct into the duodenum and mix with the *chyme*. Bile does not contain enzymes; its action is purely mechanical. It works on fat, acting as a sort of liquid crowbar that splits the bits of fat into even smaller particles so

the pancreatic digestive juices can act more efficiently. The pancreatic juice contains a number of enzymes including lipase, amylase, and trypsin.

### **Lipase**

Following the physical division of fats into tiny particles by the action of bile, the powerful pancreatic lipase does almost all the digesting of fats. In this process, fats are usually broken down into two simpler compounds, glycerol and fatty acids, which are more readily absorbable. If pancreatic lipase is absent, fats are expelled with the feces in undigested form.

### **Amylase**

This changes starch to sugar.

### **Trypsin**

Trypsin splits proteins into *amino* acids. The amino acids enable the proteins to enter the blood stream. The intestinal juice contains a number of enzymes, including three that act on complex sugars to change them into a simpler form for absorption. These are *maltase*, *sucrase*, and *lactase*.

**NOTE:** Most of the chemical changes in foods are caused by the pancreatic juice (which could probably adequately digest all foods even if no other digestive juice were produced) and occur in the intestinal tract.

This, in a nutshell, is the process of digestion. Note that the food materials the enzymes break down to absorbable forms are carbohydrates (such as sugars and starches) fats, and proteins. Mineral salts dissolve in water and are absorbed as is. Vitamins behave differently according to their type. Some are incorporated in fats and absorbed along with the fats. Other vitamins are dissolved in water and absorbed in much the same way as mineral salts. Still other vitamins (such as vitamin K) are produced by bacterial action in the colon and are absorbed via the large intestine (See following table).

<b>Digestive Juices and Enzymes</b>			
Juices and Glands	Place of Action	Enzymes	Changes in Foods
Saliva from three pairs of salivary glands	Oral cavity	Salivary amylase (ptyalin)	Begins starch digestion
Gastric juice from the stomach wall	Stomach	Pepsin	Begins protein digestion
Pancreatic juice from the pancreas	Small intestine	Amylase, Trypsin, Lipase	Acts on starches Acts on proteins Acts on fats
Intestinal juice from the small intestine (tubular glands)	Small intestine	Lactase, Maltase, Sucrase	Breaks down complex sugars into simpler forms
Bile from the liver	Small intestine	None	Breaks down fats physically so that lipase can digest them

### **Absorption**

Digested food reaches the bloodstream by a process known as *absorption*. The small intestine is the chief organ of absorption. This process takes place through the mucosa by means of its countless minute projections known as villi. The villi are so small and numerous that they give a velvety appearance to the lining of the small intestine. Each villus is epithelium underlaid with connective tissue. Within each villus is a system of miniature arteries and veins, bridged with capillaries. The basic food materials, including water and salts, with the exception of most fats, are absorbed into the bloodstream through the capillary walls of the villi. From here, they pass by way of the portal system to the liver to be stored and used as needed.

Fats have an alternative method of reaching the bloodstream. As noted, some fat is absorbed by way of the blood capillaries of the villi. However, most fats are absorbed by way of the lymphatic

capillaries of the villi, which are called *lacteals*. The word "lacteal" means "like milk," an apt description of its appearance. After a quantity of fat has been digested, a mixture of lymph and fat globules appear which comes from the small intestine. This mixture of fat and lymph, called *chyle*, collects in the cisterna chyli and eventually reaches the bloodstream.

In summary, the products of the digestive process, (simple sugars, amino acids, fatty acids, and glycerol) are absorbed into the capillaries of the villi.

### **The large intestine**

Once the processes of digestion and absorption take place in the stomach and small intestine, all that remains is water and food particles that are of no use to the body. These materials and anything else that may be indigestible will pass out of the body through the large intestine.

From the small intestine, the materials to be eliminated continue through the ileocecal valve and enter the small pouch at the beginning (proximal) of the large intestine. This pouch is called the *cecum* and is located in the lower iliac region of the abdomen. A small blind tube called the *vermiform appendix* is attached to the cecum. "Vermiform" means worm-like.

The next part of the large intestine is called the *colon*. The colon has four subdivisions:

1. Ascending colon.
2. Transverse colon.
3. Descending colon.
4. Sigmoid colon.

The *ascending colon* extends upward from the cecum along the right side toward the liver. There it bends, extending across the abdomen to the left side, forming the *transverse colon*. At this point, the colon bends sharply and extends downward on the left side of the abdomen into the pelvis. This part is called the *descending colon*. The lower part of the colon bends posteriorly in an S shape and continues downward, forming the *sigmoid colon*. The sigmoid colon empties into the *rectum*, a portion about 15 cm to 20 cm long. The rectum serves as a temporary storage area for the indigestible and unabsorbable food residue. A narrow portion of the distal part of the large intestine is called the *anal canal*, which leads to the outside of the body through an opening called the *anus*.

No enzymes are secreted by the large intestine. Its walls are lined with mucous membrane and contain layers of involuntary muscle that move the solid waste products, called *fecal matter*, toward the rectum. Absorption of large amounts of water takes place through the walls of the large intestine. The action of bacteria within the large intestine aids in the production of vitamin K and some of the B-complex vitamins.

## **412. Digestive system structures**

### **Accessory system structures**

Accessory structures of the digestive system are the:

- Liver.
- Gallbladder.
- Pancreas.

### **The liver**

The liver, or *hepar*, is the largest of the glandular organs of the body. It is located under the dome of the diaphragm so that, if normal size, it cannot be felt through the abdominal wall. The human liver is the same brownish red color as the animal livers seen in the market. It has a large right lobe and a somewhat smaller left lobe, as well as two other lesser lobes. The liver has a double blood supply: the portal vein and the hepatic artery. These two vessels deliver about 1 and 1/2 quarts of blood to the liver every minute. The hepatic artery carries oxygenated blood, while the portal system of veins



carries blood that is rich in the end products of digestion as well as in other raw materials required for metabolic activities in the liver. This most remarkable organ has so many functions that only some of its major activities are listed below:

1. Stores glucose (simple sugar) in the form of *glycogen*, an animal starch. When the blood sugar level falls below normal, the liver cells convert *glycogen* to glucose and releases it into the bloodstream. This restores the normal concentration of blood sugar.
2. Produces albumin, fibrinogen, and certain other blood plasma proteins.
3. Synthesizes *urea*, a waste product of protein metabolism. Urea is released into the bloodstream for transport to the kidneys for elimination.
4. Modifies fats so they can be more efficiently used by cells all over the body.
5. Manufactures bile. Liver cells synthesize bile salts, the substances that aid in the digestion of fats. *Bilirubin*, a pigment released during red blood cell destruction in the spleen, is extracted from the bloodstream and eliminated in the bile.
6. Detoxifies (removal of poisonous properties) harmful substances such as alcohol and certain drugs. The end products resulting from these activities are eliminated in the bile.
7. Manufactures heparin, a substance that prevents clotting of blood.

### ***The gallbladder***

The gallbladder is a muscular sac that serves as a storage pouch for bile. The liver may manufacture bile continuously; however, the need for it is likely to arise only a few times a day. Consequently, bile from the liver flows into the liver ducts and then up through the duct connected with the gallbladder. When chyme enters the duodenum, the gallbladder contracts, squeezing bile into a duct leading to the duodenum.

### ***The pancreas***

The pancreas produces the pancreatic juice, an extremely powerful substance because it contains digestive enzymes. Since it is usually confined to its proper channels, the action of the pancreatic enzymes will not damage body tissues. However, it may happen that the pancreatic duct becomes blocked, and these enzymes will then back up in the tissues that are not suppose to receive them. Also, the pancreas manufactures a substance called *insulin* which is released directly into the blood and has the function of regulating the amount of sugar that is "burned" in the tissues.

### ***The peritoneum***

The *peritoneum* is a serous membrane that covers the surface of most of the abdominal organs to form the visceral serosa and lines the abdominal wall to form the parietal layer. In addition to these parts of the peritoneum, there are more complex double layers of membrane that separate the abdomen into areas and spaces and, in some cases, help support the organs and hold them in place.

The *mesentery* is a double-layered peritoneal structure shape somewhat like a fan, with the handle portion attached to the back wall. The expanded long edge is attached to the small intestine. Between the two layers of membrane that form the mesentery are the blood vessels, nerves, and other structures that supply the intestine.

Another double-layered peritoneal structure, called the *greater omentum*, hangs downward from the lower border (greater curvature) of the stomach. This double layer of peritoneum extends into the pelvic part of the abdomen and then loops back and up to the transverse colon. It has been aptly described as an apron inside the abdomen. It can, in some cases, serve to prevent the spread of infection inside the abdominal cavity. There is also a peritoneal structure called the *lesser omentum*, which extends between the stomach and the liver.

### 413. Conditions associated with the digestive system

There are a wide variety of disorders associated with the digestive system. This lesson begins with a discussion of diseases of the mouth and teeth, then discusses the stomach and intestinal disorders. Next, it covers disorders of the accessory structures, and finally disorders of the peritoneum.

#### Diseases of the mouth and teeth

This lesson talks about diseases that are common in the mouth and teeth. These include gingivitis, pyorrhea, and tooth decay.

#### Gingivitis

Infection of the gum is called *gingivitis*, while infection of the rest of the mucous lining of the mouth is called *stomatitis*. Stomatitis is a problem for people who use antibiotic types of lozenges. These medicated wafers may encourage fungus infections of the mouth and tongue.

*Vincent's angina* (trench mouth) is a kind of gingivitis, causing redness and ulceration of the mucous membrane of the mouth and gums. It is contagious and is caused by a spirochete.

#### Pyorrhea

*Pyorrhea* is an inflammation involving the tooth socket or *alveolus*. It is accompanied by discharge of pus, so the name is really *pyorrhea alveolaris*.

#### Tooth decay

Tooth decay or dental *caries*, which means "rotteness," has a number of causes. It is a prevalent disease in persons consuming high quantities of sugar. In addition to diet, such factors as heredity, mechanical problems, and endocrine disorders are believed to play a part. Since a baby's teeth begin to develop before birth, the diet of the mother during pregnancy also is very important in ensuring the formation of healthy teeth in her baby.

#### Stomach disorders

These disorders are becoming more and more common as our lifestyles become more stressful.

#### Heartburn and GERD

Almost everyone has suffered from heartburn or "acid indigestion" at one time or another. For most people, the burning feeling from behind their breastbone comes only once in a while, perhaps after eating greasy fast food or a huge Thanksgiving dinner. For others, the gnawing burn is a daily occurrence that requires a constant supply of antacids to stop the pain.

All true cases of heartburn are caused by the back flow of digestive juices from the stomach into the esophagus. We've already discussed what is in the digestive juices—diluted hydrochloric acid and the enzyme, pepsin. The combination of the two would eat through the wall of the stomach if it weren't lined with thick mucous. The esophagus isn't as well protected. When the lower esophageal sphincter relaxes (it does this several times daily in healthy people), some digestive juices may slosh up into the esophagus. This upward flow is called *acid reflux* or *gastroesophageal reflux*. Usually, the juices don't stay in the esophagus long enough to cause problems. Gravity and peristalsis push them back down and swallowed saliva, a natural antacid, neutralizes any remaining acid.

From time to time people with normal acid reflux may get heartburn, particularly if the digestive juices stay pooled in the esophagus for long periods. That happens most commonly while lying down, because gravity can't help drain fluid out of the esophagus. People may also get occasional heartburn if they do something that relaxes the lower esophageal sphincter or forces it open. A large meal that distends the stomach puts upward pressure on the sphincter muscle. Drinking alcohol and eating fatty foods make the muscle relax. It's no wonder that the worst cases of occasional heartburn occur when these circumstances overlap. Heartburn could be at its worst when we indulge in a large meal of rich foods and alcohol shortly before bedtime.



In about one in 50 adults stomach fluid refluxes into the esophagus more frequently than normal. The repeated backflow of digestive fluids can cause problems more troubling than simple heartburn. This condition is called gastroesophageal reflux disease (GERD). While alcohol, fatty foods, and eating before bedtime may make GERD worse, the precise cause of GERD is not fully understood. Researchers think that a combination of factors, including one's genetic makeup, may all play a role.

### **Peptic ulcer**

An ulcer is an area of the skin or mucous membrane in which the tissues are gradually disintegrating. Peptic ulcers occur in the mucous membrane of the esophagus, stomach, or duodenum—the first part of the small intestine. Peptic ulcers in the stomach are gastric ulcers; those in the duodenum are duodenal ulcers. An ulcer may be the result of the acid action of the gastric juice. Peptic ulcers are found most frequently in people between the ages of 30 and 45. Duodenal ulcers are much more common in males. Emphasis is now being placed on mental and emotional factors as a contributing cause of ulcers. The person suffering from a peptic ulcer needs the best medical and nursing care, and most certainly should not depend on over-the-counter (OTC) medicines, such as antacids.

*Helicobacter pylori* (*H. pylori*) is a type of bacteria. Researchers recently discovered that *H. pylori* causes almost all peptic ulcers, accounting for 80 percent of stomach ulcers and more than 90 percent of duodenal ulcers. *H. pylori* infection is common in the United States. About 20 percent of people under 40 and half of people over 60 are infected with it. Most infected people, however, do not develop ulcers. Why *H. pylori* doesn't cause ulcers in every infected person is unknown. Most likely, infection depends on characteristics of the infected person, the type of *H. pylori*, and other factors yet to be discovered. Researchers are not certain how people become infected with *H. pylori*, but they think it may be through food or water. Researchers have found *H. pylori* in some infected people's saliva, so the bacteria may also spread through mouth-to-mouth contact such as kissing.

*H. pylori* weakens the protective mucous coating of the stomach and duodenum, which allows acid to get through to the sensitive lining beneath. Both the acid and the bacteria irritate the lining and cause a sore, or ulcer. *H. pylori* is able to survive in stomach acid because it secretes enzymes that neutralize the acid. This mechanism allows *H. pylori* to make its way to the "safe" area—the protective mucous lining. Once there, the bacterium's spiral shape helps it burrow through the mucous lining.

*H. pylori* peptic ulcers are treated with drugs to kill the bacteria, to reduce stomach acid, and to protect the stomach lining. Antibiotics are used to kill the bacteria. Two types of acid-suppressing drugs might be used: H<sub>2</sub>-blockers and proton pump inhibitors.

<b>Drugs Used to Treat <i>H. pylori</i> Peptic Ulcers</b>	
<b>Antibiotics</b>	metronidazole, tetracycline, clarithromycin, amoxicillin
<b>H<sub>2</sub>-blockers</b>	cimetidine, ranitidine, famotidine, nizatidine
<b>Proton pump inhibitors</b>	omeprazole, lansoprazole
<b>Stomach-lining protector</b>	bismuth subsalicylate, sucralfate
You may see these drugs used as dual or triple therapy. Standard therapy lasts for 14 days.	

### **Intestinal disorders**

Inflammation, diarrhea, dysentery, constipation, and cancer of the colon and rectum are disorders associated with the intestine. We will take a brief look at each one of these disorders in this lesson.

#### **Inflammation**

Difficulties with digestion or absorption may be due to *enteritis*, an intestinal inflammation. When both the stomach and the small intestine are involved, the illness is called *gastroenteritis*. The symptoms include nausea, vomiting, and diarrhea as well as acute abdominal pain or colic. Gastroenteritis may be caused by a variety of pathogenic organisms including viruses, bacteria, and protozoa. Chemical irritants, such as alcohol, spray residues (on fruits and vegetables), and other toxins have been known to cause this disorder.

*Appendicitis* is inflammation of the vermiform appendix. It can result from infection of the appendix mucosa by organisms causing enteritis or from obstruction by accumulated, hardened fecal material or occasionally by pinworms.

### ***Diarrhea and dysentery***

*Diarrhea* is a symptom characterized by abnormally frequent watery bowel movements. *Dysentery* usually refers to an inflammation of the mucosal lining, although deeper tissues also may be affected.

The two main types of dysentery are bacillary dysentery and amebic dysentery. *Bacillary dysentery* is caused by rod-shaped bacteria that are transferred to food and water primarily by human carriers.

*Amebic dysentery* is due to an infestation by a one-celled animal called *Entamoeba histolytica*.

Bacillary dysentery may be prevented by a combination of water chlorination, milk pasteurization, and by using sanitary practices when handling food. Restaurant workers need to receive periodic examinations and observe ordinary precautions such as frequent hand washing, particularly after every trip to the bathroom. Amebic dysentery is especially prevalent in areas where human waste is used to fertilize food grown in fields. When traveling in countries where this is the custom, one should avoid eating raw food and drinking unboiled or unsterilized water. The travelers need to carry chemical tablets to kill contaminants in water if they are unable to boil it.

Diarrhea is a symptom found in many conditions in addition to the dysenteries. Some of these disorders include the following:

1. *Bacterial infection of the intestinal wall*, due to ingested pathogens such as staphylococci, common in food poisoning, or the spread of pathogens from other infected sites, such as the respiratory tract.
2. *Bacterial infection of the intestinal wall*, due to ingested pathogens such as staphylococci, common in food poisoning, or to the spread of pathogens from other infected sites, such as the respiratory tract.
3. *Putrid poisoning*, which is sometimes confused with the bacterial food poisoning caused by staphylococci but is actually due to putrid meat. It is now rather rare.
4. *Nutritional deficiency diseases* such as pellagra or sprue.
5. *Acute emotional disturbances*, such as those sometimes experienced by students just before and during an important test ("State Board" diarrhea).
6. *Ulcerative colitis*, a chronic inflammatory disease causes ulceration of the intestinal wall and frequent bleeding.
7. *Cancer*, constipation may alternate with diarrhea.

Intestinal excretions may need to be examined to determine the cause of the diarrhea. Various terms are used to refer to this bowel waste including feces, fecal material, excrement, and most commonly, stool. A stool examination may reveal the presence of amoebae, bacteria, the ova of worms, or blood.

### ***Constipation***

Millions of dollars are spent each year in an effort to remedy a condition called *constipation*. What is constipation? Many people erroneously think of themselves as constipated if they have days during which there are no bowel movements. Normal people vary greatly; one person may be perfectly well although they have a bowel movement only once in two or three days, while another may be equally well with more than one movement daily.

On the basis of its onset, constipation may be classified as acute or chronic. Acute constipation occurs suddenly and may be due to an intestinal obstruction, such as a tumor associated with cancer, or an inflammation of the saclike bulges (diverticula of the intestinal wall) as seen in *diverticulitis*. Avoid laxatives and enemas and immediately consult with a physician.

Chronic constipation has a more gradual onset and may be divided into two groups: spastic and flaccid constipation.

1. *Spastic constipation* —The intestinal musculature is over-stimulated so that the canal becomes narrowed and the space (lumen) inside the intestine is not large enough to permit the passage of fecal material.
2. *Flaccid constipation*—Characterized by a lazy or *atonic* intestinal muscle. Elderly persons and those on bed rest are particularly susceptible to this condition.

The overactive spastic type of constipation is probably much more common than the atonic lazy kind. Nervous tensions, excessive amounts of bulky foods, and the use of laxatives increase the muscle tone of the intestine. Moderate exercise, an increase in vegetables and other bulky foods, and an increase in fluid intake may help the person who has sluggish intestinal muscles.

The use of enemas and so-called colonic flushings are unnecessary and should be discouraged for most persons. Streams of water that remove the normal protective mucus can injure the lining of the intestine. Also, enemas aggravate piles (hemorrhoids). Enemas should be used sparingly and only on the order of a physician.

### ***Cancer of the colon and rectum***

Tumors of the colon and rectum are among the most common types of cancer in the United States. These tumors usually arise from the mucosal lining and are called adenocarcinomas. The occurrence of cancer of the colon is evenly divided between the sexes, but malignant tumors of the rectum are more common in men. Tumors may be detected by examining the rectum and lower colon with an instrument called a *sigmoidoscope*. Early detection and treatment of tumors is a key to increasing survival rates.

### **Disorders involving the accessory structures (liver, gallbladder, and pancreas)**

#### ***Liver diseases***

This section discusses three liver diseases: hepatitis, cirrhosis, and cancer of the liver.

#### ***Hepatitis***

Inflammation of the liver is called *hepatitis*. A virus causes epidemic hepatitis. Outbreaks of this disease, which are more common in the fall and winter, occur in military establishments, prisons, and in other populous institutions. It varies in severity from mild cases that are so mild as to be scarcely recognizable to serious infections where the liver may become permanently damaged. A more prevalent type of virus infection is called serum hepatitis.

The infection is transmitted by administration of:

1. Infected blood.
2. Plasma or blood products.
3. Improperly sterilized needles and syringes (as used by drug addicts).

Since blood from the intestinal tract passes through the liver, any toxins or microorganisms that may get into the intestinal (mesenteric) veins enter the liver. The most important of these organisms is the *Entamoeba histolytica*, which causes amebic colitis at first. If it is carried into the liver, it causes the same tissue destruction that it does in the colon. However, since the liver is not open to the outside as the colon is, the softened and liquid area becomes an abscess. This condition is very hard to treat.

#### ***Cirrhosis***

*Cirrhosis* of the liver is a chronic disease that replaces active liver cells with inactive scar tissue (connective tissue). The most usual type is *portal cirrhosis*, which is fairly common in alcoholics. Many believe that the cause is related to poor nutrition. Destruction of the liver cells curtails the portal circulation, causing blood to accumulate in the spleen and the gastrointestinal tract and in the peritoneal cavity fluid. This fluid may have to be removed periodically by puncture, or *paracentesis*.





3. What three pairs of glands manufacture saliva?
4. What is the "soft palate"?
5. What term is used to describe the mixture of gastric juices and food?
6. What are the three functions of hydrochloric acid in stomach juices?
7. What is the longest part of the alimentary canal?
8. What enzyme is found in saliva?
9. What is absorption?
10. What are the four subdivisions of the colon?

**412. Digestive system structures**

1. What is the largest glandular organ of the body?
2. What organ is a muscular sac that serves as a storage pouch for bile?
3. What organ manufactures insulin?
4. What is the peritoneum?
5. What is the mesentery?
6. Where is the "greater omentum" located?



**413. Conditions associated with the digestive system**

1. What term is used to describe an infection of the mucous lining of the mouth (excluding the gums)?
2. What type of pathogen causes Vincent's angina?
3. What is pyorrhea?
4. What causes heartburn?
5. What is GERD?
6. In what age group are peptic ulcers most commonly found?
7. What term is used to describe inflammation of the intestine?
8. What are the symptoms of gastroenteritis?
9. List the causes of appendicitis.
10. What type of dysentery is caused by rod-shaped bacteria that is transferred to food and water primarily by human carriers?
11. What is ulcerative colitis?
12. What type of constipation is characterized by a lazy or *atonic* intestinal muscle?
13. How is serum hepatitis transmitted?

14. Describe cirrhosis of the liver.
15. What term is used to describe the presence of stones in the gallbladder?
16. Define peritonitis.
17. What term is used to describe an accumulation of fluid in the peritoneal cavity?
18. List one possible cause of ascites.

## 2-2. Prevention and Treatment of Digestive System Conditions

The three classes of drugs that we will discuss are the antiulcer agents, laxatives, and antidiarrheals. The information about each class will include indications, warnings, drug interactions, and patient information.

### 414. Nutrition

Good nutrition is absolutely essential for the maintenance of health. We must continually eat an adequate quantity of food materials that are necessary for the life and growth of body cells. If one or more of these vital materials are not supplied, the body will suffer in a number of ways, the effect being *malnutrition*. One commonly thinks of a malnourished person as one who does not have enough to eat; but malnutrition can occur just as easily from eating too much of the wrong foods. Malnutrition can be avoided by adhering to a balanced diet, which ensures that most diets include adequate quantities of the basic nutrients.

In order that homemakers and others who plan meals may understand more easily how to provide a balanced diet, food groupings have been publicized. One grouping arranges foods as protective foods, protein foods, and energy foods.

<i>Food Groups</i>	
Types of Foods	Description
Protective foods	High in vitamins and mineral salts. Includes citrus and other fruits, plus a variety of vegetables (particularly leafy green and yellow ones). Especially valuable in preventing disease.
Protein foods	Required for growth and repair of tissues. Cannot be stored, so include them daily.
Energy foods	Contain fats and carbohydrates. Needed in larger amounts by those who are extremely active physically.

Many assertions about food combinations, such as the common one that cherries and ice cream or fish and milk are poisonous mixtures, are not based on the laws of nature; nor can any scientific basis be found for such ideas. For the normal, healthy person, a balanced diet including a variety of fruits, vegetables, and cereals, together with adequate amounts of such protein foods as milk and milk products, eggs, and meats, will maintain nutritional health.

Infants may need supplements of certain vitamins, but normal, healthy children and adults should be able to get adequate amounts of vitamins from a well-balanced diet. When required, vitamin supplements should be selected by a physician to fit the particular need of the individual. The so-called megavitamin dosages now fashionable in some quarters may cause unpleasant reactions and in some cases are hazardous. Vitamins A and D have both been found to cause serious toxic effects, and a relatively small excess of vitamin D may result in the appearance of dangerous symptoms.

A few people develop severe allergic (hypersensitive) manifestations if they eat certain foods. Some find that strawberries cause such a response. In others, shellfish cause a reaction resembling poisoning. However, the great majority of people can eat any food. The most common causes of temporary digestive disturbances are overeating, bacterial contamination, and virus infections.

#### 415. Reflux and antiulcer agents

You learned what reflux and ulcers are in previous lessons. With all of the acid floating around in our digestive system, it's hard for lesions to heal. This lesson will cover some medications that improve conditions so that ulcers can close up and acid can be kept out of the esophagus. We'll take a look at antacids, histamine-2 blockers, proton pump inhibitors, GI stimulants, and protective agents. We'll start with the simplest way to treat reflux and ulcers—antacids.

##### Antacids

Antacids neutralize gastric acidity, resulting in an increase in the pH of the stomach and duodenum. Additionally, they inhibit pepsin activity by increasing the gastric pH above four. Antacids do not "coat" the mucosal lining, but may have a local astringent effect. Antacids also increase the lower esophageal sphincter tone. Aluminum ions inhibit smooth muscle contraction and gastric emptying. The drugs that we'll examine in this class include magnesium and aluminum hydroxide and calcium carbonate.

##### Indications

All antacids are indicated for hyperacidity. They treat symptomatic relief of upset stomach associated with hyperacidity (heartburn, gastroesophageal reflux, acid indigestion, and sour stomach) and hyperacidity associated with peptic ulcer and gastric hyperacidity.

<i>Antacids</i>			
Drug	Common Name	Dosage Form	Dosage
Magnesium hydroxide	Milk of Magnesia	311 chewable tabs 400 and 800 mg/5ml liquid	600 – 1,200 mgs up to 4 times daily
Aluminum hydroxide	Amphogel	300, 400, 500, 600 mg chewable tabs 320, 450, 600 mg/5ml liquid	500 to 1,500 mg 3 to 6 times daily, between meals and at bedtime.
Calcium carbonate	Tums, Maalox, Mylanta tabs	various strengths 300 – 1,250 mg tabs 1,250 mg/5ml liquid	500 – 1,500 mg as needed

##### Warnings

Antacids may cause dose-related rebound hyperacidity since they may increase gastric secretion or serum gastrin levels. If a patient is using aluminum antacids for prolonged periods, a phosphate deficiency may occur. Phosphate is essential for the maintenance of healthy bones.

**Pregnancy:** There is no class assigned to antacids. However, pregnant women should consult their provider before taking an antacid. There are no problems with lactating women and antacids.

##### Drug interactions

Antacids may interfere with drugs by altering their disintegration, dissolution, or solubility and can change gastric emptying time. The absorption of weak acidic drugs is decreased and basic drug

absorption is increased, possibly to toxic levels. Antacids also bind some drugs to their surface, resulting in decreased bioavailability. Magnesium is the worst of the three discussed for this interaction. Urinary pH is also changed by antacids, which may inhibit the excretion of basic drugs and enhance that of acidic ones. A staggering of two hours in administration time from antacids to other medications is usually enough to offset these effects. The following table lists the specific antacids and some of their more significant medication interactions. The table states if the drug actions are increased or decreased by antacids. If the column is blank, the drug is unaffected by that particular antacid.

<b>Antacid Interactions</b>			
<b>Drugs</b>	<b>Aluminum</b>	<b>Calcium</b>	<b>Magnesium</b>
Corticosteroids	Decreased		Decreased
Digoxin	Decreased		Decreased
Fluoroquinolones		Decreased	
Histamine H <sub>2</sub> antagonists	Decreased		Decreased
Hydantoins		Decreased	Decreased
Iron salts	Decreased	Decreased	Decreased
Quinidine			Increased
Salicylates			Decreased
Sulfonylureas			Increased
Tetracyclines	Decreased	Decreased	Decreased
Thyroid hormones	Decreased	Decreased	

#### **Patient information**

- Chewable tablets: Thoroughly chew before swallowing. Follow with a glass of water.
- Drug interaction precaution: Antacids may interact with certain prescription drugs. If you are presently taking a prescription drug, check with your physician or pharmacist before taking an antacid.
- Magnesium-containing products can act as a saline cathartic in larger doses and produce a laxative effect and can cause diarrhea. Aluminum and calcium-containing products can cause constipation. Magnesium/aluminum antacid mixtures are used to avoid bowel function changes.
- Notify physician if relief is not obtained or if there are any symptoms that suggest bleeding, such as black tarry stools or "coffee ground" vomitus.
- Taking too much of these products can cause the stomach to secrete excess stomach acid. Consult your physician or pharmacist about the appropriate dose. Do not use the maximum dosage of antacids for > 2 weeks, except under the supervision of a physician.

#### **Histamine-2 blockers**

Histamine-2 blockers, or H<sub>2</sub> blockers, have become one of the fastest growing drugs in terms of usage and in treating common indigestion. Our discussion will only cover prescription doses for the treatment of ulcerative diseases. We will look at the two H<sub>2</sub> blockers appearing on the DOD Basic Core Formulary, cimetidine and ranitidine.

H<sub>2</sub> blockers are highly selective. They act only on the H<sub>2</sub> receptors, which are found in the parietal lining of the stomach. They have no effect on H<sub>1</sub> receptors (the ones found in the rest of the body, responsible for allergic reactions), nor do they have any anticholinergic effects. Potent inhibitors of all phases of gastric acid secretion inhibit secretions caused by histamine, muscarinic agonists and gastrin. They also inhibit fasting and nocturnal secretions and secretions stimulated by food, insulin, and caffeine.



### Indications

Both of our  $H_2$  blockers are indicated for duodenal and gastric ulcer, GERD, erosive esophagitis, and a few other hypersecretory conditions. They are also indicated in the therapy for *heliobacter-pylori* infection. The first table below is for cimetidine, and the second is for ranitidine.

<b>Cimetidine Indications</b>		
Indication	Dosage	Duration of treatment
Duodenal ulcer	Acute: 400 mg twice daily or 800 mg at bedtime	A: 4 – 6 weeks
	Maintenance: 400 mg at bedtime	M: ongoing
Gastric ulcer	Acute: 800 mg at bedtime	A: 8 weeks
	Maintenance: not used	M: n/a
GERD	1,600 mg daily (divided)	12 weeks

<b>Ranitidine Indications</b>		
Indication	Dosage	Duration of treatment
Duodenal ulcer	Acute: 150 mg twice daily or 300 mg at bedtime	A: 4 – 6 weeks
	Maintenance: 150 mg at bedtime	M: ongoing
Gastric ulcer	Acute: 150 mg twice daily	A: 8 weeks
	Maintenance: 150 mg at bedtime	M: ongoing
GERD	150 mg twice daily	12 weeks
Erosive esophagitis	150 mg 4 times daily	12 weeks
	150 mg twice daily	Ongoing

### Contraindications

$H_2$  blockers are contraindicated when the patients have sensitivity to them or their components.

### Warnings

**Pregnancy:** Cimetidine and ranitidine are in pregnancy category B. Cimetidine crosses the placenta. There are no adequate and well-controlled studies with these agents in pregnant women. Use only when clearly needed and when the potential benefits outweigh the potential hazards to the fetus.

**Lactation:** Cimetidine is excreted in breast milk with milk: plasma ratios of approximately 5:1 to 12:1. Potential daily infant ingestion is approximately 6 mg so do not nurse.

Ranitidine is excreted in breast milk with milk: plasma ratios of 1:1 to 6.7:1. Exercise caution when administering to a nursing mother.

### Drug interactions

These two drugs differ in this area so we'll cover them separately.

Cimetidine may increase the toxic effects (respiratory depression) of narcotic analgesics but it decreases the absorption and pharmacologic effects of:

1. Digoxin.
2. Fluconazole.
3. Iron salts.
4. Indomethacin.
5. Ketoconazole.
6. Tetracyclines.

Ranitidine *increases* the effects of both glipizide and warfarin, possibly through a reduction in clearance and reduces the GI absorption of diazepam, *decreasing* its pharmacologic effects.



**Patient information**

- Inform physician or pharmacist of any concomitant drug therapy, especially when taking cimetidine.
- Stagger doses of antacids and cimetidine or ranitidine.
- May be taken without regard to meals.

**Proton pump inhibitors (PPIs)**

H<sub>2</sub> blockers stop the acid-producing signal from reaching the receptor site. PPIs work later in the process. They suppress gastric acid secretion by specifically inhibiting the enzymes at the surface of the gastric parietal cell. PPIs get their name because this enzyme is the "acid (proton) pump" within the system, the final step of acid production. Omeprazole and lansoprazole are the two PPIs. Omeprazole is the only PPI that we will discuss.

**Indications**

Omeprazole is:

1. Indicated for treatment or symptomatic relief of various gastric disorders including gastric and duodenal ulcers, GERD, or pathological hypersecretory conditions.
2. Is enteric coated.
3. Available in 10 mg and 20 mg delayed-release capsules.

<b>Omeprazole Dosing</b>		
Indication	Dosage	Duration
Duodenal ulcer	20 mg daily	4 – 8 weeks
Gastric ulcer	40 mg once daily	4 – 8 weeks
GERD	20 mg daily	4 – 8 weeks
Erosive esophagitis	20 mg daily	4 – 8 weeks
Pathological hypersecretions	60 – 360 mg daily (divided into 3 doses)	As long as required

**Contraindications**

Sensitivity to the drug or its formulation is the only contraindication.

**Warnings**

**Pregnancy:** Omeprazole is in pregnancy category C. There is no adequate or well-controlled studies with omeprazole in pregnant women. Use during pregnancy *only* if the potential benefit justifies the risk to the fetus.

**Lactation:** We don't know if omeprazole is excreted in breast milk. Because of the potential for serious adverse reactions in nursing infants, and the potential for tumorigenicity shown in rat carcinogenicity studies, decide whether to discontinue nursing or to discontinue the drug. Before making a decision, determine the importance of the drug to the mother.

**Drug interactions**

Omeprazole affects the liver enzymes, especially the P450. This enzyme is important in the metabolism of some medications. Omeprazole inhibits this enzyme, decreasing the metabolism of benzodiazepines, phenytoin, and warfarin. The decreased metabolism means that the drug is around longer (longer half-life) and the effects of the medications are greatly increased.

Omeprazole *increases* the clearance of theophylline, lowering its effects.

A strange interaction between omeprazole and clarithromycin happens. Levels and effects of both drugs are increased when administered concurrently.

**Patient information**

- Take before eating.
- Swallow omeprazole capsule whole: do not open, chew, or crush.
- Antacids may be used while taking omeprazole.

**GI stimulants**

This class of drugs does exactly as its name implies. These drugs effectively reduce irritation of the stomach (ulcers) and prevent reflux by quickly moving substances through the digestive system. They *stimulate* peristalsis. The drug that we are going to cover in this section is metoclopramide.

**Metoclopramide**

Metoclopramide's mechanism of action is complex. Following are actions of this medication:

1. Enhances gastric motility without stimulating gastric secretions.
2. Helps with the natural cholinergic activity by either causing the release of more acetylcholine or by sensitizing the receptors on the smooth muscle of the digestive system.
3. Helps with keeping the lower esophageal sphincter closed, but its actions are greater during the day than at night.
4. Increases the tone and amplitude of gastric contractions.
5. Relaxes the pyloric sphincter and the duodenal bulb.
6. Increases peristalsis of the duodenum and jejunum, resulting in accelerated gastric emptying and intestinal transit.
7. Is an anti-emetic because of its dopaminergic receptor blocking.

**Indications**

Metoclopramide is indicated in symptomatic gastroesophageal reflux. It is also used in diabetic patients who suffer from gastroparesis. Its anti-emetic affects are useful for the prevention of postoperative nausea, and nausea and vomiting associated with chemotherapy. Metoclopramide is available in 10-mg tablets, 5mg/5ml syrup, 10mg/ml concentrated solution and 5 mg/ml injection.

<b>Metoclopramide Dosing</b>	
<b>Indication</b>	<b>Dosage</b>
Diabetic gastroparesis	10 mg 30 minutes before each meal and at bedtime for 2 – 8 weeks.
Gastroesophageal reflux	10–15 mg orally up to 4 times daily 30 minutes before each meal and at bedtime for up to 12 weeks.
Postoperative nausea	Inject 10–20 mg near the end of surgery.
Chemotherapy nausea	2mg/kg infused IV 30 minutes before beginning chemotherapy, repeated ever 2 hours for 2 doses and then every 3 hours for 3 doses

**Contraindications**

Metoclopramide shouldn't be used when GI motility stimulation might be dangerous (e.g. when there is a GI hemorrhage, mechanical obstruction, or perforation).

**Warnings**

IV metoclopramide may exacerbate hypertension.

**Pregnancy:** Metoclopramide is in pregnancy category B. Metoclopramide crosses the placenta. However, there are no adequate and well-controlled studies on pregnant women. In several case reports, no effects occurred in the fetus when pregnant women used this drug for treating nausea, vomiting, and reflux esophagitis. Use only when clearly needed and when the potential benefits outweigh the potential hazards to the fetus.

**Lactation:** Metoclopramide is excreted into breast milk. The dose that an infant receives is much less than the maximum recommended infant dose. There appears to be no risk to an infant when the mother's dose is less than 45 mg/day.

#### *Drug interactions*

Metoclopramide *decreases* the absorption of cimetidine and digoxin. Faster gastric transit time is the primary reason for the interaction.

Metoclopramide *increases* the rate of absorption of alcohol by decreasing the time that it takes alcohol to reach the small intestine and be absorbed.

#### *Patient information*

- May produce drowsiness and dizziness; observe caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity.
- Notify physician if involuntary movement of eyes, face, or limbs occurs.
- Take medication 30 minutes before each meal.

#### **Protective agents**

Protective agents are the last of our anti-ulcer agents. The only drug that will be discussed here is Sucralfate. Sucralfate works locally rather than systemically. The sucralfate molecule has an aluminum ion that splits off when it hits stomach acid. This aluminum ion is non-absorbable and adheres to the ulcer. It pretty much forms a band-aid over the sore to protect it.

#### *Indications*

Sucralfate is indicated for the short-term treatment of active duodenal ulcers and for maintenance therapy at reduced dosage. The dosage for an active duodenal ulcer is 1 gm 4 times daily on an empty stomach, one hour before meals and at bedtime. After eight weeks of treatment, use 1 gm twice daily for maintenance therapy. Sucralfate is available in 1 gm tablets and 1 gm/10ml suspension.

#### *Contraindications*

There are no contraindications listed for sucralfate.

#### *Warnings*

It's very common for a patient to take antacids while taking sucralfate. Small amounts of aluminum are absorbed from sucralfate. If a patient has impaired kidney function, the additional aluminum could cause serious problems.

**Pregnancy:** Sucralfate is in category B. There are no adequate and well-controlled studies in pregnant women. Use this drug during pregnancy only if clearly needed.

**Lactation:** It is not known whether this drug is excreted in breast milk. Exercise caution when sucralfate is administered to a nursing mother.

#### *Drug interactions*

Sucralfate's drug interactions are not from systemic causes. The following drugs bind to sucralfate in the GI tract and are not well absorbed:

Anticoagulants	Digoxin	Hydantoins
Ketoconazole	Quinidine	Quinolones

#### *Patient information*

- Take on an empty stomach at least one hour before meals and at bedtime.
- Do not take antacids one-half hour before or after taking sucralfate.

#### **416. Laxatives**

Many of us, at one time or another, have needed a laxative. Laxatives promote bowel evacuation. A misunderstanding of normal bowel functions frequently cause misuse of nonprescription laxatives.

Restrict self-medication with laxatives to short-term constipation therapy. Self-medication with laxatives should be restricted to short-term therapy of constipation; chronic use of laxatives, particularly stimulants, may lead to dependence. Most people could probably avoid using laxatives if they would be sure to take in enough fluids, have proper dietary habits, including enough bulk or roughage, and have some daily exercise. This class will be covered a little differently. We won't discuss specific doses of specific drugs. Under the laxative class, we'll discuss the sub-classes of saline laxatives, irritant/stimulants, bulk producing, lubricants, surfactants, and miscellaneous laxatives. You will be given some examples of each and told how and where each of them work.

<b>Laxatives</b>				
<b>Laxatives</b>		<b>Onset of action (hrs)</b>	<b>Site of action</b>	<b>Mechanism of action</b>
Saline	Magnesium citrate	0.5 – 3	Sm & Lg intestine	Attracts and retains water in intestine, increasing pressure.
	Sod. Phosphate/biphosphate enema	0.03 – 0.25	Colon	
Irritant/stimulant	Senna	6 – 10	Colon	Direct action on intestinal mucosa, alters water and electrolyte secretion. Causes contractions, supplements peristalsis.
	Phenolphthalein	6 – 10	Colon	
	Bisacodyl tabs	6 – 10	Colon	
	Bisacodyl supp	0.25 – 1	Colon	
	Castor oil	2 – 6	Sm intestine	
Bulk producing	Methylcellulose	12 – 24	Sm & Lg intestine	Holds water in stool.
	Psyllium	12 – 24		
Lubricant	Mineral oil	6 – 8	Colon	Keeps fecal water from being absorbed.
Surfactant	Docusate	24 – 72	Sm & Lg intestine	Detergent activity, lets water mix into stool to soften.

### Indications

Laxatives are indicated for the short-term treatment of constipation. Certain stimulant, lubricant and saline laxatives are used to evacuate the colon for rectal and bowel examinations. Lubricant laxatives or fecal softeners are useful prophylactically in patients who should not strain during defecation (i.e., following anorectal surgery or myocardial infarction). Psyllium is also useful in patients with irritable bowel syndrome, diverticular disease, spastic colon and hemorrhoids.

### Contraindications

Laxatives are contraindicated in patients who are hypersensitive to any ingredient. Do not use laxatives with patients having nausea, vomiting or other symptoms of appendicitis, acute surgical abdomen, fecal impaction (except mineral oil enema), intestinal obstruction, or undiagnosed abdominal pain.

### Warnings

Excessive laxative use may lead to significant fluid and electrolyte imbalance. Preparations containing sodium should not be used by individuals on a sodium-restricted diet or in the presence of edema, congestive heart failure, or hypertension. Chronic use of laxatives, particularly stimulants, may lead to laxative dependency, which in turn may result in fluid and electrolyte imbalances, steatorrhea, osteomalacia, and vitamin/mineral deficiencies.

**Pregnancy:** Docusate sodium, mineral oil, and senna are in pregnancy category C. Do not use castor oil during pregnancy; its irritant effect may induce premature labor. Mineral oil may decrease absorption of fat-soluble vitamins. Improper use of saline cathartics can lead to dangerous electrolyte imbalance. If needed, limit use to bulk-forming or surfactant laxatives.

**Lactation:** All of the covered laxatives are safe in breastfeeding women except docusate sodium and lactulose. It is not known whether either of these is excreted in breast milk.



**Drug interactions**

Mineral oil: Surfactants may facilitate absorption, thus increasing the toxicity of mineral oil.

Milk or antacids: Concomitant administration of bisacodyl tablets may cause the enteric coating to dissolve, resulting in gastric lining irritation or dyspepsia.

Lipid soluble vitamins (vitamins A, D, E, and K): Absorption may decrease during prolonged administration with mineral oil.

Tetracycline: Laxatives containing aluminum, calcium, or magnesium impair absorption of tetracycline, due to release of free calcium.

**Patient information**

Attention to proper dietary fiber intake, adequate fluids, and regular exercise reduces the need to use laxatives.

Individuals using laxatives must understand the following information:

1. Do *not* use in the presence of abdominal pain, nausea, or vomiting.
2. Laxative use only a temporary measure: do not use longer than one week. When regularity returns, discontinue use. Prolonged or excessive use may result in dependence or electrolyte imbalance.
3. Notify physician if unrelieved constipation, rectal bleeding, or symptoms of electrolyte imbalance occurs (muscle cramps or pain, weakness, dizziness).
4. Pink-red, red-violet, or red-brown discoloration of alkaline urine may occur with cascara sagrada, phenolphthalein, or senna.
5. Yellow-brown discoloration of acid urine may occur with cascara sagrada or senna.
6. Refrigerate magnesium citrate solutions to retain potency and palatability.
7. Take with a full glass of water or juice.
8. Administer mineral oil on an empty stomach.
9. Swallow bisacodyl tablets whole; do not take within one hour of taking antacids or drinking milk.

**417. Antidiarrheals**

Diarrhea is not the most pleasant subject in the world. It's something that we as medics have to deal with though. In the last lesson, we saw that most of the laxatives worked by either complimenting peristalsis or retaining water in the bowel. The antidiarrheals do just the opposite. They either decrease motility or remove excess water from the bowel. The antidiarrheals that we will discuss are diphenoxylate with atropine, and kaolin/pectin. These are probably the most common antidiarrheals that we will encounter. Loperamide and diphenoxylate will be covered together, as they both decrease motility. Kaolin/pectin, the adsorbent, will be covered separately.

**Loperamide and diphenoxylate**

Both of these drugs work directly on the muscles of the intestinal tract. They treat diarrhea by slowing peristalsis. This action prolongs transit time, reduces fecal volume, increases fecal viscosity and density, and diminishes the loss of fluid and electrolytes.

Diphenoxylate is structurally related to meperidine. There is a possibility of abuse when using diphenoxylate. Atropine is added to diphenoxylate in subtherapeutic levels to discourage deliberate over-dosage. If too much is taken, the atropine will cause a severe dry mouth and throat, dry, hot, and flushed skin, and a general excitement (not a very comfortable feeling). The amount of atropine is too small to interfere with the constipating effect of diphenoxylate, except when taken in very large doses.



### Indications

Both of these drugs are indicated in the control and management of acute diarrhea. Loperamide is also indicated for chronic diarrhea.

<i>Antidiarrheals</i>		
Drug	Dosage	Dosage forms
Diphenoxylate	5 mg 4 times daily	2.5 mg tabs and 2.5 mg/5ml
Loperamide	A: 4 mg followed by 2 mg after each unformed stool. Do not exceed 16 mg/day. C: Use acute dosing until diarrhea is controlled, then individualize to 4–8 mg/day.	2 mg tabs 1 mg/5 ml and 1 mg/ml liquid

### Contraindications

Diphenoxylate is contraindicated in children under two years old due to a greater variability of response. Both drugs are contraindicated in patients who have a sensitivity to their components.

### Warnings

These antidiarrheal drugs may prolong or aggravate diarrhea associated with organisms that penetrate the intestinal mucosa. In some patients with ulcerative colitis, these drugs may induce toxic megacolon, a condition of extreme dilation of a portion of the colon.

Pregnancy: Diphenoxylate is in category C, loperamide is in B.

Lactation: Do not use diphenoxylate with lactating mothers. It isn't known if diphenoxylate is excreted in breast milk, but the atropine is excreted. Safety for use of loperamide by nursing mothers has not been established.

### Drug interactions

There are no listed drug interactions for loperamide. Diphenoxylate may cause a hypertensive crisis if used with monoamine oxidase inhibitors. It may also potentiate the depressant action of barbiturates, tranquilizers, and alcohol.

### Patient information

- May cause drowsiness or dizziness; patients need to be cautious while driving or performing other tasks requiring alertness, coordination, or physical dexterity.
- May cause dry mouth. Drink plenty of clear fluids to help prevent dehydration, which may accompany diarrhea.
- Notify physician if diarrhea does not stop after a few days or if abdominal pain or distention or fever occurs. Do *not* exceed prescribed dosage.

### Kaolin/pectin

Kaolin and pectin are used as antidiarrhea agents because of their adsorbent properties. They adsorb the bacteria, toxins, and excess fluid from intestine. Since kaolin and pectin are not absorbed, the toxins are passed out with the fecal matter.

### Indications

Kaolin and pectin are indicated for the symptomatic relief of mild to moderate diarrhea. These medications come in many various strengths. The usual adult dosage is 60–120 ml of regular strength suspension or 45–90 ml of concentrated suspension.

### Contraindications, warnings, and drug interactions

There are no contraindications, warnings, or drug interactions listed for kaolin and pectin.

### Patient information

Patients should get plenty of rest, fluids, and an appropriate diet. Shake the suspension well before taking.

## Self-Test Questions

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

### 414. Nutrition

1. What is malnutrition?
2. Define protective foods.
3. What type of food is required for the growth and repair of tissues?
4. What group of foods contains fats and carbohydrates?
5. What are the most common causes of temporary digestive disturbances?

### 415. Reflux and antiulcer agents

1. What are the indications for magnesium hydroxide?
2. How do antacids interact with other drugs?
3. What is one of the fastest growing and most popular drugs for treating common indigestion?
4. How do PPIs work?
5. What is metoclopramide's mechanism of action?
6. For what disorder is sucralfate indicated?

**416. Laxatives**

1. What are the four types of laxatives and how do they work?
2. What are the contraindications for laxatives?

**417. Antidiarrheals**

1. In general, how do antidiarrheals work?
2. Where does loperamide act?
3. How does kaolin and pectin work?

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### Answers to Self-Test Questions

**411**

1. The mouth, pharynx, esophagus, the stomach, small intestine, and large intestine.
2. To dissolve the food and to facilitate the processes of mastication (chewing) and deglutition (swallowing).
3. The parotid, submandibular, and sublingual glands.
4. The muscular tissue that forms the back of the roof of the oral cavity.
5. Chyme.
6. Softens the connective tissues in meat, kills bacteria and thus destroys many potential disease-producing agents, and activates at least one of the stomach enzymes, which are chemicals that begin the digestion of food.
7. Small intestine.
8. Amylase or ptyalin.
9. The means by which the digested food reaches the bloodstream.
10. Ascending colon, transverse colon, descending colon, and sigmoid colon.

**412**

1. The liver.
2. The gallbladder.
3. The pancreas.
4. A serous membrane that covers the surface of most of the abdominal organs to form the visceral serosa and lines the abdominal wall to form the parietal layer.
5. A double-layered peritoneal structure shaped somewhat like a fan, with the handle portion attached to the back wall. The expanded long edge is attached to the small intestine.
6. It hangs downward from the lower border of the stomach.

**413**

1. Stomatitis.
2. A spirochete.
3. An inflammation involving the tooth socket.
4. A backflow of digestive juices from the stomach into the esophagus.

5. When stomach fluid refluxes into the esophagus more frequently than normal, causing more problems than simple heartburn.
6. People between the ages of 30 and 45.
7. Enteritis.
8. Nausea, vomiting, and diarrhea as well as acute abdominal pain or colic.
9. It may result from infection of the appendix mucosa by organisms causing enteritis or from obstruction by accumulated, hardened fecal material or occasionally by pinworms.
10. Bacillary dysentery.
11. A chronic inflammatory disease with ulceration of the intestinal wall frequently causing bleeding.
12. Flaccid constipation.
13. By administration of infected blood, plasma or blood products, or by improperly sterilized needles and syringes (as used by drug addicts).
14. It is a chronic disease in which the active liver cells are replaced by inactive scar tissue (connective tissue).
15. Cholelithiasis.
16. Inflammation of the peritoneum.
17. Ascites.
18. Obstruction of the portal flow.

**414**

1. When one or more of the fundamental food materials necessary for the life and growth of body cells is not supplied.
2. Foods that are especially high in vitamins and mineral salts.
3. Protein foods.
4. Energy foods.
5. Overeating, bacterial contamination, and virus infections.

**415**

1. It treats upset stomach associated with hyperacidity.
2. They interfere by altering disintegration, dissolution, or solubility and changing gastric emptying time.
3. Histamine 2 blockers.
4. They suppress gastric acid secretion by specific inhibition of the enzymes at the surface of the gastric parietal cell.
5. Metoclopramide works by either causing the release of more acetylcholine or sensitizing receptors on the smooth muscle of the digestive system.
6. Short-term treatment of active duodenal ulcers.

**416**

1. Saline, by attracting and retaining water in the intestine; irritant/stimulant, by direct action on the intestinal mucosa to cause contractions; bulk producing, by holding water in the stool; lubricant, keeps fecal water from being absorbed; surfactant, detergent activity lets water mix into stool.
2. Hypersensitivity, nausea and vomiting, symptoms of appendicitis, acute surgical abdomen, fecal impaction, or intestinal obstruction.

**417**

1. They decrease motility or remove excess water from the bowel.
2. Directly on the muscle of the intestinal tract to slow peristalsis.
3. They adsorb water and toxins from the bowel.

**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.

29. (411) What sphincter valve connects the stomach to the small intestine?
  - a. Upper esophageal.
  - b. Lower esophageal.
  - c. Pyloric.
  - d. Duodenal.
30. (411) Where does most of the digestive and absorptive processes occur?
  - a. Stomach.
  - b. Small intestine.
  - c. Large intestine.
  - d. Esophagus.
31. (411) Approximately what percentage of an adult's body is composed of water?
  - a. 33.
  - b. 44.
  - c. 55.
  - d. 66.
32. (411) What substance is mixed with chyme in the duodenum during the digestive process?
  - a. Bile.
  - b. Lipase.
  - c. Amylase.
  - d. Tripsin.
33. (412) Heparin is manufactured in the
  - a. gall bladder.
  - b. pancreas.
  - c. stomach.
  - d. liver.
34. (412) In what organ is insulin manufactured?
  - a. Gall bladder.
  - b. Pancreas.
  - c. Stomach.
  - d. Liver.
35. (412) What membrane separates the abdomen into different areas to help support the abdominal organs?
  - a. Colon.
  - b. Pancreas.
  - c. Peritoneum.
  - d. Appendix.
36. (412) Which area of the peritoneum supplies blood and nerves to the intestine?
  - a. Greater omentum.
  - b. Lesser omentum.
  - c. Abdomen.
  - d. Mesentery.



37. (413) What disease is problematic for people who use antibiotic lozenges?
- Stomatitis.
  - Gingivitis.
  - Dental caries.
  - Pyorrhea.
38. (413) What disease is inflammation of the tooth socket?
- Dental caries.
  - Gingivitis.
  - Stomatitis.
  - Pyorrhea.
39. (413) The part of the alimentary canal that relaxes allowing digestive juices to enter the esophagus is the
- lower esophageal sphincter.
  - upper esophageal sphincter.
  - stomach.
  - colon.
40. (413) What disorder refers to an inflammation of the intestinal mucosal lining?
- Diarrhea.
  - Dysentery.
  - Appendicitis.
  - Ulcerative colitis.
41. (413) Which intestinal disorder occurs when the intestinal musculature is overstimulated?
- Piles.
  - Diverticulitis.
  - Flaccid constipation.
  - Spastic constipation.
42. (413) The disorder caused when destructed liver cells curtail portal circulation is
- hepatitis.
  - cirrhosis.
  - pancreatitis.
  - cholecystitis.
43. (413) Peritonitis often follows an infection of what organ?
- Appendix.
  - Gall bladder.
  - Pancreas.
  - Liver.
44. (413) What disorder is presented as an accumulation of fluid in the peritoneal cavity?
- Hepatitis.
  - Appendicitis.
  - Ascites.
  - Gall stones.
45. (414) Which items are considered *protective foods*?
- Carbohydrates.
  - Citrus fruits.
  - Milk.
  - Fats.

46. (414) Which item is considered *energy food*?
- Fat.
  - Protein.
  - Citrus fruit.
  - Milk.
47. (415) The treatment for GERD is for how many weeks?
- 6.
  - 8.
  - 10.
  - 12.
48. (415) At the *final* step in its production, which class of drugs inhibits stomach acid?
- Antacids.
  - GI stimulants.
  - Protective agents.
  - Proton pump inhibitors.
49. (415) What drug does omeprazole interact with, causing an *increase* in the levels of both drugs?
- Clarithromycin.
  - Theophylline.
  - Phenytoin.
  - Warfarin.
50. (415) Which antiulcer drug works locally rather than systemically?
- Proton pump inhibitors.
  - Protective agents.
  - H<sub>2</sub> blockers.
  - Antacids.
51. (416) Psyllium falls into which category of laxative?
- Irritant/stimulant.
  - Bulk producing.
  - Surfactant.
  - Lubricant.
52. (416) What is the mechanism of action for surfactant laxatives?
- Direct action on intestinal mucosa to supplement peristalsis.
  - Keeps fecal water from being absorbed.
  - Attract and retain water in intestine.
  - Lets water mix into stool to soften.
53. (417) Which antidiarrheal is structurally related to meperidine?
- Loperamide.
  - Diphenoxylate.
  - Kaolin.
  - Pectin.
54. (417) Atropine is added to dipheoxylate to
- enhance absorption.
  - decrease side effects.
  - increase therapeutic effects.
  - discourage intentional overdose.

Please read the unit menu for unit 3 and continue →

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## Student Notes

## Unit 3. The Urinary System

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**T**HE urinary system consists of organs that produce urine and eliminate it from the body. The excretion of urine and its elimination from the body are vital functions. since together they constitute one of the most important mechanisms for maintaining homeostasis. This unit will discuss the anatomy and physiology of the urinary system, the conditions associated with this system, and the drugs used to treat those conditions.

### 3-1. Anatomy, Physiology, and Disorders of the Urinary System

This section begins with an introduction to the urinary system. The next lessons discuss the structure and function of the kidneys and ureters.

#### 418. Introduction to the urinary system

The urinary system is also called the excretory system. and one of its main functions is to remove certain waste products from the blood and eliminate them from the body.

The terms *elimination* and *excretion* are often used interchangeably. Excretion is the function that removes useless substances (i.e., the waste products of cell metabolism) from the blood and lymph. This is done by not only filtering the waste products from the blood but also by a type of cellular activity similar to when glands produce secretions. On the other hand, elimination indicates the actual emptying of the hollow organs where these waste products have been temporarily stored. Thus, the kidney is said to excrete, while the urinary bladder eliminates. The main parts of the urinary system shown in figure 3-1 are:

Parts	Function
Two kidneys	These are the glandular organs that are necessary for life. The kidneys, in addition to other things, extract wastes from the blood.
Two ureters	These are tubes that conduct the secretion from the kidneys to the urinary bladder.
The urinary bladder	This is the reservoir that receives the urine brought to it by the two ureters.
The urethra	This is the excretory tube for the bladder. The urine is conducted to the outside of the body and eliminated through the urethra.



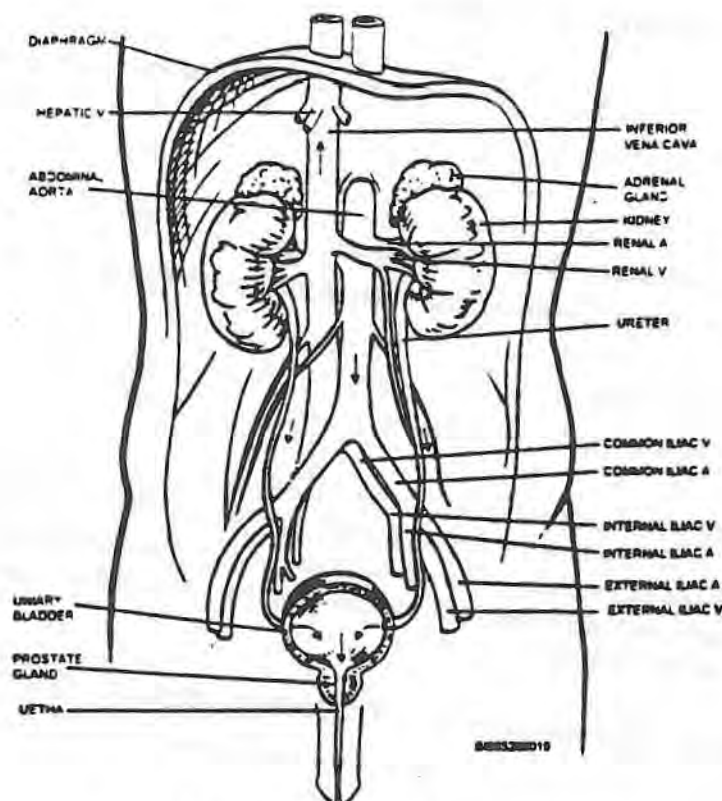


Figure 3-1. The urinary system, with blood vessels.

#### 419. Kidneys

The two kidneys lie against the muscles of the back in the upper abdomen. The lower ribs and the rib (costal) cartilages protect them since they are up under the dome of the diaphragm. Each kidney is enclosed in a membranous capsule made of fibrous connective tissue; it is loosely adherent to the kidney itself. In addition, there is a crescent of fat around the lateral perimeter of the organ. It is called the adipose capsule, and is one of the chief supporting structures of the kidney. The peritoneum lies in front of the kidneys, which means the kidneys and several other structures are not in the peritoneal cavity. This area is known as the *retroperitoneal* space, indicating that it is behind the peritoneum.

##### Structure

The kidney is a somewhat flattened organ about 10 cm (4 inches) long, 5 cm (2 inches) wide, and 2.5 cm (1 inch) thick. There is a notch, called the hilus, on the inner or medial border where the artery, the vein, and the ureter connect with the kidney. The outer or lateral border is convex (curved outward), giving the entire organ a bean-shaped appearance.

The three regions of the kidney are:

1. Renal cortex.
2. Renal medulla.
3. Renal pelvis.

The renal *cortex* is the outer portion of the kidney. The renal *medulla* consists of several cone-shaped structures called *pyramids*. The tip of each pyramid points toward the renal pelvis. The renal *pelvis* is a funnel-shaped basin that forms the upper end of the ureter. Cup-like extensions of the renal pelvis project from the pelvis to surround the tips of the pyramids. These extensions are called *calyces*,

singular *calyx*. The urine collects in the pelvis and then passes down the ureters to the bladder (see fig. 3-2).

The kidney is a glandular organ with most of the tissue being epithelium and just enough connective tissues to serve as a framework. As is the case with most organs, the most fascinating aspect of the kidney is too small to be seen with the naked eye. This basic unit of the kidney, where the kidney's business is actually done, is called a *nephron* (see fig. 3-3). The nephron is primarily a tiny coiled tube with a bulb at one end called the *Bowman's capsule*. This bulb surrounds a cluster of capillaries called the *glomerulus*. A kidney is composed of about a million nephrons. If all these coiled tubes were separated, straightened out, and laid end to end, they would span some 120 kilometers (75 miles)!

A small blood vessel, called the *afferent arteriole*, supplies the glomerulus with blood; another small vessel, called the *efferent arteriole*, carries blood from the glomerulus to the capillaries surrounding the coiled tube of the nephron. Since these capillaries surround the tube, they are called the *peritubular capillaries*.

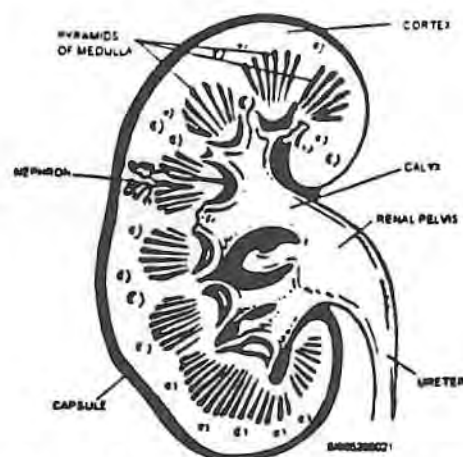


Figure 3-2. Longitudinal section through the kidney showing its internal structure.

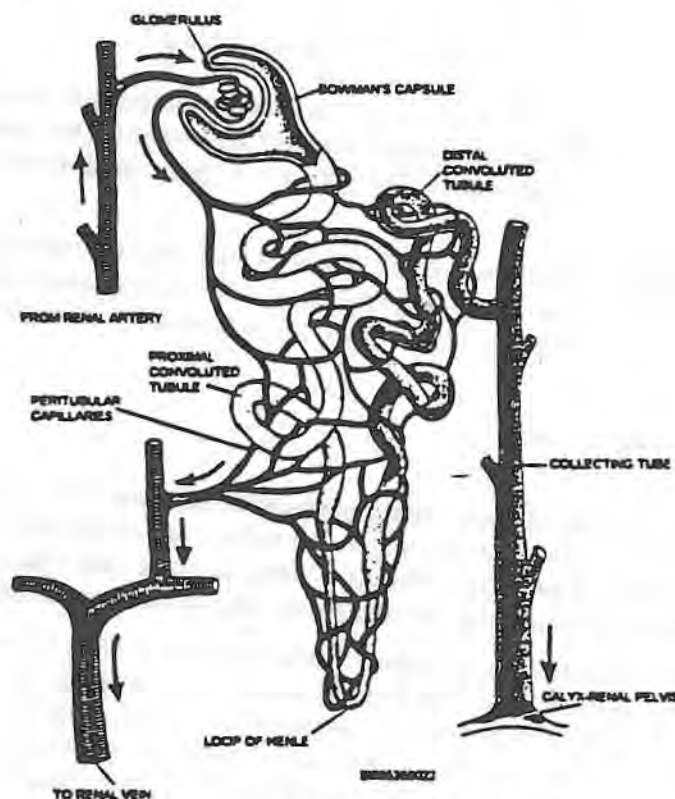


Figure 3-3. A simplified nephron.

The tubular part of the nephron consists of several portions. The coiled portion leading from the Bowman's capsule is called the *proximal convoluted tubule*, and the coiled portion at the other end is called the *distal convoluted tubule*. Between these two coiled portions is the *loop of Henle* (see fig. 3-4).

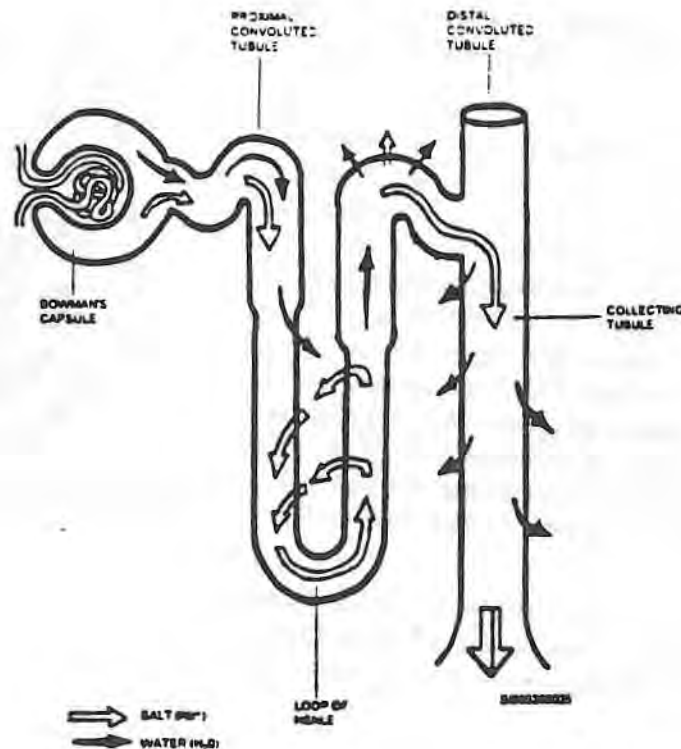


Figure 3-4. The loop of Henle.

The distal convoluted tubule curls back toward the glomerulus between the afferent and efferent arterioles. At the point where the distal tubule contacts the arterioles are specialized glandular cells that form the *juxtaglomerular apparatus*. The function of these specialized cells is discussed later in this lesson.

The glomerulus, Bowman's capsule, and the proximal and distal convoluted tubules of each nephron are within the renal cortex. The loop of Henle extends varying distances into the medulla. The distal end of each tubule empties into a collecting duct, which continues through the medulla toward the renal pelvis.

### Physiology of the renal system

#### *Glomerular filtration*

The process of urine formation begins in the glomerulus and Bowman's capsule. The membranes forming the walls of the glomerular capillaries are sieve-like and permit a free flow of water and soluble materials through them. These capillary walls, as is the case with other capillaries, are impermeable to blood cells and large protein molecules, so these substances remain in the blood.

The afferent arteriole, entering the glomerulus, allows blood to enter more rapidly than it can leave through the efferent arteriole. Thus, the blood's pressure in the glomerulus is about three to four times as high as it is in other body capillaries. Consequently, the fluid in the blood is constantly being "squeezed" into the Bowman's capsule. This process is known as glomerular filtration, and the fluid that enters the Bowman's capsule is called the glomerular filtrate. This filtrate then begins its journey along the tubular system of the nephron. In addition to water and the normal soluble substances in the blood, other substances, such as drugs, may also be filtered and become part of the glomerular filtrate.

#### *Tubular reabsorption and secretion*

The process of filtration that occurs in the renal corpuscle is followed by the processes of reabsorption and secretion during the journey of the filtrate through the tubular system. The filtrate is very much like the blood plasma; since it contains glucose, amino acids, mineral salts, water, and

other needed substances. These are removed by the cells of the proximal convoluted tubule and returned to the tissue fluids and to the blood in the peritubular capillaries by *reabsorption*. As this modified filtrate continues its journey through the loop of Henle and the distal convoluted tubule, more waste materials and often drugs are removed from the blood by an active process called *secretion*. The original dilute filtrate has now become urine, ready for excretion from the body.

### Functions of the kidneys

The following is a list of the kidney's functions:

1. Excretes unwanted substances such as waste products from cell metabolism and excess salts.
2. Helps to maintain water balance.
3. Helps to regulate the acid-base balance.
4. Produces hormones including the hormone renin, which is important in the regulation of blood pressure.

The use of proteins (in the form of amino acids) by the body cells produces, among other things, waste materials that contain the element nitrogen. Chief among these nitrogen-containing products is *urea*. The kidneys provide a specialized mechanism for the elimination of these nitrogenous waste products.

A second function of the kidneys involves the maintenance of water balance. Although the amount of water consumed in a day can vary tremendously, the kidneys can adapt to these variations so that the volume of body water remains remarkably stable from day to day. Water is constantly lost in many ways: from the skin, the respiratory system during exhalation, and the intestinal tract. Normally, the amount of water taken in or produced (intake) is approximately equal to the amount lost (output).

A third function of the kidneys is to aid in regulating the acid-base balance of the body fluids. Acids are constantly being produced by cell metabolism and, in addition certain foods can cause acids or bases to form in the body. Bases in the form of antacids, such as baking soda, may also be ingested. However, if the body is to function normally, a certain critical proportion of acids and bases must be maintained at all times.

The fourth function of the kidneys involves the production of hormones, which is accomplished by the juxtaglomerular apparatus. If the blood pressure is low, the juxtaglomerular apparatus cells release renin into the blood. There it acts as an enzyme which activates a protein that causes blood vessels to constrict and thus raise the blood pressure. When the kidneys do not get enough oxygen, they release another hormone-like substance that acts as an enzyme to produce erythropoietin. Erythropoietin serves to stimulate the development of red bone marrow and thus prevents anemia.

### Dialysis and kidney transplants

#### *Dialysis*

*Dialysis* means the diffusion of dissolved molecules through a semipermeable membrane. These molecules tend to pass from the area of greater concentration to one of less concentration. In patients who have defective kidney function, the accumulation of urea and other nitrogen waste products can be reduced by passing the patient's blood through a dialysis machine. This is where the principle of *molecules leaving the area of greater concentration* operates to remove the excess products from the blood.

Hemodialysis and peritoneal dialysis are the two methods in use. Both are based on the principle of diffusion of dissolved molecules through a semipermeable membrane. In hemodialysis, the membrane is made of cellophane; in peritoneal dialysis, the surface area of the peritoneum acts as the membrane. An amendment to the Social Security Act in 1973 provides federal financial assistance for persons who have chronic renal disease and require dialysis. Recent improvements have made home dialysis possible for many patients. Access to the bloodstream has been made safer and easier, and the size of the equipment has been reduced. Currently, researchers are developing a portable hemodialysis unit



that patients can wear when they are away from home or hospital. With improved methods of peritoneal dialysis, chronic as well as acute renal failure can be treated. Permanent catheters can be implanted into the abdomen, and machines have been developed that can administer the dialyzing fluid automatically.

### ***Kidney transplants***

Many hundreds of kidney transplants have been done successfully during the last several years. Kidneys have so much extra functioning tissue that in the normal individual no problem is posed by losing one kidney. Records show the percentage of transplant successes is greatest when living, closely related donors are used. However, organs from a deceased donor have also proved satisfactory in many cases.

## **420. Ureters**

The two ureters are long, slender, muscular tubes that extend from the kidney basin down to and through the lower part of the urinary bladder.

### **Structure and function**

The ureters' length naturally varies with the size of the individual and so may be anywhere from 25 cm to 32 cm (10 to 12 inches) long. Nearly 2.5 cm (one inch) of the lower part enters the bladder by passing obliquely through the bladder wall. They are entirely extraperitoneal, and that is behind and at the lower part, below the peritoneum.

The walls of the ureters include a lining of epithelial cells, a relatively thick layer of involuntary muscle, and finally, an outer coat of fibrous connective tissue. The lining is continuous with that of the renal pelvis and the bladder. The muscles of the ureters are capable of the same rhythmic contraction (peristalsis) found in the digestive system. At frequent intervals, peristalsis moves the urine along the ureters from the kidneys to the bladder. Because of the oblique direction of the last part of each ureter through the lower bladder wall, compression of the ureters by the full bladder prevents back-flow of urine.

### **Urinary bladder**

The urinary bladder is a temporary reservoir for urine, just as the gallbladder is a storage bag for bile. An empty bladder is located below the parietal peritoneum and behind the pubic joint. A filled bladder pushes the peritoneum upward and may extend well into the abdominal cavity proper.

The bladder wall has many layers and is lined with mucous membrane. When the receptacle is empty, the lining (like the stomach lining) is thrown into folds called rugae. Beneath the mucosa is a layer of connective tissue. Following the connective tissue is a three-layered coat of involuntary muscle tissue that is capable of stretching to a great extent. Finally, there is an incomplete coat of peritoneum that covers only the upper portion of the bladder. When the bladder is empty, the muscular wall becomes thick and the entire organ feels firm. As the organ fills, the muscular wall becomes thinner and the organ may increase from a length of 5 cm (2 inches) up to as much as 12.5 cm (5 inches) or even more. A moderately full bladder holds about 470 ml (one pint) of urine.

Near the outlet of the bladder circular muscle fibers contract to prevent emptying, and form what is known as the *internal sphincter*. In an infant, a center in the lower part of the spinal cord receives impulses from the bladder and sends motor impulses out to the bladder musculature; the organ is emptied in a reflex action. However, with training, the child learns to control this reflex.

### **Urethra**

The *urethra* is the tube that empties the bladder. It extends from the bladder to the outside. The urethra differs in men and women, since in men it is also a part of the reproductive system and it is much longer.

The female urethra is a thin-walled tube about 3.75 cm long. It is behind the pubic joint embedded in the muscle of the front wall of the vagina. The external opening is called the urethral meatus and is located just in front of the vaginal opening or within the lower part of the front wall of the vagina.

The male urethra is about 20 cm long. Early in its course, it passes through the prostate gland, where the two ducts carrying the male sex cells (semen) join it. From here it leads through the *penis* to the outside. The male urethra serves the dual purpose of conveying the semen and draining the bladder.

The process of expelling urine through the urethra is called *urination or micturition*. It is controlled by the action of circular muscles continuous with those in the walls of the bladder and in the urethra. These form valve-like structures that are aided by external muscles in the pelvic floor.

## Urine

In this lesson we learned some of the main constituents of urine. Here they are summarized in a more detailed manner.

Urine is a yellowish liquid that is about 95percent water. A number of solids and gases are dissolved in this water. The amount of these dissolved substances is indicated by the *specific gravity*. If urine were pure water, the specific gravity would be 1.000. However, because of the dissolved materials, the specific gravity of urine normally varies from 1.002 for very dilute urine to 1.040 for very concentrated urine. When the kidneys are diseased, they lose the ability to concentrate urine and the specific gravity will not vary as it does when the kidneys function normally.

Some of the dissolved substances normally found in the urine are the following:

- Nitrogenous waste products—These include urea, uric acid, and creatinine.
- Mineral salts—These include sodium chloride (as in common table salt) and different kinds of sulfates and phosphates. They are excreted in appropriate amounts to keep the blood concentration of the mineral salts constant.
- Yellow pigment—Derived from certain bile compounds.

One of the most important parts of a person's physical evaluation is the urine examination. Among the most significant abnormal substances found in the urine are the following:

<b>Abnormal Substances in Urine</b>	
<b>Substance</b>	<b>Characteristics</b>
Glucose	An indication of a disease known as <i>diabetes mellitus</i> where blood sugar is not oxidized (burned) in the body cells but is excreted in the urine instead. Glucose in the urine is known as <i>glycosuria</i> .
Albumin	Normally retained in the blood. May indicate a kidney disorder such as nephritis. Albumin in the urine is known as <i>albuminuria</i> .
Blood	An important indicator of urinary system disease including nephritis. Blood in the urine is known as <i>hematuria</i> .
Acetone	Produced when fats are incompletely oxidized. Often seen in diabetes mellitus and in starvation.
Pus cells ( <i>leukocytes</i> )	Evidence of infection. Can be seen by microscopic examination of a centrifuged specimen. Pus in the urine is known as <i>pyuria</i> .
Casts	Molds formed in the microscopic kidney tubes. Usually evidence of disease of the nephrons.

## 421. Disorders associated with the urinary system

This lesson deals with disorders of the kidney, ureters, bladder, and urethra.

### Kidney disorders

Kidney disorders may be acute or chronic. Acute conditions usually arise suddenly and, most frequently, are the result of infection with inflammation of the nephrons. These diseases commonly

run a course of a few weeks followed by complete recovery. Chronic conditions arise slowly and often are progressive with gradual loss of kidney function.

#### ***Acute glomerulonephritis***

*Acute glomerulonephritis* is the most common kidney disease. One to four weeks after a streptococcal infection of the throat, this condition usually occurs in children. Antibodies formed in response to the streptococci attach to the glomerular membrane and injure it. These damaged glomeruli allow protein, especially albumin, to filter into the Bowman's capsule and ultimately appear in the urine (albuminuria). They also allow red blood cells to filter into the urine (hematuria). Usually, the patient recovers without permanent kidney damage. Sometimes, in an adult patient, the disease becomes chronic with a gradual decrease in the number of functioning nephrons leading to chronic renal failure.

#### ***Pyelonephritis***

*Pyelonephritis* refers to an inflammation of the kidney pelvis and the tissue of the kidney itself. It may be either acute or chronic. In acute pyelonephritis, the inflammation results from a bacterial infection. Bacteria most commonly reach the kidney by ascending along the lining membrane from an infection in the lower part of the urinary tract. More rarely, bacteria can be carried to the kidney by the blood. Acute pyelonephritis is often seen in persons with partial obstruction of urine flow with stagnation (urinary stasis). This may occur during pregnancy in the female or it may be due to an enlarged prostate in the male. Usually, the disease responds to the administration of antibiotics, fluid replacement, rest, and fever control. Chronic pyelonephritis is a more serious disease and is frequently seen in patients with urinary tract blockage. It may be caused by persistent or repeated bacterial infections. There is progressive of kidney tissue damage eventually leading to chronic renal failure.

#### ***Hydronephrosis***

*Hydronephrosis* refers to the distension of the renal pelvis and calyces caused by an accumulation of fluid due to an obstruction of normal urine flow. The obstruction may occur at any level in the urinary tract. The most common causes of obstruction are (in addition to pregnancy or an enlarged prostate):

- Kidney stone formed in the pelvis and dropped into the ureter.
- Tumor pressing on a ureter.
- Scars caused by inflammation.

There can be complete recovery if the obstruction is removed within a few weeks before the kidney is damaged. If the obstruction is not removed, the kidney will be permanently damaged.

#### ***Acute renal failure***

*Acute renal failure* may result from a medical or surgical emergency or from toxins that damage the tubules. This condition is characterized by a sudden, serious decrease in kidney function, which may be fatal without immediate medical treatment.

#### ***Chronic renal failure***

*Chronic renal failure* results from a gradual loss of nephrons. As more and more nephrons are destroyed, the kidneys gradually lose the ability to perform their normal functions. As the disease progresses, nitrogen waste products accumulate to high levels; this condition is known as *uremia*.



A few of the characteristic signs and symptoms of chronic renal failure are in the following table.

<i>Symptoms of Renal Failure</i>	
Sign or Symptom	Characteristics
Dehydration	Excessive loss of body fluid may occur early in renal failure when the kidneys cannot concentrate the urine and large amounts of water are eliminated.
Edema	When the kidneys cannot eliminate water in adequate amounts, accumulation of fluid in tissue spaces may occur late in chronic renal disease
Hypertension	May occur as the result of fluid overload and the increased production of renin.
Anemia	Occurs when the kidneys cannot produce the hormone to activate red bone marrow cell production.
Increased amounts of nitrogen waste products in the blood	If these levels are very high, urea can be changed into ammonia in the stomach and intestine and cause ulcerations and bleeding.

Even without kidney disease, the kidneys lose some of their ability to concentrate urine because of the aging process. More water is needed to excrete the normal amount of waste products. Older persons find it necessary to drink more water, and they eliminate larger amounts of urine (polyuria) even at night (nocturia).

#### ***Kidney tumors***

Kidney tumors usually grow rather slowly, but occasionally rapidly invading types are found. Blood in the urine and dull pain in the kidney region are warnings that must be immediately heeded. Immediate surgery may be lifesaving. A *polycystic* kidney is one in which many fluid-containing sacs develop in the active tissue and gradually, by pressure, destroy the functioning parts. This disorder runs in families, and until now treatment has not proved very satisfactory, except for the use of dialysis machines or kidney transplants.

#### ***Kidney stones***

Kidney stones, or *calculi*, are made of certain substances, such as uric acid and calcium salts, that precipitate out of the urine instead of remaining in solution. They usually form in the renal pelvis, although the bladder can be another site of formation. The causes of this precipitation of stone-building materials include infection of the urinary tract and stagnation of the urine. These stones may vary in size from tiny grains resembling bits of gravel up to large masses that fill the kidney pelvis and extend into the calyces. These are described as *staghorn calculi*. There is no way of dissolving these stones, since substances that would be able to do so also would destroy the kidney tissue. Sometimes, instruments can be used to crush smaller stones allowing them to be expelled with the urine. More often surgical removal is required.

#### ***Disorders of the ureters***

Ureter structure abnormalities include double portions at the kidney pelvis and constricted or abnormally narrow parts, called *strictures*. Narrowing of the ureter may also be caused by abnormal pressures from tumors or other masses outside the tube. Ureter obstruction can be caused by stones from the kidneys or a kinked tube from a dropped kidney, a condition known as *ptosis*.

The passage of a small stone along the ureter causes one of the most excruciating pains known. This intense pain is called renal colic and usually requires morphine or an equally powerful drug for relief. The first "barber surgeons," operating without benefit of anesthesia, were permitted by their patients to cut through the skin and the muscles of the back to remove stones from the ureters. "Cutting for stone" in this way was relatively successful, in spite of lack of sterile technique, because of the approach through the back and the avoidance of the peritoneal cavity, with the possibility of deadly peritonitis. Modern surgery for a kidney stone, including the use of special instruments threaded through the urinary tract from the outside, may cause temporary disability and a short convalescence.



### Disorders involving the bladder

A full (distended) bladder lies in an unprotected position in the lower abdomen, and a blow may rupture it, necessitating immediate surgical repair. Infection and tumors may involve the bladder; common symptom is blood in the bladder. Inflammation of the bladder is called *cystitis* and is 10 times as frequent in women as in men. This may be due, at least in part, to the very short urethra in the female (compared with that of the male). Usually, bacteria (e.g., colon bacilli) ascend from the outside through the urethra into the bladder. Pain, urgency, and frequency are common symptoms.

Obstruction, by an enlarged prostate gland or from a pregnancy, may lead to stagnation and cystitis. Reduction of the general resistance to infection, as in diabetes, may lead to cystitis. The danger is that the infection may ascend to other parts of the urinary tract.

Another disorder involving the bladder is overactive bladder. Overactive bladder is a widespread medical condition characterized by the following symptoms:

- Urgency (sudden, strong desire to urinate).
- Frequency (frequently urinating more than eight times in 24 hours).
- Urge incontinence (sudden and total involuntary loss of urine).

Many men and women develop this condition as they grow older, but overactive bladder is not a normal part of aging, and it does not have to be endured. Overactive bladder can be effectively treated, just like other chronic medical conditions such as hypertension or adult-onset diabetes.

There are different kinds of bladder control problems. Each has different cause and exhibits different symptoms. In order to get the proper medical treatment, it is important that a healthcare provider identify which type a person has. Most bladder control problems happen when muscles are either too weak or too active. Problems also may occur when nerve signals don't work properly.

### Disorders of the urethra

Congenital *anomalies* (defects) present at birth involve the urethra as well as other parts of the urinary tract. The opening of the urethra to the outside may be too small, or the urethra itself narrowed. Occasionally, it happens that there is an abnormal valve-like structure located at the point where the urethra enters the bladder. These valve-like folds of tissue can cause a backpressure of the urine with serious consequences if they are not removed surgically. A condition in the male where the urethra opens on the under surface of the penis instead of at the end is called *hypospadias*.

Inflammation of the mucous membrane and the glands of the urethra is called *Urethritis*. This condition is more common in the male than in the female and is often due to gonorrhea, although many other bacteria may be responsible for the infection.

"Straddle" injuries to the urethra are common in men. This type of injury occurs when, for example, a man walking along a raised beam slips and lands with the beam between his legs. Such an accident may catch the urethra between the hard surfaces of the beam and the pubic arch, and rupture the urethra. A ruptured urethra is fairly common in accidents where the bones of the pelvis are fractured.

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## Self-Test Questions

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

### 418. Introduction to the urinary system

1. What is another name for the urinary system?
2. What are the main parts of the urinary system?

**419. Kidneys**

1. What is the "adipose capsule?"
2. What are the three regions of the kidney?
3. What is a nephron?
4. What blood vessel supplies the kidney's glomerulus with blood?
5. List the functions of the kidneys.
6. Define dialysis.

**420. Ureters**

1. How is urine moved along the ureter from the kidneys to the bladder?
2. Where is the urine bladder located when it is empty? Full?
3. What is the "urethra?"
4. What percentage of urine is water?
5. What is hematuria?

**421. Disorders associated with the urinary system**

1. What is the most common disease of the kidneys?
2. What causes acute pyelonephritis?

3. What is "hydronephrosis?"
4. What causes chronic renal failure?
5. What are the characteristic signs and symptoms of chronic renal failure?
6. Describe a polycystic kidney.
7. What is ptosis?
8. What is renal colic?
9. What term is used to describe inflammation of the bladder?
10. What two disorders can be caused by bladder obstruction?
11. The condition in males in which the urethra opens on the under surface of the penis instead of at the end is called what?
12. Is the condition urethritis more common in males or females?

### **3-2. Drugs Used to Treat Conditions Associated with the Urinary System**

Now that you have learned about all the things that can go wrong within the urinary system, let's look at some drugs used to treat those disorders. This section will cover urinary antispasmodics, urinary tract analgesics, and urinary alkalinizers.

#### **422. Urinary antispasmodics**

Some of the antispasmodics that are indicated for GI problems also work in the urinary tract. This lesson covers two agents that are specifically recommended for urologic conditions. We'll look at flavoxate and oxybutinin. Once again, these two drugs are different enough that they'll be covered separately.

**Flavoxate**

- Counteracts smooth muscle spasms of the urinary tract.
- Relaxes smooth muscle by cholinergic blockade.
- Exerts a direct effect on the muscle.
- Contains anticholinergic, local anesthetic, and analgesic properties.

**Indications**

Flavoxate is indicated for the symptomatic relief of dysuria, urgency, nocturia, frequency, and incontinence that can be found in cystitis, prostatitis, urethritis, and urethrocystitis. Dosing for flavoxate is 100 or 200 mg, 3 or 4 times daily. The dose is reduced when symptoms improve.

Flavoxate is available in 100 mg and 200 mg tablets.

**Contraindications**

Flavoxate is contraindicated when there is any urinary obstruction, intestinal obstruction, or GI hemorrhaging.

**Warnings**

Since flavoxate has some anticholinergic effects, it may disrupt the drainage mechanism of the eye. Therefore, do not use flavoxate in patients suspected of having glaucoma.

Pregnancy: There are no well-controlled studies in pregnant women. Flavoxate should be used during pregnancy only when clearly needed.

Lactation: It is not known whether this drug is excreted in breast milk. Use caution when flavoxate is administered to a nursing woman.

Children: Safety and efficacy in children < 12 years of age have not been established.

**Drug interactions**

There are no listed drug interactions for flavoxate.

**Patient information**

- May cause drowsiness or blurred vision; observe caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity.
- May cause dry mouth.

**Oxybutinin**

- Exerts direct antispasmodic effect on smooth muscle.
- Inhibits the action of acetylcholine on smooth muscle.
- Exhibits anticholinergic activity.
- Increases vesical capacity in patients characterized by involuntary bladder contraction.
- Diminishes frequency of uninhibited contractions of the detrusor muscle and delays initial desire to void.
- Decreases urgency and the frequency of both incontinent episodes and voluntary urination.

**Indications**

Oxybutinin is indicated for the relief of symptoms of bladder instability associated with voiding in patients with urinary urgency, frequency, leakage, urge incontinence, and dysuria. Dosing for oxybutinin is 5 mg 2–3 times daily. Oxybutinin is available in 5 mg tablets and 5 mg/5 ml liquid.



**Contraindications**

Oxybutinin is contraindicated:

- Whenever there is a GI or urinary tract obstruction.
- In patients with glaucoma or an unstable coronary condition.

**Warnings**

Oxybutinin decreases sweating. This reaction is severe enough to cause heat prostration in high temperature environments.

**Pregnancy:** Oxybutinin is in category B. Safety for use during pregnancy has not been established. Use only when clearly needed and when the potential benefits outweigh the potential hazards to the fetus.

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

**Drug interactions**

Oxybutinin may cause a slight delay in the absorption of oral acetaminophen. This decreases the effectiveness of acetaminophen.

Oxybutinin increases the levels and actions of atenolol and digoxin. It also increases the concentration of nitrofurantoin, which increases adverse side effects.

**Patient information**

- Drowsiness, dizziness or blurred vision, alcohol or sedatives may enhance drowsiness. Observe caution while driving or performing other tasks requiring alertness, coordination or physical dexterity.
- Dry mouth.

**423. Urinary tract analgesics**

Infections can hurt! The urinary tract is a sensitive area and sometimes when a patient has an infection, the pain needs to be treated before the antibiotic takes effect. Enter urinary analgesics. The only drug in this class that we'll discuss is phenazopyridine (try saying that one three times fast).

After absorption, phenazopyridine is excreted in the urine where it exerts a topical analgesic effect on urinary tract mucosa; therefore, it is used only for relief of symptoms. Its mechanism of action is unknown. Phenazopyridine is compatible with antibacterial therapy and can help relieve pain and discomfort before antibacterial therapy controls the infection.

**Indications**

Phenazopyridine is indicated for the symptomatic relief of pain, burning, urgency, frequency, and other discomforts arising from irritation of the lower urinary tract mucosa caused by infection, trauma, surgery, endoscopic procedures, or passage of sounds or catheters. Its analgesic action may reduce or eliminate the need for systemic analgesics or narcotics. The dosing for phenazopyridine is: Adults: 200 mg 3 times/day after meals. Do not administer for > 2 days when used concomitantly with an antibacterial agent for the treatment of urinary tract infection (UTI).

Children (six to 12 years): 12 mg/kg/day divided into three oral doses for two days.

Phenazopyridine is available in 100 and 200 mg tablets.

**Contraindications**

Sensitivity to drug and kidney problems is the only contraindication for phenazopyridine.

**Warnings**

**Pregnancy:** Phenazopyridine is in category B. There are no adequate and well-controlled studies in pregnant women. Use during pregnancy only if clearly needed.

**Lactation:** No information is available on the appearance of this drug or its metabolites in breast milk.

**Drug interactions**

There are no drug interactions; however, since phenazopyridine is a dye, it may interfere with some urinalysis testing.

**Patient information**

- May cause GI upset; take after meals.
- May cause a reddish-orange discoloration of the urine and may stain fabric. This is not abnormal and represents no cause for alarm. Staining of contact lenses has also occurred.
- Do not use long-term to treat undiagnosed urinary tract pain. This product treats painful symptoms but not the source or cause of the pain.

**424. Urinary alkalinizers**

This lesson covers little-known information or information that is not covered in your training. We're going to learn about potassium citrate. I know, you're asking yourself, "Why are we reading about potassium and citric acid when we're discussing the urinary tract?" That's a good question. Potassium citrate is absorbed and metabolized to potassium bicarbonate. This is used to buffer gastric acidity and as a systemic alkalinizer. There are times when it is necessary to keep the urine more basic. It's not used often, but you need to know why you have the potassium and citric acid combinations (Bi-citra and Polycitra) in stock.

**Indications**

This drug is used in conditions where long-term maintenance of alkaline urine is desirable. It is used in the treatment of patients with uric acid and cystine calculi of the urinary tract and in conjunction with uricosurics in gout therapy to prevent uric acid nephropathy (damage to the kidneys from too much uric acid). The urinary alkalinizers come in either crystals for reconstitution, solution, or 5 mEq and 10 mEq tablets. The exact type and dosing is determined by the severity of the condition. Dosing for severe hypocitruria is 60 mEq/day in three or four doses. For mild to moderate hypocitruria: 30 mEq/day (10 mEq three times/day with meals).

Do not exceed 100 mEq/day.

**Contraindications**

This drug is contraindicated in patients with kidney problems or untreated Addison's disease.

**Warnings**

**Pregnancy:** Potassium levels are important when using this drug in pregnant women. There should be no problems as long as the dosage given does not cause hyperkalemia.

**Lactation:** Exercise caution when used by a nursing mother.

**Drug interactions**

Urinary alkalinizers may increase the excretion and decrease the serum level of the following drugs, possibly decreasing their pharmacologic effects:

- Lithium.
- Methotrexate.
- Salicylates.
- Tetracyclines.

Conversely, alkalinizers may decrease the excretion and increase serum levels, increasing the pharmacologic effects of these drugs:

- Anorexiant.
- Quinidine.
- Sympathomimetics.

**Patient information**

- Dilute with water: follow with additional water, if desired.
- Take after meals.
- Notify physician if diarrhea, nausea, stomach pains, vomiting or convulsions occur.

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**Self-Test Questions**

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

**422. Urinary antispasmodics**

1. For what disorder is flavoxate indicated?
2. Which, if any antispasmodic, exerts a direct antispasmodic effect on urinary smooth muscle?
3. What condition is oxybutynin used to treat?
4. What possible drug interaction can occur between oxybutynin and nitrofurantoin?

**423. Urinary tract analgesics**

1. How is phenazopyridine used with antibacterial therapy?
2. Phenazopyridine is used to treat what conditions?

3. What information should be given to patients who are taking phenazopyridine and also wear contact lenses?

#### 424. Urinary alkalinizers

1. How is potassium used in the urinary system?
2. How does gout therapy effect the urinary tract?
3. What caution must be observed when treating pregnant patients with urinary alkalinizers?

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### Answers to Self-Test Questions

#### 418

1. The excretory system.
2. The two kidneys, two ureters, the urinary bladder, and the urethra.

#### 419

1. A crescent of fat around the lateral perimeter of the kidney.
2. The renal cortex, the renal medulla, and the renal pelvis.
3. A nephron is the basic unit of the kidney, a tiny coiled tube with a bulb at one end.
4. Afferent arteriole.
5. Excretion of unwanted substances such as waste products from cell metabolism and excess salts; aid in the maintenance of water balance; aid in regulating the acid-base balance; production of hormones, including the hormone renin, which is important in the regulation of blood pressure.
6. The diffusion of dissolved molecules through a semipermeable membrane.

#### 420

1. By peristalsis at frequent intervals.
2. Empty—below the parietal peritoneum and behind the pubic joint; full—it pushes the peritoneum upward and may extend well into the abdominal cavity proper.
3. The tube that extends from the bladder to the outside, and is the means by which the bladder is emptied.
4. 95 percent.
5. Blood in the urine.

#### 421

1. Acute glomerulonephritis.
2. A bacterial infection.
3. The distension of the renal pelvis and calyces caused by an accumulation of fluid due to an obstruction to normal urine flow. The obstruction may occur at any level in the urinary tract.
4. A gradual loss of nephrons.
5. Dehydration, edema, hypertension, anemia, and an increased amount of nitrogen waste products in the blood.

6. A kidney in which many fluid-containing sacs develop in the active tissue and gradually, by pressure, destroy the functioning parts.
7. A kinking of the ureter due to a dropping of the kidney.
8. Intense pain caused by the passage of a small stone along the ureter.
9. Cystitis.
10. Stagnation and cystitis.
11. Hypospadias.
12. Males.

**422**

1. Symptomatic relief of disuria, urgency, nocturia, frequency, and incontinence in cystitis, prostatitis, urethritis, and urethrocystitis.
2. Oxybutinin is the only one of the two discussed antispasmodics which exhibits direct antispasmodic effects.
3. Symptoms of bladder instability associated with urgency, frequency, and incontinence.
4. It increases nitrofurantoin levels, increasing side effects.

**423**

1. It is used to relieve symptoms until the antibacterial therapy controls the infection.
2. Symptoms only, pain and burning and other discomforts from urinary tract irritation.
3. Contact lenses may be discolored.

**424**

1. It buffers the pH of the urinary tract.
2. Uricosuric agents remove uric acid from the body and excrete them through the urinary system. Too much uric acid may damage the kidneys.
4. Pregnant patients must be monitored for hyperkalemia.



## 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.**

55. (418) What tube conducts secretions from the kidneys to the urinary bladder?
- a. Urethra.
  - b. Ureter.
  - c. Excretory vein.
  - d. Nephron.
56. (418) What is the name of the excretory tube for the bladder?
- a. Urethra.
  - b. Ureter.
  - c. Excretory vein.
  - d. Nephron.
57. (419) What is the name of the functional unit of the kidney?
- a. Renal medulla.
  - b. Glomerulus.
  - c. Nephron.
  - d. Hilus.
58. (419) What hormone is released by the kidney to increase blood pressure?
- a. Anti-diuretic hormone.
  - b. Erythropoietin.
  - c. Aldosterone.
  - d. Renin.
59. (420) What causes urine to move through the ureter?
- a. Bladder muscle contractions.
  - b. Kidney muscle contractions.
  - c. Peristalsis.
  - d. Gravity.
60. (420) What percent of urine is water?
- a. 65.
  - b. 75.
  - c. 85.
  - d. 95.
61. (421) What is the most common disease of the kidneys?
- a. Acute glomerulonephritis.
  - b. Chronic renal failure.
  - c. Hydronephrosis.
  - d. Pyelonephritis.

62. (421) Dehydration, edema, hypertension, anemia, and an increased amount of nitrogen waste products in the blood are the characteristic symptoms of what kidney disorder?
- Acute glomerulonephritis.
  - Chronic renal failure.
  - Hydronephrosis.
  - Pyelonephritis.
63. (421) What is renal colic?
- Kinking of the ureter.
  - Blockage of the ureter.
  - Narrowing of the ureter.
  - Passage of a stone through the ureter.
64. (421) What disease occurs when bacteria ascend from the outside through the urethra into the bladder?
- Stagnation.
  - Ptosis.
  - Cystitis.
  - Stricture.
65. (421) A condition in males where the urethra opens on the under surface of the penis instead of at the end is
- cystitis.
  - ptosis.
  - calculi.
  - hypospadias.
66. (422) Which urinary antispasmodic *relaxes* smooth muscle through cholinergic blockade?
- Cyclobenzaprine.
  - Carisoprodol.
  - Oxybutinin.
  - Flavoxate.
67. (422) Which urinary antispasmodic *decreases* sweating and may cause heat prostration?
- Cyclobenzaprine.
  - Carisoprodol.
  - Oxybutinin.
  - Flavoxate.
68. (423) What part of urinary disorders is phenazopyridine used to treat?
- Causes and symptoms.
  - Symptoms only.
  - Bacteria only.
  - Causes only.
69. (423) What information should patients who wear contact lenses be given when taking phenazopyridine?
- Excess internal pressure may cause some discomfort.
  - Excess internal moisture may fog lenses.
  - Lenses may become abnormally dry.
  - Lenses may become stained.

70. (424) Which condition can be prevented in gout patients by using potassium and citric acid?
- a. Uric acid nephropathy.
  - b. Systemic alkalosis.
  - c. Lactic acidosis.
  - d. Cystine calculi.

## Student Notes

## Student Notes



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