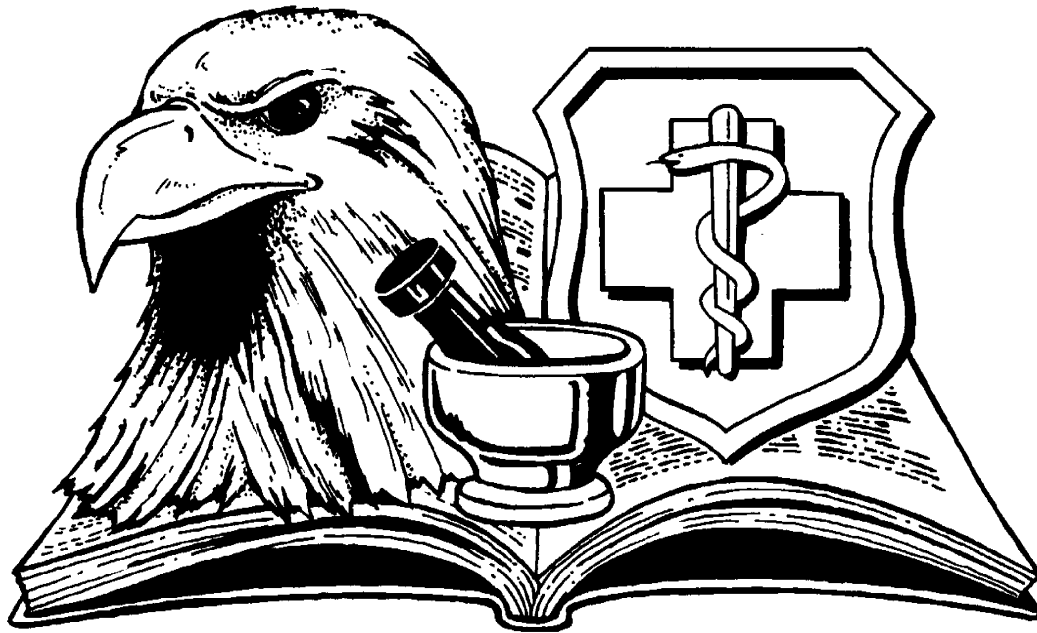


CDC 4P051B

Pharmacy Journeyman

Volume 2. Anatomy, Physiology, and Pharmacology



Air Force Institute for Advanced Distributed Learning

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This volume starts the presentation of the systems of the body. The rest of this course will cover the systems anatomy and physiology followed by conditions affecting that system. We'll then look at the drugs that are used to treat those conditions. I have tried to format the drug section in a way that looks like the reference books that you use every day. The DoD Basic Core Formulary is the document that I used to decide which drugs to discuss.

Unit 1 covers the integumentary system. Structure and functions of skin, hair and nails is followed with a discussion on conditions affecting this area: burns and infections are two examples of what you'll see. We'll then take a look at the drugs that treat these conditions.

Unit 2 discusses the skeletal system. Bone structure and function, divisions of the skeleton, bone landmarks, and joints are also covered. This is followed by two discussions: bone and joint disorders and analgesics.

Unit 3 moves on to the muscular system. Skeletal muscles' characteristics, attachments, movement, and functions are discussed. Muscular disorders are covered, with the main drug class of skeletal muscle relaxants being discussed.

Unit 4 goes into the circulatory system. This is a long unit due to the large amount of information to cover. We have to look at the heart, blood, blood vessels, and the circulation process. Disorders that accompany each of these areas are then discussed. There are then many drugs to look at in the discussion of the circulatory system.

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This volume is valued at 18 hours and 6 points.

Acknowledgment

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

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

NOTE:

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

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Unit 1. The Integumentary System

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THIS unit discusses the skin and its appendages—hair, nails, and skin glands—as an organ system. By studying the skin and its appendages before you proceed to the more traditional organ systems discussed in the next units, you will improve your understanding of how structure is related to function.

The format of the information presented in this unit is one that we will follow throughout this volume. First, we discuss the anatomy and physiology of the organ system; then, conditions associated with the system; and finally, drugs used to treat those conditions associated with the system. Let's begin with the integumentary system (skin).

1–1. Anatomy and Physiology

Another name for skin is *integument*. *Integumentary system* is a term used to denote the skin and its appendages. A variety of adjectives may be used to describe the body's largest, thinnest, and one of its most important organs—vital, diverse, complex, extensive—the list can go on and on. This section focuses on that complex organ—the skin—its functions, structure, appendages, and observation.

200. Skin structure

The thin, relatively flat, organ we call the skin is classified as a membrane, specifically, the cutaneous membrane. The skin's two main layers are made up of an outer, thinner layer called the *epidermis*; and an inner, thicker layer called the *dermis*. Figure 1–1 is a microscopic view of a longitudinal section of the skin. See if you can find the epidermis and dermis in this illustration. The area where the cells of the epidermis meet the connective tissue cells of the dermis is known as the *dermal-epidermal junction*. A loose *subcutaneous layer*, rich in fat and areolar tissue, lies beneath the dermis. Sometimes, it is called the *hypodermis* or *superficial fascia*. The hypodermis' fat content varies with the state of nutrition of the person. In obese individuals, certain areas may exceed 10 cm in thickness. The density and arrangement of fat cells and collagen fibers in this area determine the relative mobility of the skin.

Epidermis

The skin's epidermis is composed of stratified squamous epithelium. The “thin skin,” which covers most of the body surface, has a total depth of 1 to 3 mm. The outer dermis is much thinner than most of us think—less than 0.17 mm thick (1/200 inch) in most areas. This is true in most areas, except for the soles of the feet and the palms of the hands, which are chronically exposed to pressure and friction. Here this “thick skin” has a total thickness of 4 to 5 mm, and is increasingly thicker (1 to 1.3 mm) than the thin skin that covers the majority of the body.

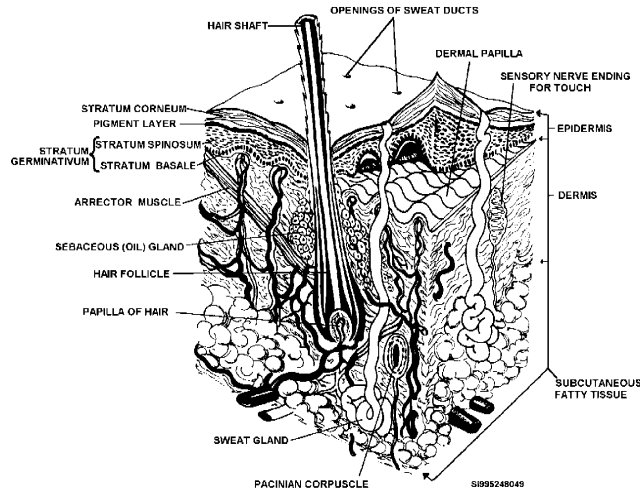


Figure 1-1. Microscopic view of the skin in longitudinal section.

Cell types

Three primary types of cells make up the epidermis:

1. Keratinocytes.
2. Melanocytes.
3. Langerhans' cells.

Of these three cell types, the keratinocytes, arranged in distinct strata (layers), are by far the most important. They constitute over 90 percent of the epidermal cells, and form the principal structural element of the outer skin.

Melanocytes serve to filter ultra-violet light and also contribute color to the skin. Even though they make up over five percent of the epidermal cells,

they may be completely absent from the skin in certain non-lethal conditions.

Langerhans' cells are believed to play a limited role in immunological reactions that affect the skin. They may also serve as a defense mechanism for the body.

Cell layers

Even though the subcutaneous layer, or hypodermis, is not part of the skin itself, it carries the major blood vessels and nerves to the skin above. Due to its rich blood supply and loose spongy texture, it is an ideal site for the rapid and relatively pain-free absorption of injected material. Liquid medicines like insulin are often administered by subcutaneous injection into this spongy and porous layer beneath the skin.

There are five divisions of the epidermis. Let's begin by discussing the *stratum corneum*.

Stratum corneum (horny layer)

This is the most superficial layer of the epidermis. The stratum corneum is made up of very thin squamous (flat) cells that are dead at the skin's surface. They are continually being shed and replaced. *Keratin*, a water-repellent protein, replaces cytoplasm in these cells. Furthermore, these cell membranes become thick and chemically resistant. *Desmosomes*, which are specialized junctions that hold adjacent keratinocytes together, strengthen this layer even more and permit it to withstand considerable wear and tear. The term *keratinization* is used to describe the process by which cells in this layer are formed from cells in deeper layers of the epidermis, and then filled with keratin and move to the surface. *Barrier area* is a term used to describe the stratum corneum, because it functions as a barrier to water loss and many environmental threats ranging from microorganisms and harmful chemicals to physical trauma. The effectiveness of the skin as a protectant is greatly reduced when this barrier layer becomes damaged, allowing most contaminants to easily pass through the lower layers of the cellular epidermis. Some skin diseases cause the stratum corneum layer of the epidermis to thicken far beyond its normal limits. This condition is called *hyperkeratosis*. The skin becomes thick, dry, and scaly, and is inelastic and subject to painful fissures.

Stratum lucidum (Latin *lucidus*, "clear")

This layer contains keratinocytes that are closely packed and clear. Ordinarily, the nuclei are absent, and the cell outlines are indistinct. These cells are filled with *eleidin*, a soft gel-like substance that is eventually transformed to keratin. Eleidin is rich in protein-bound lipids and serves as a barrier to

water penetration or loss. Thin skin does not have this layer, but it is quite evident in sections of thick skin from the soles of the feet or palms of the hands.

Stratum granulosum (granular cell layer)

Keratinization begins in this layer. Cells in this layer are arranged in a sheet, two to four layers deep, and filled with heavily staining granules called *keratohyalin*. Keratohyalin is necessary for keratin formation. In the stratum granulosum layer, the cells have started to degenerate. As a result, the cytoplasm contains high levels of lysosomal enzymes, and the nuclei are missing or degenerated. This layer, like the stratum lucidum, may be missing in some layers of thin skin.

Stratum spinosum (prickle cell layer)

This layer of the epidermis is made of eight to ten layers of irregularly shaped cells. These cells have very prominent intercellular bridges or desmosomes. If you look at this layer under a microscope, you will see the desmosomes joining adjacent cells, giving the layer a spiny or prickly appearance (Latin *spinosus*, “spinelike”). Cells in the stratum spinosum layer are rich in ribonucleic acid (RNA) and, consequently, well equipped to initiate protein synthesis necessary for production of keratin. This layer and the innermost layer of the epithelium called the *stratum basale*, which we will discuss next, are sometimes referred to as the *stratum germinativum*.

Stratum basale

The stratum basale is a single layer of columnar cells. The cells of this deepest layer of the epithelium are the only cells that undergo *mitosis*. Due to this regenerative activity, cells migrate or transfer from the basal layer through the other layers until they are shed from the skin surface.

Epidermal growth and repair

Protection—the most important function of the integument—largely depends on the special structure features of the epidermis and its ability to create and repair itself following injury or disease. Two terms used to describe the time period required for a population of cells to mature and reproduce are *turnover* and *regeneration time*. As the surface cells of the stratum corneum are lost, replacement of keratinocytes by myotic activity must occur. In order to maintain a constant thickness of the epidermis, new cells must be formed at the same rate that old keratinized cells flake off from the stratum corneum. Cells push upward from the stratum basale into each successive layer, die, become keratinized, and eventually desquamate (shed), just as their predecessors did. What an amazing physiological principle: while life continues, the body’s work is never done. Even when the body is at rest, it is producing millions upon millions of new cells to replace the old ones.

Dermis

The *corium*, another term for the dermis, is also called the “true skin.” The dermis is made up of a thin *papillary* and a thicker *reticular* layer. This dermis is much thicker than the epidermis, and may exceed 4 mm on the soles and palms. The dermis is thinnest on the eyelids, seldom exceeding 0.5 mm. Generally speaking, the dermis on the ventral surface of the body and over the appendages is usually thinner than on the dorsal surface. The skin’s mechanical strength is in the dermis. Besides serving a protection function against mechanical injury and compression, the dermis provides a reservoir storage area for water and important electrolytes. Sensory information, such as pain, pressure, touch, and temperature are processed by a specialized network of nerves and nerve endings in the dermis. At various levels of the dermis, there are muscle fibers, hair follicles, sweat and sebaceous glands, and many blood vessels. Because of its rich vascular supply, the dermis plays a critical role in the regulation of body temperature.

Papillary layer

Look at figure 1–1 again. Notice that the thin superficial layer of the dermis is thrown upward into folds called *dermal papillae* which project into the dermis. This layer takes its name from the papillae arranged in rows on its surface. The dermal-epidermal junction lies between the sculptured surface of

the papillary layer and the stratum basale. The papillary layer is made essentially of loose connective tissue elements and a fine network of thin collagenous and elastic fibers.

Reticular layer

Below the papillary layer of the dermis, you will find the thick reticular layer, consisting of a much denser reticulum than the papillary layer. This dense layer of tough, interlacing white collagenous fibers in animal skin is used to make leather. Even though most of the fibers in this layer are of the collagenous type, giving toughness to the skin, there are also elastic fibers present. These elastic fibers make the skin stretchable and elastic.

The dermis is made up of both skeletal and smooth muscle fibers. A number of skeletal muscles can be found in the skin of the face and scalp. These muscles allow for a wide variety of facial expressions and are also responsible for voluntary movement of the scalp. Smooth muscle fiber distribution in the dermis is much more extensive than the skeletal variety. There is a small bundle of involuntary muscles attached to each hair follicle. They are known as the *arrector pili muscles*. When these muscles contract, it makes your hair “stand on end”—as in extreme fright or in the cold. When the hair is pulled into an upright position, it raises the skin around it into what we call “goose pimples or goose bumps.”

There are millions of specialized nerve endings in the dermis of all skin areas known as *receptors*. Receptors allow the skin to serve as a sense organ transmitting sensations of pain, pressure, touch, and temperature to the brain.

201. Skin functions

The skin forms a self-repairing and protective boundary between the often hostile external world and your body. The skin surface is as large as the body itself. An average sized adult has an area of skin between 17 to 20 square feet. Its thickness varies from a little less than 0.05 cm (1/50 inch) to a little more than 0.3 cm (1/8 inch).

The skin’s functions are diverse and also crucial to the maintenance of homeostasis and to survival itself. They include the following processes:

1. Protection.
2. Temperature regulation.
3. Synthesis of important chemicals and hormones (such as vitamin D).
4. Excretion of water and salts.

We now know that certain substances can be absorbed through the skin. These include:

1. Fat-soluble vitamins (A, D, E, and K).
2. Estrogens and other sex hormones.
3. Corticoid hormones.

Sensory receptors in the skin allow it to function as a sophisticated sense organ. These sensory receptors act as antennas that detect stimuli leading to sensations of heat, cold, pressure, touch, and pain.

The skin also produces the following substances:

Substance	Description
Melanin	The pigment that serves as an extremely effective screen against potentially harmful ultraviolet light.
Keratin	One of nature’s most flexible yet enduring protective proteins.

The epidermis is composed of (get ready for this one) keratinized stratified squamous epithelial tissue. This tissue makes it a formidable barrier. It also protects underlying tissues against invasion by a vast amount of microorganisms, bars entry of most harmful chemicals, and minimizes mechanical injury of the underlying structures.

Your skin plays a very significant role in the maintenance of homeostasis of your body's temperature. Basically, the blood vessels in the dermis dilate, and sweat secretions increase as the body temperature rises above normal. Therefore, more heat is lost by radiation from the larger volume of blood in the skin, in addition to the evaporation of sweat on the skin's surface. Collectively, these changes tend to decrease blood temperature back to normal. When blood temperature falls below normal, the skin's blood vessels constrict and sweat decreases.

202. Appendages of the skin

The skin's appendages are the hair, nails, and skin glands. We will also discuss the surface film of the skin in this lesson. Let's begin our discussion of the skin's appendages with the hair.

Hair

There are only a few skin areas that are hairless—notably the palms of the hands and soles of the feet. There is also no hair on lips and some areas of the genitalia.

It has been stated that human body hair performs no apparent function. As humans, we feel the hair on our head serves a cosmetic purpose. It also provides some protection against the cold, ultraviolet rays, and mechanical injury. Our eyelashes, and hairs in our nose and ears, keep out some dust and insects.

Months before birth, hair follicles begin to develop on most parts of the skin. The developing fetus, by about the sixth month of pregnancy, is covered with an extremely fine, soft hair coat called *lanugo*. Before birth, most of this hair is lost. After birth, what lanugo that is left on the body is lost and replaced with a more pigmented stronger hair. This replacement hair appears first on the scalp, eyelids, and eyebrows. At puberty, the coarse pubic and axillary hair that develops is known as *terminal hair*.

Hair growth starts when the cells of the epidermis grow down into the dermis. This forms a small tube, known as the *follicle*. The stratum germinativum develops into the follicle's innermost layer and forms a cap-shaped cluster of cells known as the *germinal matrix* at the bottom of the follicle. A small mound of the dermis, called the *hair papilla*, protrudes into the germinal matrix. The hair papilla is a highly important structure since it contains the blood capillaries that nourish the germinal matrix. Figure 1-2 A shows the relationship of a hair follicle and related structures to the epidermal and dermal layers of the skin, and 1-2 B shows an enlarged view of a hair root cut in longitudinal section.

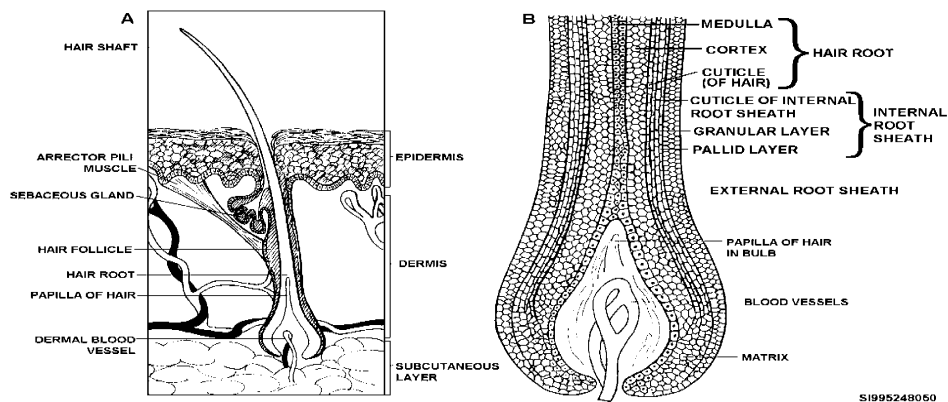


Figure 1-2. Hair follicle.

The cells of the germinal matrix are responsible for forming hairs. They undergo repeated mitosis, push upward in the follicle, and become keratinized to form a hair. As long as the cells of the germinal matrix remain alive, hair will regenerate even though it is cut or plucked, or any other method of removal is used. A portion of the hair, namely the root, lies hidden in the follicle. The visible part of the hair is called the *shaft*, the inner core is the *medulla*, and the outer portion around it is the *cortex*. The cortex is made up of layers of keratinized cells. Varying amounts of *melanin*, the pigment responsible for brown or black hair, is deposited in these cells. Depending on the shape of the shaft, the hair will be straight or wavy. Straight hair has a round, cylindrical shaft, and wavy hair, in contrast, has a flat shaft that is not as strong. As a result, wavy hair is more easily broken and damaged than straight hair. An oily substance, called *sebum*, is secreted by two or more small sebaceous glands into each hair follicle. These secretions lubricate the hair and keep it from becoming dry, brittle, and easily damaged.

Our hair alternates between periods of growth and rest. On an average, hair on the head grows a little less than a quarter-inch per month (4 mm), or about 3 inches per year. The hair on our bodies grows much slower. Reportedly, head hairs live between 2 and 6 years, die and then are shed. However, new hairs usually replace those that are lost. Baldness can develop, as we all know! The most common type of baldness occurs only when two requirements are met: (1) genes for baldness must be inherited, and (2) the male sex hormone, testosterone, must be present. When the right combinations of causative factors exist, common baldness (*male pattern baldness*) inevitably results.

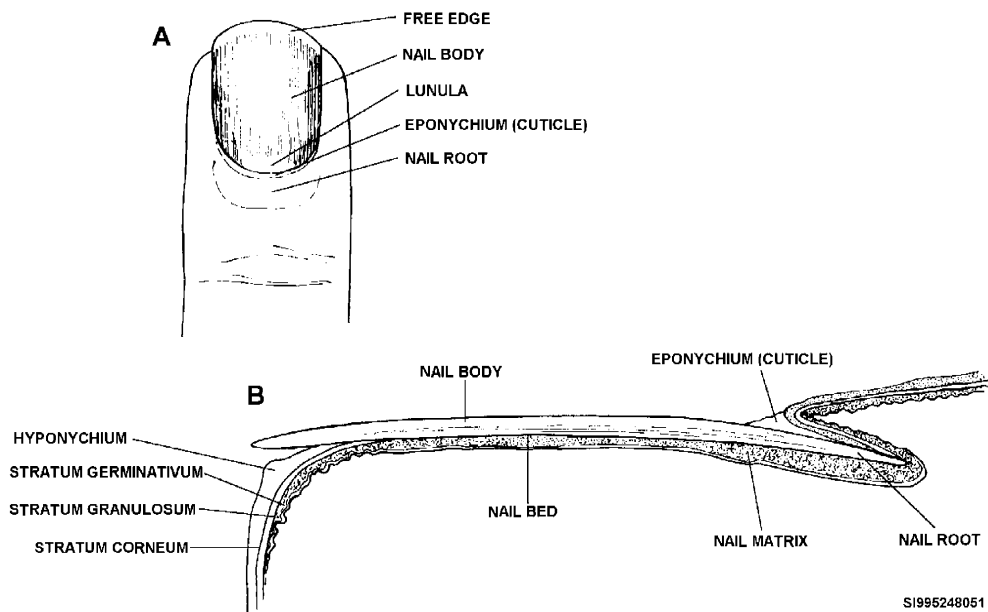


Figure 1-3. Structure of a nail.

Nails

Fingernails and toenails are composed of heavily keratinized epidermal cells. The part of each nail that you see is called the *nail body*. The rest of the nail, the *root*, lies in a groove hidden by a fold of skin called the *cuticle*. The part of the nail body that is nearest the root has a crescent-shaped white area known as the *lunula*, or “little moon.” The *nail bed*, a layer of epithelium, lies under the nail. Figure 1-3A shows the fingernail viewed from above, and 1-3 B shows a sagittal section of the fingernail and associated structures. The nail bed contains an abundant amount of blood vessels, and, therefore, appears pink in color through the translucent nail bodies. Nails grow because of cellular mitosis in the stratum germinativum beneath the lunula. For the most part, nails grow an average of about 0.5mm a week. Fingernails, however, grow faster than toenails, and both grow faster in the summer than in the winter.

Skin glands

Three kinds of microscopic glands make up the skin glands. They are the sudoriferous, sebaceous, and ceruminous.

Sudoriferous glands

The most numerous of the skin glands are the *sweat* or *sudoriferous glands*. They can be classified into two groups—the *eccrine* and the *apocrine* (fig. 1-4). Their classification is based on the type of secretion, location, and nervous system connections.

Eccrine sweat glands

These glands are by far the most numerous, important, and widespread sweat glands in the body. Eccrine sweat glands are quite small, have a secretory portion that is less than 0.4 mm in diameter, and are distributed over the entire body surface, with the exception of the lips, ear canal, glans penis, and nail beds. These glands are simple, coiled, tubular glands. Their function in life is to produce a transparent water liquid that we call *perspiration* or *sweat*. Sweat is rich in salts, ammonia, uric acid, urea, and other wastes. Sweat also plays an important role in helping the body maintain a constant core temperature. Histologists estimate that a single square inch of skin on the palms of the hands contains about 3,000 sweat glands. Eccrine sweat glands are also very abundant on the soles of the feet, forehead, and upper torso. If you have a good magnifying glass, you can locate the opening of the sweat gland ducts on the skin ridges of the palms and on the skin of the palmar surfaces of the fingers.

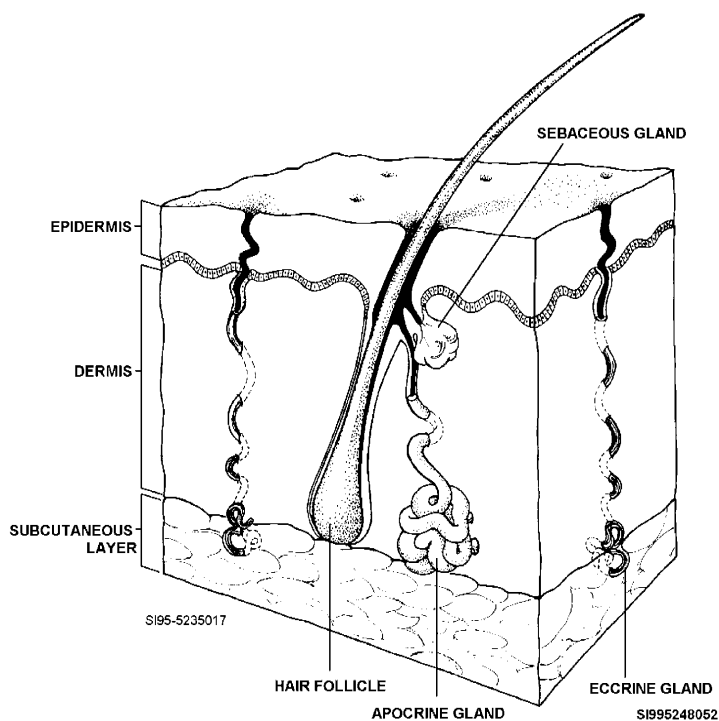


Figure 1-4. Skin glands

Apocrine sweat glands

These glands are located deep in the subcutaneous layer of the skin in the axilla (armpit), the areola of the breast, and the pigmented skin areas around the anus. The apocrine sweat glands are much larger than the eccrine glands and often have secretory units that reach 5 mm or more in diameter. They are classified as simple, branched tubular glands and are connected with hair follicles. Apocrine glands enlarge and begin to function at puberty. They produce a more viscous and colored secretion than the eccrine glands. Apocrine gland secretions show cyclic changes that are linked to the menstrual cycle in females. Odors that are associated with the apocrine gland secretion often are not caused by the secretion itself. Instead, are caused by contamination and decomposition of

the secretion by skin bacteria.

Sebaceous glands

These glands secrete oil for the hair and skin. There are sebaceous glands wherever hair grows from the skin—at least two for each hair. The oil or *sebum* keeps hair supple and skin soft and pliant. The sebum also serves as nature's own protective skin cream by preventing excessive water loss from the epidermis. The sebum is rich in chemicals, such as triglycerides, waxes, fatty acids, and cholesterol

that have an anti-fungal effect. Therefore, it also contributes to the fungistatic activity of the skin surface film. This helps protect the skin from numerous types of fungal infections.

Sebaceous glands are simple branched glands of varying size that are found in the dermis except in the skin of the palms and soles. Sebaceous glands are almost always associated with hair follicles, although some specialized sebaceous glands do open directly on the skin surface in such areas as the lips and eyelids. Increased blood levels of the sex hormones stimulate sebum secretion during adolescence, thereby increasing sebum secretions during this period. Sebum frequently accumulates in and enlarges some of the ducts of the sebaceous glands, forming white pimples. This accumulated sebum darkens with oxidation, forming a *blackhead*.

Ceruminous glands

These glands are a special variety or modified apocrine sweat gland. They appear, histologically, as simple coiled tubular glands with excretory ducts that open into the free surface of the skin in the external ear canal or with sebaceous glands into the necks of hair follicles in this area. The mixture of sebaceous and ceruminous secretions form a brown waxy substance called *cerumen*. Even though cerumen serves a useful purpose in protecting the skin of the ear canal from dehydration, excess cerumen can harden and cause an impaction or blockage in the ear. This could result in a hearing loss.

Surface film

There is a thin film of emulsified material spread over the skin's surface. The proper functioning of this *surface film* affects the ability of the skin to act as a protective barrier against a wide array of potentially damaging assaults from the environment. Surface film is created by the mixing of residue and secretions from sweat and sebaceous glands with epithelial cells continually being cast off from the epidermis. *Desquamation* is the term used to describe the shedding of epithelial elements from the skin surface. The functions of the surface film are:

1. Antibacterial and antifungal activity.
2. Blockade of many toxic agents.
3. Buffering of caustic irritants.
4. Hydration of the skin surface.
5. Lubrication.

The surface film's chemical composition includes:

1. Amino acids, sterols, and complex phospholipids from the breakdown of sloughed epithelial cells.
2. Fatty acids, triglycerides, and waxes from the sebum.
3. Water, ammonia, lactic acid, urea, and uric acid from sweat.

Samples taken from skin covering one body area will often have a different "mix" of chemical components than film covering skin in another area. This difference aids in explaining the unique and localized distribution patterns of certain skin diseases and why the skin covering one area of the body is sometimes more susceptible to attack by certain bacteria or fungi.

203. Observation of the skin

What can the skin communicate to you? What do the skin's color, texture, and other attributes indicate? If you are a keen observer, you can learn quite a bit! As a matter of fact, the first sign of serious systemic disease may be a skin disorder.

The color of skin depends on a number of factors, including:

1. Amount of pigment in the epidermis.
2. Quantity of blood circulating in the surface blood vessels.

3. Composition of the circulating blood:
 - a) Presence or absence of oxygen.
 - b) Concentration of hemoglobin
 - c) Presence of bile, silver compounds, or other chemicals.

Pigment of the skin

The pigment of the skin is called *melanin*. Melanin is also found in the hair, the iris of the eye, and in some tumors. It is common to all races, but darker people have a much larger quantity of it distributed in these tissues. As a result of exposure to the sun, a normal increase in skin pigment occurs. Abnormal increases in the quantity of melanin may occur in localized areas or over the entire body surface. Scattered spots of pigmentation may be characteristic of some endocrine disorders.

Discoloration of the skin

The presence of excessive quantities of bilirubin (bile pigment) in the blood may be the cause of a yellow discoloration of the skin. This condition is called *jaundice* and may be a symptom of a number of disorders, such as:

1. A tumor pressing on the common bile duct or a stone within the duct, either of which would obstruct the flow of bile into the small intestine.
2. Inflammation of the liver (hepatitis).
3. Certain diseases of the blood in which the red blood cells are rapidly destroyed.
4. The excessive intake of carrots and other deeply colored vegetables can also cause a yellowish discoloration of the skin. This condition is called *carotinemia*.
5. Grayish or brown discoloration of the skin may be caused by chronic poisoning.
6. Addison's disease, a malfunction of the adrenal glands, presents a peculiar bronze cast to the skin.

There are many more diseases that cause discoloration of the skin but we do not have room to list them all.

Injuries to the skin

A local injury or wound is called a *lesion*. Some skin lesions that should be noted by healthcare providers include:

Lesion	Description
Excoriations	May be evidence of scratching
Lacerations	Rough, jagged wounds made by tearing the skin
Ulcers	Sores associated with disintegration and death of tissue.
Erythema	Areas of redness, as well as other discoloration.
Spots	Any type of spots.

Skin eruptions

Skin rashes (eruptions) may be localized as in a diaper rash, or they may be generalized as in measles and other systemic infections. The following terms are often used to describe skin eruptions.

Term	Explanation
Macules or macular rash	The spots are neither raised nor depressed, typical of measles and also descriptive of freckles.
Papules or papular rash	Firm raised areas, as in some stages of chickenpox and in the second stage of syphilis. Characteristic of pimples.
Vesicles or vesicular eruptions	Blisters or small sacs are full of fluid, such as those found in some of the eruptions of chickenpox.
Pustules or pustular lesions	May follow the vesicular stage of chickenpox.
Crusts	Made of dried pus and blood and commonly referred to by a layperson as scabs.

Self-Test Questions

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

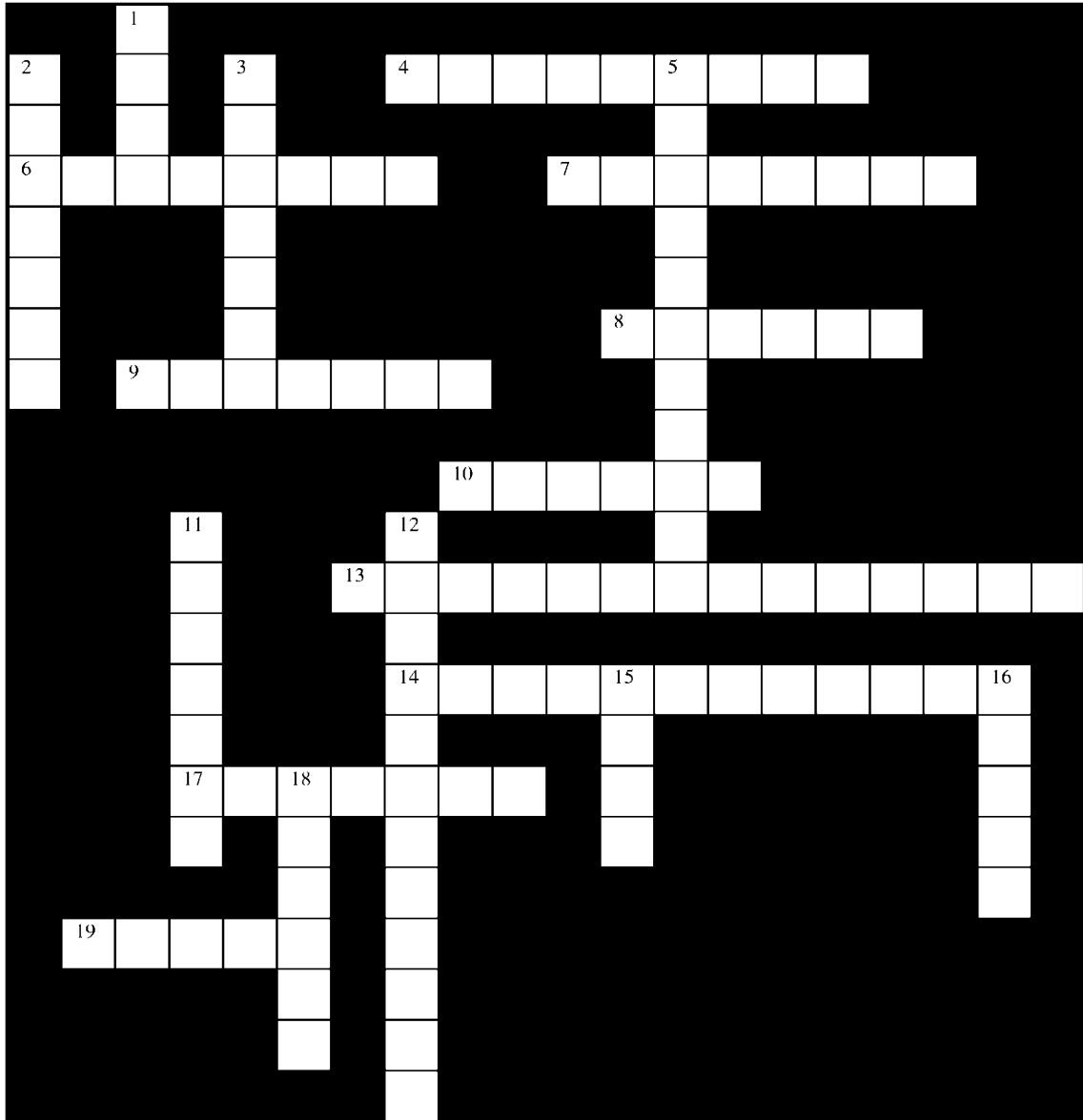
200. Skin structure

1. What type of membrane is the skin classified as?
2. What are the two main layers of the skin?
3. What term is used to describe the area where the cells of the epidermis meet the connective tissue cells of the dermis?
4. What are the two terms used to describe the loose subcutaneous layer, rich in fat and areolar tissue, that lies beneath the dermis?
5. What are the three primary types of cells that make up the epidermis?
6. What is the most superficial layer of the epidermis, and what is it made of?
7. Define keratinization.
8. In what layer of the skin does keratinization begin?
9. Which layer of the skin has cells that undergo mitosis?

10. What is the most important function of the skin?
11. What two other terms are synonymous with “dermis?”
12. Which is thicker—the dermis or epidermis?
13. What types of muscle fibers make up the dermis?

201. Skin functions

1. List the functions of the skin.
2. What is melanin?
3. What type of tissue is the epidermis composed of?



<i>ACROSS</i>	<i>DOWN</i>
4. Darkened accumulated sebum	1. Not found on palms of hands
6. Hair that develops at puberty	2. Fold of skin that hides the nail root
7. Visible part of nail	3. Layer of epithelium under nail
8. Fine, soft hair covering fetus	5. Contains blood capillaries that nourish the germinal matrix
9. Inner core of hair	11. Brown waxy substance
10. Crescent-shaped area of nail body	12. Sweat
13. Follicular cap-shaped cluster of cells	15. Hidden by cuticle
14. Most numerous of the skin glands	16. Oil that keeps the hair supple
17. Most numerous of the sweat glands	18. The outer portion of the medulla
19. Visible part of hair	

1. List factors that affect the skin's color.

2. What is another name for the pigment of skin?
3. What skin discoloration is seen in Addison's disease?
4. What term is used to describe areas of redness of the skin?
5. What type of skin eruption appears as a blister or small sac full of fluid?

1-2. Conditions Associated With the Integumentary System

The skin is the body's largest, thinnest, and one of its most important organs. It forms a self-repairing, protective boundary between the body and an often hostile, external world. This hostile, external world often includes burns, baldness, athlete's foot, blisters, common acne, decubitus ulcers, dermatosis, dermatitis, eczema, impetigo, skin cancer, sunburn, and a few other skin disorders. We discuss all of these disorders in this section.

204. Burns

Most often we think of a burn as a thermal injury or lesion caused by contact of the skin with some hot object or fire. Overexposure to ultraviolet light (sunburn) or contact with an electric current or corrosive chemicals will also cause injury or death to skin cells. The injuries that result can all be classified as burns.

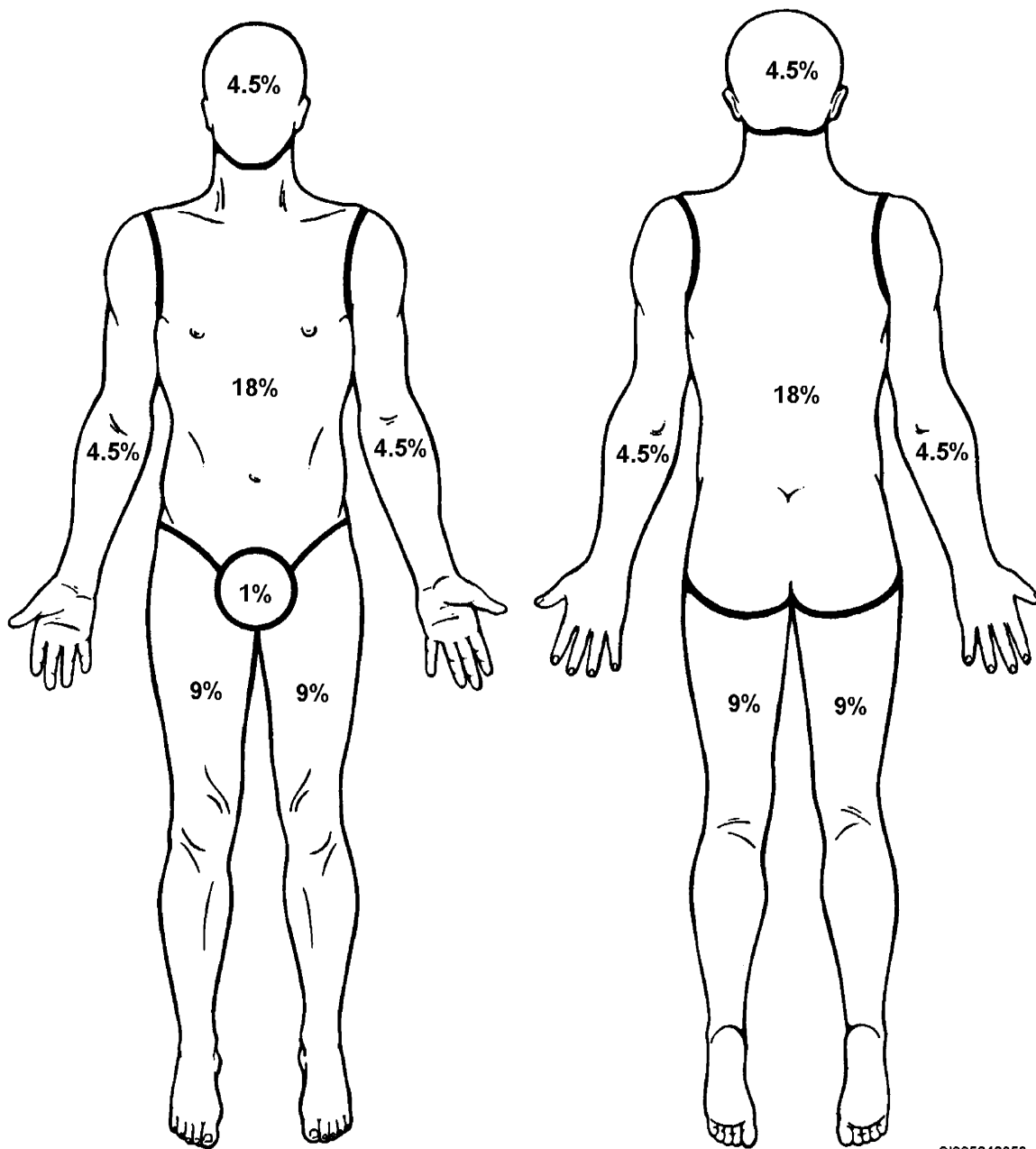
When burns involve large areas of the skin, treatment and prognosis for recovery depends greatly on the total area involved and the severity of the burn. First, we will discuss how to determine the extent of body surface area involved, then describe the different severity levels of a burn.

Estimating body surface area

The depth of the lesion, as well as the extent (percent of body surface area burned) determines the severity of a burn. There are several ways to estimate the extent of body surface area burned. We will only discuss one here.

Rule of nines

This is an accurate method of determining the extent of burn injury. When using this technique, the body is divided into 11 areas of nine percent with the area around the genitals, called the *peritoneum*, representing the additional one percent of body surface area. To estimate the extent of the burn, add up the number of areas burned, and multiply by nine. As figure 1-5 shows, nine percent of the skin



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Figure 1-5. Rule of nines

covers the head and each upper extremity, to include front and back surfaces. Eighteen percent, or twice as much, of the total skin area covers the front and back of the trunk and each lower extremity, to include front and back surfaces. The rule of nines works well with adults but does not reflect the differences in body surface area seen in small children. Special tables, called *Lund-Browder Charts*, take into account the large surface area of certain body areas (such as the head) in the growing child. Physicians use these charts to estimate burn percentages in children.

Degree of severity of the burn

The depth of a burn injury depends on the tissue layers of the skin that are involved. A *first-degree burn* (typical sunburn) will cause minor discomfort and some reddening of the skin. Even though the

surface layers of the burned area may peel in one or two days, no blistering occurs, and actual tissue destruction is minimal.

Second-degree burns involve the deep epidermal layers and always cause injury to the upper layers of the dermis. In deep second-degree burns, damage to sweat glands, hair follicles, and sebaceous glands may occur, but tissue death is not complete. Blisters, severe pain, generalized swelling, and edema characterize this type of burn. Scarring is common. Both first- and second-degree burns are called *partial-thickness burns*.

Third-degree or full-thickness burns are characterized by destruction of both the epidermis and dermis. Tissue death extends below the hair follicles and sweat glands. Burning may involve underlying muscles, fasciae, or even bone. A distinction between second- and third-degree burning is the fact that the third-degree lesion is insensitive to pain immediately after injury because of the destruction of nerve endings. Scarring is a serious problem.

205. Other skin conditions

Alopecia (baldness)

Baldness may be due to infection as well as many other factors. In males, particularly, it may be inherited. It may be a manifestation of aging, in which case it normally begins at the crown of the head and is associated with atrophy of the structures of the scalp. Baldness may be the result of such systemic diseases as syphilis and myxedema. Severe infections, such as scarlet fever, may cause a loss of hair. In these cases, recovery from the disease usually means regrowth of the hair. Chronic fungal infections that involve the oil glands and hair follicles may result in alopecia. In these cases constant attention to skin hygiene and frequent shampooing may prevent balding.

Blisters

Blisters may be the result of injury to cells in the epidermis or from separation of the dermal-epidermal junction. Despite their cause, blisters represent a basic reaction of the skin to injury. Blister formation is initiated when any irritant damages the physical or chemical bonds that hold adjacent skin cells or layers together. *Desmosomes* are the specialized junctions that serve to hold adjacent cells in the epidermis together, and they are also essential for the integrity of the skin.

Common acne

Acne is usually a disease of the oil glands of the hair follicles of the skin called *acne vulgaris*. Individuals between the age of 14 and 25 are its usual victims. This infection of the oil glands manifests itself in the form of pimples, which generally surround blackheads. Certain endocrine glands in the body control the secretions of the sebaceous glands and are particularly active in adolescence, causing acne to be most severe during this time. Thorough and frequent cleansing of the skin with abrasive soaps and warm water, followed by the use of a clean pillowcase changed daily, may be effective treatment in some cases. Some patients also require antibiotic treatment; we discuss that later in this course.

Decubitus ulcers

Older people confined to bed for prolonged periods are particularly susceptible to *bedsores* or *decubitus ulcers*. Patients with this condition have skin covering bony prominences (e.g., ankles, heels, and buttocks) that is subject to constant pressure caused by body weight for long periods of time. If the patient is not turned or cannot change bed positions, the blood supply to the skin in these pressure areas will be reduced, and tissue damage, infection, and ulceration will occur.

Dermatosis and dermatitis

Dermatosis is a common term referring to any skin disease. *Dermatitis* is a term used to describe inflammation of the skin. This inflammation may be due to many kinds of irritants, such as the oil of poison oak or poison ivy plants, detergents, strong acids or alkalines, or other chemicals. The most

effective prevention and treatment involve prompt removal of the irritant. Where plant oils are concerned, a thorough bath with soap and water as soon as possible after contact may prevent the development of the itching eruptions.

Eczema

This is a very unpleasant disease that can be found in people of all ages and shows no gender preference. It is more common, however, in the very young and the elderly. Any and all parts of the skin surface may be affected by eczema. It may exhibit itself by redness (erythema), blisters (vesicles), and pimple-like (papular) lesions; it is not a contagious disease. Patients with eczema may also have scaling and crusting of the skin surface. It may also cause excessive sensitivity to detergents, soaps, and other chemicals. For instance, when used frequently, even the mildest soap may cause irritation. The skin may also overreact to heat, dryness, rough fabrics (especially wool), and even to perspiration.

Impetigo

This is an acute, contagious disease of staphylococcal or streptococcal origin that may be serious enough to cause death in newborn infants. Impetigo manifests itself as blister-like lesions that become filled with pus and contain millions of virulent bacteria. Impetigo is most frequently found in poor and undernourished children. These children may re-infect themselves or others. Contaminated linen or dishes sometimes spread the infection. For instance, in the nursery, utmost care in handling infants to prevent the spread of the disease from baby to baby is extremely important. Fatalities from impetigo have occurred at various times in the United States, despite ordinary precautions. This disease is so contagious that children who develop impetigo should not be permitted to return to school until a health professional certifies that the condition is cured.

Fungal infections

Fungal infections of the hair, skin, and nails are a major problem throughout the world. It is estimated that fungal infections account for about five percent of new outpatient referrals to dermatologists in the temperate climates, and as many as 20 percent in tropical climates. Most fungal infections are caused by either dermatophytes or yeast

Dermatophytes are fungi that cause skin infections. They obtain nutrients from keratin found, for example, in the stratum corneum. Some dermatophytes cause a wide inflammatory response; others produce inflammation only in specific locations. Factors that make you more susceptible to fungal infections include:

1. Debilitating diseases.
2. Diabetes mellitus.
3. Use of immunosuppressive drugs.
4. Impaired circulation.
5. Occluded skin.
6. Poor hygiene.
7. Poor nutrition, trauma.
8. Tropical climates.
9. Warm, moist skin.

Tinea pedis

The most prevalent cutaneous fungal infection, also known as athlete's foot, includes itching, burning, scaling, cracking or stinging, and sometimes weeping or oozing, or pain. Some individuals will suffer no ill effects when exposed to pathogenic fungi. Other people will experience a severe skin infection when subjected to a mild exposure. Excessive sweating of the feet may make the problem worse. The following procedures will discourage infection:

1. Frequent changing of hose and shoes.
2. Thorough drying of the feet, with particular attention to the spaces between the toes.
3. Dusting powders in the shoes and on the feet.

Medicines may or may not be effective.

Tinea corporis

Tinea corporis, or body ringworm, begins as a red macule or papule. It develops into a ring or bow-shaped lesion with sharply edged, raised red borders with papules or vesicles and center. Tinea corporis can occur on the neck, body, arms and legs. It is most common in children, especially those exposed to animals with ringworm (e.g., cats, dogs). The infection may be either asymptomatic or mildly pruritic.

Tinea cruris

Tinea cruris, or jock itch, is an infection of the groin area and is more common in men. Bilateral erythematous plaques (papular lesions >1 cm in diameter) occur in the groin area and upper inner thigh, which may spread to the buttocks. The penis and scrotum are not usually involved

Onychomycosis

This is a fungus, similar to ringworm, that attacks your nails. It first appears as a distinct white or yellow spot on your nail. Then gradually, it can consume your entire nail bed. Depending on the type of fungus, your nail may turn yellow, gray, brown or black in color. Often, the nail becomes thick and brittle, and cracks or separates from its bed. Your surrounding skin can be red, itchy or swollen. As you age, your nails thicken and grow more slowly, making them more susceptible to infection.

Your risk of a fungal toenail infection also increases if:

1. Your feet perspire excessively.
2. You wear socks or hose made from polyester or nylon, which don't absorb foot perspiration well.
3. You wear shoes with rubber soles, instead of leather, which don't allow ventilation.
4. You walk barefoot around public pools, showers and locker rooms.

Fungal fingernail infections usually result from overexposure to water and detergents. Moisture trapped under artificial nails can also allow fungus to grow. Once an infection begins, it can persist indefinitely if not treated.

Candidia

This type of fungus, like all others, thrives on dark, damp places. It can affect the mouth, causing an infection called thrush; another version of candidia attacks the vagina (candidiasis). Candidiasis can be passed as a sexually transmitted disease.

Parasitic infestation

We'll take a quick look at scabies and lice. Scabies are a small, parasitic animal that burrows into the skin to lay eggs. After hatching, the larvae exit the burrows and start the process over again. The life cycle from an egg to an adult parasite is 8 to 15 days.

There are actually two types of lice that infect humans, head lice and pubic lice. The lice feed on the blood of their host, leaving their eggs (nits) on hair follicles. The glue that holds the nits onto the hair is very strong and can't be removed without chemical treatment. Lice can infect clothing under the right conditions.

Skin cancer

There are three major types of skin cancer. From a practical standpoint, it is of the utmost importance to differentiate among them. The most common forms are called *squamous cell carcinoma*, *basal cell carcinoma*, and *malignant melanoma*.

All three types apparently result from cell changes in the epidermis and are referred to as epithelial cancers. Cancers of the sweat glands, hair follicles, and sebaceous glands do occur, but they are relatively uncommon.

Skin cancers are the most common neoplasms, or abnormal growths, seen in humans. They account for nearly 14 percent of reported cancers in women, and almost one-fourth of all cancer in men. The higher incidence in males may be due to a more extensive and chronic occupational exposure to sunlight. Cancer may be the result of x-rays or cell damage caused by carcinogenic, or cancer-causing chemicals (e.g., arsenic, soot, tar, and certain lubricating oils used by machinists and metal lathe workers).

Squamous cell carcinoma

This type of cancer is the most common form of skin cancer. It usually begins as a small lump with a scaly or warty appearance. It may appear anywhere on the body, but it occurs most often in the skin exposed to the sun—especially on the dorsum of the hand, ears, and face. An ulceration often develops as the tumor grows, and underlying tissues are invaded and destroyed. Squamous cell carcinomas will spread to other areas of the body if left untreated, a process called *metastasis*, and death may be the result.

Basal cell carcinoma

Basal cell carcinoma comes from cells in the deep basilar layer of the epidermis. Most often, it shows up on the skin of the lips, eyelids, chin, and nose. Infiltration into adjacent tissues occurs, once the carcinoma is established. Its growth is slower than squamous cell carcinoma, but it is very destructive to surrounding structures. Advanced lesions may destroy bone and cartilage. Fortunately, this cancer is not spread by metastasis and is easily cured, if treated early.

Malignant melanoma

This is the most common type of pigment cell skin cancer. Malignant melanomas are usually preceded by a flat hairless mole that begins to darken as it undergoes malignant change. If treatment is initiated before deep invasion of underlying tissue occurs, this so-called “superficial spreading melanoma” can be cured by surgical excision. If you notice changes in a mole involving pigmentation or alteration of surface characteristics, seek medical evaluation immediately. When previously smooth moles become rough or develop a notched edge and change color, they are almost always undergoing cancerous changes. Malignant melanomas metastasize and then become one of the most difficult cancers to cure when treatment is delayed.

Sunburn and its complications

The skin may undergo both chemical and biological changes due to sunlight. First, the skin becomes reddened (erythematous) and then it may become swollen and blistered. Some people become seriously ill and suffer severe sunburn. There is quite a bit of evidence to back up the notion that continued excessive exposure to the sun is a leading cause of skin cancer. Currently, there seems to be a fad for tanning; consequently, the skin is required to protect itself by producing considerably more than its usual amount of melanin. This increase in pigmentation can have the effect of lowering the ability of the body to profit from the desirable smaller amounts of sun available during some parts of the year.

Other skin disorders

In addition to the skin conditions we discussed, there are other disorders. We will discuss a few of them very briefly.

Furuncles

This is another name for “boils.” Furuncles are localized collection of pus in cavities formed by the disintegration of tissue. They are caused by bacteria that enter hair follicles or sebaceous glands.

Carbuncles

Carbuncles are pus-producing lesions that result from extensions of infectious processes, such as boils. They involve both the skin and subcutaneous tissues and have numerous drainage channels that extend to the skin surface.

Psoriasis

Psoriasis is characterized by sharply outlined, red, flat areas (plaques) covered with silvery scales. The cause of this chronic, recurrent skin disease is unknown.

Herpes simplex

This disease is characterized by the formation of water vesicles (cold sores, fever blisters) on the skin and mucous membranes, including the genital area.

Urticaria

This is an allergic reaction characterized by the transient appearance of elevated red patches (hives) often accompanied by severe *pruritus* (itching).

Scleroderma

This disease and some of the metabolic diseases, such as certain forms of lupus erythematosus, cause thickening of the dermis.

Self-Test Questions

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

204. Burns

1. How is the severity of a burn determined?
2. Using the rule of nines, how do you approximate the percentage of body surface area burned?
3. Describe a second-degree burn.

205. Other skin diseases

1. What type of patient is particularly susceptible to decubitus ulcers?
2. Define dermatosis and dermatitis.
3. What is impetigo, and how does it manifest itself?

4. What is the most common cause of athlete's foot?
5. List the three most common forms of skin cancer.
6. What is the most common form of skin cancer?
7. What skin condition has a pus-producing lesion that results from extensions of infectious processes, such as boils?

1-3. Drugs used to treat conditions associated with the Integumentary System

The pharmacological basis of therapeutics in dermatology is unique and fascinating. The majority of drugs used to treat dermatological diseases are also used systemically to treat disorders of other organ systems. The topical pharmacology and use of these drugs is emphasized in this section. The basic features of the systemic pharmacology of these drugs will be discussed elsewhere in this course. Discussion on each drug in this section, and the remaining volumes of this course, will be formatted in the following manner: discussion of class, indications, contraindications, warnings, interactions, and patient information. Please note that some drugs have many interactions that you may never come across in your duties. In order to save you some time, this course won't cover 100% of interactions and warnings. The drugs and interactions listed are those most used; they will become valued reference material in your pharmacy. Become familiar with the format and use your references on the job!

Before we get started with the actual therapeutic classification of the drugs, there are some specific things you need to remember about drug therapy.

206. Drug therapy

Drug therapy is different—yet the same—in different disease states. There *are* some basic rules of drug therapy regarding concepts, goals, maintenance, and acute therapy; factors determining the length of therapy and dosage intervals; and drug therapy in non-disease states. Let's start off with a discussion of drug therapy concepts.

Concepts

Disease is defined as a condition of the living animal or one of its parts that impairs the performance of a vital function. We will discuss four different types of disease:

Type	Description
Acute	Diseases with a rapid onset and short duration.
Chronic	Diseases with a slow onset and long duration.
Infectious	Diseases acquired from overgrowth of microorganisms.
Congenital	Diseases present from birth.

Goals of drug therapy

A drug is any substance that will modify one or more body functions when taken into a living organism. Therapy is the treatment of disease. The goals of drug therapy are to (1) treat the symptoms, (2) prolong life, and (3) cure disease.

Maintenance and acute therapy

Maintenance therapy refers to chronic diseases. The goal of maintenance therapy is to slow or stop progression of the disease and to maintain a patient's health or comfort.

Acute therapy refers to diseases with a rapid onset, often with severe symptoms, and the symptoms usually have a short duration. The goal of acute therapy is to relieve symptoms and cure the disease state within a reasonable period of time.

Factors determining the length of therapy and dosage intervals

Drug regimen refers to the amount of drug given and the time interval between doses. Factors affecting the length of therapy and dosing include:

1. The patient's age, weight, sex, health, etc.
2. The drug half-life, route of administration, absorption rate, excretion rate, etc.

Pregnancy categories

Throughout this course and your work in pharmacy you must be constantly aware of pregnancy categories. There are some medications that are just not safe to give to pregnant women. Some drugs may cause an abortion or damage the fetus. Care must also be taken for breast-feeding women. Many drugs are absorbed and excreted into breast milk (you don't want your baby to get mom's antibiotic). The FDA has established the following categories:

Category	Description
A	Adequate studies in pregnant women have not demonstrated a risk to the fetus in the first trimester of pregnancy and there is no evidence of risk in later trimesters.
B	Animal studies have not demonstrated a risk to the fetus but there are no adequate studies in pregnant women or animal studies showing an adverse effect, but adequate studies in pregnant women have not demonstrated a risk to the fetus during the first trimester of pregnancy and there is no evidence of risk in later trimesters.
C	Animal studies have shown an adverse effect on the fetus but there are no adequate studies in humans; the benefits from the use of the drug in pregnant women may be acceptable despite its potential risks or there are no animal reproduction studies and no adequate studies in humans.
D	There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.
X	Studies in animals or humans demonstrate fetal abnormalities or adverse reaction reports indicate evidence of fetal risk. The risk of use in a pregnant woman clearly outweighs any possible benefit.

Regardless of the designated Pregnancy Category or presumed safety, no drug should be administered during pregnancy unless it is clearly needed and potential benefits outweigh potential hazards to the fetus.

Drug therapy in non-disease states

Drugs are used in non-disease states. Some examples include:

1. Contraceptive to prevent pregnancy.
2. Antibiotics to prevent infection during surgery (prophylaxis) or susceptible recurring infections.
3. Immunization against disease.
4. Smoking deterrents to prevent future illness.
5. Sunscreens to reduce the risk of skin cancer.

This refresher is intended to keep these thoughts current in your mind as you are studying these drugs. Now let's get started on our first therapeutic drug class that affects the integumentary system.

207. Drug therapy in integumentary disease states**Antihistamines**

Antihistamines are drugs that oppose the action of histamine. Many of the first antihistamines were noted for their side effects of drowsiness and dry mouth.

Systemic antihistamines elicit a favorable response for many patients suffering from pruritus (itching), although their major beneficial effect may be due to sedation. There is disagreement over which antihistamine agent is more effective in the treatment of pruritus. There is little evidence that antihistamines are effective in treating pruritus that is not caused by histamine except that their inherent sedative effect may be somewhat beneficial in all pruritic conditions. Antihistamines can also be used to treat urticaria (skin eruptions). The skin eruptions that were discussed back at the beginning of this unit may be caused by an allergic (histamine) reaction. Antihistamines will only help an allergic urticaria.

Although there are many antihistamines, we will discuss only two in this section. Diphenhydramine and Hydroxyzine are both used orally for both systemic and integumentary conditions. Diphenhydramine is also used topically for its drying effect.

Indications and usage

Both of these agents are indicated for pruritis, diphenhydramine is also indicated for urticaria.

DRUG	DOSE (mg)	INTERVAL (hrs)	SEDATION	ANTIHISTAMINE EFFECT	ANTICHOLINERGIC EFFECT
Diphenhydramine	25-50	4-6	moderate	low	moderate
Hydroxyzine	25-100	6-8	moderate	moderate	low

Contraindications

These medications are contraindicated, or should be used with caution in patients with the following conditions:

1. Asthma.
2. Hypertension.
3. Cardiac disease.
4. Glaucoma.
5. Prostatic hypertrophy.

Warnings

When using systemic antihistamines for integumentary disorders, the following cautions should be observed:

1. Patients with lower respiratory disorders such as emphysema, chronic bronchitis, and asthma should not use antihistamines because their drying effect may thicken secretions and impair expectoration.
2. Antihistamines may cause dizziness or drowsiness; this may be more severe in elderly patients.
3. In children, antihistamines may diminish mental alertness, or they can occasionally produce excitation.
4. Diphenhydramine is pregnancy category B, Hydroxyzine is pregnancy category C.

Drug interactions

Drugs that interact with antihistamines*	
Drugs	Action
Anticholinergics, anxiolytics, sedatives, hypnotics, barbiturates, ethanol	Additive CNS effects (i.e., drowsiness and sedation can occur)
Monoamine Oxidase Inhibitors (MAOIs)	MAOIs may increase and prolong the anticholinergic and CNS depressant effects of antihistamines
Phenothiazines and Tricyclic antidepressants	These drugs can add to the anticholinergic effect of antihistamines

*Only the two discussed in this section

Patient information

1. Antihistamines can cause drowsiness or dizziness. They may also cause nervous system effects such as headache and decreased mental alertness. They can impair the ability to drive or operate machinery.
2. Alcohol can reduce your body's ability to process antihistamines and increase your risk of developing serious side effects. Avoid or minimize your alcohol intake.
3. Topical use can mask the symptoms of infections or other serious skin conditions. Do not use the topical form of diphenhydramine for more than a few days without consulting your healthcare provider.
4. You should take this medication as directed. Do not increase your dosage, or take extra doses, without consulting your healthcare provider. If you miss a dose, take it as soon as possible after the dose was due. Do not take the missed dose if it is nearly time for the next dose. Do not take double doses or extra doses.
5. If you experience a dry mouth, you can reduce the effect by chewing sugarless gum, sucking on hard candy, and drinking plenty of water. If the dry mouth continues for more than two weeks, consult your physician.

Anti-inflammatory agents

Hydrocortisone or synthetic derivatives of hydrocortisone are used topically as anti-inflammatory agents. They are known as topical corticosteroids. Following topical application, corticosteroids produce anti-inflammatory, anti-pruritic, and vasoconstrictor actions

Topical corticosteroids relieve the symptoms of skin irritations. The cause of the irritation should be determined and eliminated, if possible. Skin irritations are controlled, not cured, by these drugs. Systemic corticosteroids are usually more effective in treating skin conditions; however, topical treatment is preferred in most cases because of fewer side-effects.

Topical corticosteroids are generally most effective in the treatment of acute or chronic skin conditions (e.g., seborrheic dermatitis, localized neurodermatitis, anogenital pruritus, and psoriasis).

Topical corticosteroids are effective in the late phase of allergic contact dermatitis or irritant dermatitis, but systemic corticosteroids are usually required to relieve the acute manifestations of these conditions.

Individual topical corticosteroid preparations vary in anti-inflammatory activity and in percutaneous penetration, but therapeutic efficacy of a particular drug can often be increased by increasing the concentration or by using occlusive dressing therapy. As with systemic use, some patients may respond better to one topical corticosteroid than to another.

Systemic corticosteroids will be addressed in later lessons. For now, we'll focus on topically applied corticosteroids.

Vehicles

The term "vehicle" refers to how a drug is delivered. Remember from your apprentice course, non-sterile lab, that medications can be added to any number of topical vehicles. Ointments are more occlusive (separates the wound from the air) and are preferred for dry, scaly lesions. Use creams on oozing lesions or in folds of the skin. Creams are often preferred by patients because they don't appear greasy, even though the cream tends to dry out the skin more. Gels, aerosols, and lotions are useful on hairy areas. The addition of urea adds to the absorption of some steroids by hydrating the skin. Normally, ointments and gels are more potent than lotions and creams. Medication-impregnated tapes are useful for occlusive therapy in small areas.

Occlusive dressings

Occlusive dressings such as plastic wrap increase skin penetration by as much as ten times by increasing the moisture content of the stratum corneum. Occlusive dressings must be used cautiously because the increased moisture can also cause bacterial or fungal infections. Additionally, the increased absorption may cause some systemic effects. Do not use occlusive dressings for more than 12 hours/day when using potent corticosteroids.

Potency

The potency of a product depends on several factors. Vasoconstrictor tests are used to measure the relative potency of products. This potency may, however, vary from manufacturer to manufacturer.

Relative Potency of Topical Corticosteroids

Drug	Dosage Form	Strength
Very high potency		
Augmented betamethasone dipropionate	Ointment	0.05%
Clobetasol propionate	Cream, Ointment	0.05%
Halobetasol propionate	Cream, Ointment	0.05%
High potency		
Augmented betamethasone dipropionate	Cream	0.05%
Betamethasone dipropionate	Cream, Ointment	0.05%
Betamethasone valerate	Ointment	0.1%
Medium potency		
Betamethasone dipropionate	Lotion	0.05%
Betamethasone valerate	Cream	0.1%
Hydrocortisone valerate	Cream, Ointment	0.2%

Drug	Dosage Form	Strength
Triamcinolone acetonide	Cream, Ointment, Lotion	0.025%, 0.1%
Fluocinolone acetonide	Cream, Ointment	0.025%
Low potency		
Desonide	Cream	0.05%
Fluocinolone acetonide	Cream, Solution	0.01%
Hydrocortisone	Cream, Ointment, Lotion, Solution, Aerosol	0.25%, 0.5%, 1%, 2.5%

Indications

Topical corticosteroids are indicated for contact dermatitis, atopic dermatitis, eczema, psoriasis, severe diaper rash, insect bite reactions, first and second degree localized burns, and sunburn.

Usual dose: Apply sparingly to affected areas 2 to 4 times daily.

Contraindications

1. Bacterial infection.
2. Facial use.
3. Ophthalmic use.

Warnings

Corticosteroids are pregnancy category C; caution should be used with topical corticosteroids for breast-feeding mothers.

Children may be more susceptible to topical corticosteroid-induced hypothalamic-pituitary-adrenal axis suppression (discussed in the endocrine system) than adults because of a larger skin surface to body weight ratio. Use should be limited to the smallest amount possible to get effective therapy.

Patient information

1. Apply ointments, creams or gels sparingly in a light film; rub in gently. Washing or soaking the area before application may increase drug penetration.
2. To use a lotion, solution or gel on your scalp, part your hair, apply a small amount of the medicine on the affected area and rub it in gently. Protect the area from washing, clothing, rubbing, etc., until the lotion dries. You may wash your hair as usual but not right after applying the medicine.
3. To apply aerosols, shake well and spray on affected area holding container about 3 to 6 inches away. Spray for about 2 seconds to cover an area the size of your hand. Take care not to inhale the vapors. If you are spraying your face or near your face, cover your eyes.
4. Use only as directed. Do not put bandages, dressings, cosmetics, or other skin products over the treated area unless directed by your physician.
5. Notify your physician if the condition being treated gets worse, or if burning, swelling or redness develops.
6. Avoid prolonged use around the eyes, in the genital and rectal areas, on the face, armpits, and in skin creases unless directed by your physician. Avoid contact with the eyes.
7. If you forget a dose, apply it as soon as you remember and continue on your regular schedule. If it is almost time for the next application, wait and continue on your regular schedule. Do not apply double doses.
8. For parents of pediatric patients: Do not use tight-fitting diapers or plastic pants on a child treated in the diaper area; these garments may work like occlusive dressings and cause more of the drug to be absorbed into your child's body.

Anti-infective agents

The term “anti-infective” can be defined as an agent counteracting infection. For the purpose of this course, all anti-infectives will fall into one of the following drug categories: anthelmintics, antibiotics, anti-anaerobic agents, antimycobacterials, antivirals, antiprotozoals, and scabicides. This section will only discuss *topical* anti-infectives. Systemic dosage forms of some of these drugs will be discussed in later sections of this course.

Topical Anti-infectives		
Drug	Dosage form	Indication
Acyclovir	Ointment	Herpes simplex infections
Bacitracin	Ointment	Minor skin infections
Clindamycin	Gel, solution, lotion	Acne vulgaris
Erythromycin	Gel, ointment, swabs, solution	Acne vulgaris, superficial pyogenic infections
Metronidazole	Gel	Acne rosacea
Mupirocin	Ointment	Impetigo
Silver sulfadiazine	Cream	Burns, skin infections from clean cuts (grafts, incisions)

Indications

These anti-infective preparations are used for infection prophylaxis in minor cuts, wounds, burns, and skin abrasions, as an aid to healing and for the treatment of superficial infections of the skin due to susceptible organisms responding to local treatment. Apply these medications 1–4 times daily (acyclovir, 6–7 times daily) according to provider directions. Cover with sterile bandage if needed.

Contraindications

1. Any known sensitivity to any form of these topical anti-infectives should be considered.
2. These drugs should not be applied over large areas of the body.
3. These drugs should not be applied to serious burns, deep wounds, or animal bites without consulting a health care provider.
4. Topical anti-infectives should not be used for long periods of time. Such use may lead to masking of other signs of infection or overgrowth of non-susceptible organisms.
5. Unless specifically noted, these medications are not for ophthalmic use.

Warnings

Acyclovir is pregnancy category C. Pregnancy categories are not considered with the other drugs. However, care should be exercised when breast-feeding mothers use these drugs. Some systemic absorption occurs and may be passed along in breast milk.

Interactions

Erythromycin and Clindamycin interact with other acne products containing benzoyl peroxide, tretinoin, or salicylic acid.

Patient information

1. This product should not be applied to severe burns, animal bites, or large areas of damaged skin.
2. For external use only. Avoid contact with eyes. If this preparation comes in contact with your eyes, rinse with cool water.

3. Use exactly as directed for the complete length of time prescribed. It is very important that the patient complete the full course of treatment.
4. Do not stop using unless advised by your healthcare provider.
5. Wash hands before and after use.
6. Wash affected area and gently pat dry. Apply a thin layer of the product to the affected area as often as prescribed by your healthcare provider.
7. Do not use topical (skin) products near eyes, nose, or mouth.
8. Alcohol in some products can burn and irritate the eyes or tender membranes of the mouth or nose.
9. Apply missed doses as soon as possible after the dose was due, but not if it is almost time for you next dose; do not double or use extra doses.
10. Some circumstances require individual instructions:

Special Circumstance	Instructions
Acne medications only	This medication will not cure your acne. However, keep using this product for the entire course of treatment to keep your condition under control. Do not stop using this product if your acne begins to improve within a few days.
Acyclovir only	<ol style="list-style-type: none"> 1. Ointment must thoroughly cover all lesions. Use a finger cot or rubber glove when applying ointment to prevent spread of infection. 2. May cause transient burning, stinging, itching and rash; notify physician if these become pronounced or persist. 3. Acyclovir ointment is not a cure for herpes simplex infections, and it is of little benefit in treating recurrent attacks.

Anti-fungal agents

A crucial factor for the successful treatment of fungal infection of the skin is an understanding of the kinetics of turnover of epidermal cells. Microorganisms in glabrous (non-hairy) skin inhabit the stratum corneum, which is normally replaced every two to three weeks. Since the primary effect of most antifungal agents is to prevent colonization of new tissue by the organisms, any agent should be used for a minimum of four weeks to fully kill the infection. Infections of the hair begin at the root, 3 to 4 millimeters below the surface of the skin. Because scalp hair grows about 1 millimeter per week, treatment should be continued for 4 to 6 weeks to cure infected hair. Many fungal infections of the nails begin in the matrix; a cure, therefore, consists of removing the organism from that protected site. This can take 6 to 12 months for fingernails and 12 to 24 months for toenails.

Fungal treatment can be oral or topical. This lesson will cover both routes of administration. The same drugs may appear in both sections of the lesson, but we'll try to keep them clear for you.

Oral anti-fungals

Drug	Dosage form	Indication	Duration of treatment
Griseofulvin	250,330 mg tablets (ultramicrosized)	Tinea corporis, pedis, cruris, onychomycosis	Skin- 4 to 8 weeks Nails- 4-6 months (at least)

Drug	Dosage form	Indication	Duration of treatment
Nystatin	500,000 tablet, 100,000 unit/ml suspension, 200,000 unit troche	Intestinal candidiasis (tablets) Oral candidiasis (susp, troche)	48 hours after symptoms subside
Fluconazole	50, 100, 150, 200 mg tablet; 10,40 mg/ml susp	Vaginal candidiasis	One 150 mg dose
Itraconazole	100 mg capsule	Onychomycosis	200mg daily for 12 weeks
Terbinafine	250 mg tablet	Onychomycosis	250 mg daily for 6–12 weeks

Contraindications

Hypersensitivity to any component of these drugs.

Warnings

All of the medications except nystatin are in pregnancy category C. These medications should not be given to breast-feeding mothers

Interactions

Interactions for each of these drugs is very different and will be listed separately.

Drug	Interaction
Nystatin	None
Griseofulvin	Should not be taken with or extreme caution used with: <ol style="list-style-type: none"> 1. Anticoagulants—anticoagulant activity is lowered. 2. Oral contraceptives—loss of contraceptive effectiveness. 3. Cyclosporine—reduced cyclosporine levels.
Fluconazole	<ol style="list-style-type: none"> 1. Cimetidine – reduced fluconazole levels. 2. HCTZ – increased fluconazole levels. 3. Oral contraceptives – decreased contraceptive effectiveness.
Terbinafine	<ol style="list-style-type: none"> 1. Cimetidine—increased levels of terbinafine. 2. Rifampin—decreased levels of terbinafine.
Itraconazole	<ol style="list-style-type: none"> 1. Calcium channel blockers—patients develop edema. 2. Digoxin—increased digoxin levels.

Patient information

Drug	Information
Nystatin	Continue therapy for at least 2 days after symptoms have disappeared.

Drug	Information
Griseofulvin	<ol style="list-style-type: none"> 1. Beneficial effects may not be noticeable for some time; continue taking medication for entire course of therapy. 2. Photosensitivity reactions may occur; avoid prolonged exposure to sunlight or sunlamps. 3. Notify physician if fever, sore throat, or skin rash occurs.
Fluconazole	None
Itraconazole	Take this medication after a meal.
Terbinafine	Be sure to continue this medication for the full course of therapy.

Topical anti-fungals

Drug	Dosage form	Indications
Nystatin	Cream, ointment	Topical candidial infections
Ketoconazole	Cream, shampoo	Tinea pedis, cruris, coporis (cream), dandruff (shampoo)
Clotrimazole	Cream, solution, lotion	Tinea pedis, cruris, coporis
Terbinafine	Cream	Tinea pedis, cruris, coporis
Tolnaftate	Cream, solution, gel, powder, spray	Tinea pedis, cruris, coporis
Gentian violet	solution	Anti-infective

These medications may be used alone in milder cases of fungal infections or in addition to treatment with systemic medication.

Contraindications

A history of sensitivity to any component of these medications.

Warnings

1. None of these medications is to be used near the eyes
2. Ketoconazole and Clotrimazole are pregnancy category C. Terbenifine is category B. Nystatin, Tolnaftate, and Gentian violet are not discussed in pregnancy warnings.

Interactions

The topical forms of these drugs do not interact with other medications.

Patient information

1. For external use only. Avoid contact with the eyes.
2. Apply after cleansing affected area (unless directed otherwise).
3. If condition persists or worsens, or if irritation occurs, discontinue use and notify physician.
4. Use the medication for the full treatment time even though the symptoms may have improved. Notify physician if no improvement.
5. Inform the physician if the area of application shows signs of increased irritation (e.g., redness, itching, burning, blistering, swelling, or oozing) indicative of possible sensitization.
6. For athlete's foot, wear well-fitting, ventilated shoes; change shoes and socks at least once a day.

7. Gentian violet will stain skin and clothing.
8. Do not apply gentian violet to an ulcerative lesion; may result in “tattooing” of the skin.
9. Ketoconazole shampoo: May remove curl from permanently waved hair.

Scabicides/Pediculocides

These classes of drugs get rid of those little bugs (I’m itching just thinking about them). Lindane and permethrin kill both scabies and lice by disrupting their nervous system. Crotamiton is only a scabicide; it’s unclear how it works.

Drug	Dosage form	Application time	Indication
Lindane	Lotion	12 hours	Pubic lice, scabies
	Shampoo	4 minutes	Head lice
Crotamiton	Cream (vanishing)	2 applications in 24 hours	Scabies
Permethrin	Cream	8–14 hours	Body lice, scabies
	Liquid	10 minutes	Head lice

Contraindications

Lindane is contraindicated in young children due to their low skin surface to weight ratio.

Warnings

Lindane and Permethrins are pregnancy category B; Crotamiton is in category C. Lactating mothers should stop breast-feeding while using these medications.

Interactions

These topical agents do not interact with other medications.

Patient information

1. Patient instructions and information are available with product. Do not exceed prescribed dosage.
2. For external use only (oral ingestion can lead to serious central nervous system toxicity). Do not apply to face. Avoid eyes; if there is contact, flush well with water for several minutes. Avoid unnecessary skin contact or contact with mucous membranes (e.g., nose, mouth). Wear rubber gloves, particularly when applying to more than one person.
3. Notify physician if condition worsens or if itching, redness, swelling, burning or skin rash occurs.
4. Avoid use on open cuts.
5. Treat sexual partners simultaneously.
6. Patients with scabies should routinely take a bath or shower.
7. Change clothing and bed linen the next day. Contaminated clothing and bed linen should be dry cleaned or washed in the hot cycle of the washing machine.

Topical antineoplastics

Antineoplastic agents prevent the development, growth, or proliferation of malignant cells. In this course we will discuss one topical antineoplastic—Fluorouracil. Topical fluorouracil is available in cream or solution.

Indications

Affects topically superficial basal cell carcinoma.

Contraindications

Hypersensitivity to the drug is the only contraindication

Warnings

Occlusive dressings may increase inflammation around the site of action. A porous gauze dressing may be used for cosmetic reasons without increasing inflammation.

Interactions

Fluorouracil does not interact with any other medication.

Patient information

1. Avoid prolonged exposure to ultraviolet rays or other forms of ultraviolet irradiation while under treatment; intensity of reaction may be increased.
2. If applied with fingers, wash hands immediately afterward. Apply with care near the eyes, nose and mouth.
3. Reaction in the treated areas may be unsightly during therapy and, in some cases, for several weeks following cessation of therapy.
4. This medication is for external use only.

Miscellaneous drugs

There are a few drugs we need to discuss that just don't fall nicely into the other categories. We'll discuss three of these interesting drugs you need to know about.

Minoxidil (topical)

Minoxidil wasn't always a topical agent. Its first uses were as a vasodilator anti-hypertensive. People who used minoxidil noticed the thickening of hair. More research was done and today minoxidil is better known for the alopecia indication than the hypertension indication. Topical minoxidil is available in a solution.

Indications

Topical minoxidil is indicated for alopecia on the vertex (crown area) of the head.

Contraindications

Sensitivity to minoxidil

Warnings

1. Minoxidil is pregnancy category C.
2. If over used, some systemic absorption could occur.
3. Topical minoxidil should not be used with other topical products that may increase absorption.

Interactions

Topical minoxidil does not interact with other medications

Patient information

1. Evidence of hair growth usually will take ≥ 4 months.
2. First hair growth may be soft, downy, colorless hair that is barely visible. After further treatment, the new hair should be the same color and thickness as the other hair on the scalp.
3. If there is no response to treatment after a reasonable period of time (≥ 4 months), consult physician as to whether to discontinue use.
4. If treatment is stopped, new hair will probably be shed within a few months.

5. If one or two daily applications are missed, restart twice-daily application and return to the usual schedule. Do not attempt to make up for missed applications.
6. More frequent applications or use of larger doses (> 1 ml twice a day) will not speed up the process of hair growth and may increase the possibility of side effects.
7. Minoxidil topical solution contains alcohol, which could cause burning or irritation of the eyes, mucous membranes or sensitive skin areas. If accidental contact occurs, bathe the area with large amounts of cool tap water. Consult physician if irritation persists.
8. Apply only to the scalp; do not use on other parts of the body, as absorption of minoxidil may be increased and the risk of side effects may become greater. Do not use if scalp becomes irritated or is sunburned; do not use along with other topical medication on scalp.

Tretinoin

Tretinoin has been used to treat acne vulgaris for a while. It seems to work by decreasing the cohesiveness of follicular epithelial cells. In essence, it flattens the cellular layers so that bacteria can't get stuck in the layers to form the acne. It also increases the turnover of those cells so that older layers of skin shed away quicker and new, clear skin comes to the surface..

Indications

Acne vulgaris

Contraindications

Hypersensitivity to the medication.

Warnings

1. This is for external use only and is to be kept away from the eyes and mouth.
2. Tretinoin is pregnancy category C.

Interactions

1. Sulfur, resorcinol, benzoyl peroxide or salicylic acid: Cautiously use concomitant topical medications because of possible interactions with tretinoin. Significant skin irritation may result.
2. Soaps: Cautiously use medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices, or lime because of possible interactions with tretinoin.

Patient information

1. Before application, thoroughly cleanse the area to be treated.
2. Keep away from eyes, mouth, angles of the nose, and mucous membranes.
3. Avoid excessive exposure to sunlight and sunlamps.
4. Application may cause a transitory feeling of warmth and slight stinging. Redness and peeling may occur with excessive application; if excessive redness or discomfort occurs, decrease or discontinue use temporarily.
5. Normal use of cosmetics is permissible.

Isotretinoin

Before we even start to talk about isotretinoin, it must be stated that if you are pregnant, may be pregnant, or are thinking about getting pregnant, you shouldn't take or even touch this drug. Now, it's ok for technicians to dispense a sealed box of capsules without any risk.

Isotretinoin is a metabolite of vitamin A. Improvement in cystic acne is associated with the reduction in sebum secretion. This is a temporary decrease and is related to dose and treatment duration. It

seems that isotretinoin reduces the size of the sebaceous gland and inhibits its actions. Isotretinoin may also prevent abnormal keratinization (formation of a fibrous protein, keratin, which is found in the skin and continually has to slough away).

Indications

Isotretinoin is indicated for severe cystic acne.

Contraindications

Pregnancy or a sensitivity to parabens (used as a preservative).

Warnings

1. Pregnancy category X.
2. Decreased night vision may occur.
3. Triglyceride levels may increase while taking this medication.

Interactions

1. Vitamin A: To avoid additive toxic effects, do not take concomitantly with isotretinoin.
2. Carbamazepine: Coadministration has resulted in reduced carbamazepine levels.
3. Drug/Food interactions: When taken with food or milk, the absorption of isotretinoin is increased.

Patient information

1. Prior to use, have patients complete a consent form included with package insert.
2. Take with meals. Do not take vitamin supplements containing vitamin A. Avoid alcohol consumption.
3. Women of childbearing potential should practice contraception during therapy and for 1 month before and after therapy. A pregnancy test 2 weeks prior to starting therapy is advised. Notify physician immediately if pregnancy is suspected.
4. A transient exacerbation of acne may occur during the initial period of therapy.
5. May cause photosensitivity; avoid prolonged exposure to sunlight or sunlamps.
6. Report visual disturbances, abdominal pain, rectal bleeding, severe diarrhea, difficulty in controlling blood sugar, and decreased tolerance to contact lens wear to physician immediately.
7. Do not donate blood for transfusion for 30 days after stopping therapy.

Combination drugs

Often a patient requires more than one dermatological agent to treat a condition. Rather than apply two different preparations, the patient may be prescribed a combination preparation. Multitudes of preparations are available. The most common combinations normally include a corticosteroid with an anti-fungal, anti-infective, or some other dermatologic agent (moisturizer, analgesic, etc). Rather than picking just a small sampling, we discuss some generalities of the class and you can use the knowledge that you received earlier in your training to complete the puzzle.

Corticosteroids are used often because they reduce inflammation and itching around an affected area, allowing the secondary medication to effectively cure the problem. Hydrocortisone is commonly used as the corticosteroid portion of combination products. These are normally easy to spot as they usually end in HC (e.g., Anusol HC, Lotrimin HC, Proctofoam HC). Other products may use the suffix *-one* (e.g., hydrocortis*one*, triamcinol*one*, betamethas*one*).

Self-Test Questions

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

206. Drug therapy

1. Define disease.
2. What term is used to describe a disease that has a slow onset and long duration?
3. What are the three goals of drug therapy?
4. What factors affect the length of drug therapy and dosing?

207. Drug therapy in integumentary disease states

1. What class of drugs opposes the action of histamine?
2. What dermatological condition(s) is diphenhydramine used to treat?
3. Why shouldn't patients with lower respiratory disorders use antihistamines?
4. Name four conditions that topical corticosteroids are effective in treating.
5. What are the four categories of topical corticosteroids?
6. For what condition is erythromycin solution indicated?
7. Into which pregnancy category does acyclovir fall?
8. How long is the duration of treatment for toenail fungus?

9. Which two antifungals decrease the effectiveness of oral contraceptives?
10. Which three topical anti-fungals have no pregnancy warning?
11. Which anti-fungal will remove the curl from permed hair?
12. With what medications do scabicides interact?
13. What is the indication for fluorouracil?
14. What was minoxidil used for, before being used for alopecia?
15. What type of patient should never use isotretinoin?
16. What does the suffix "HC" to the name of a drug infer?

Answers to Self-Test Questions

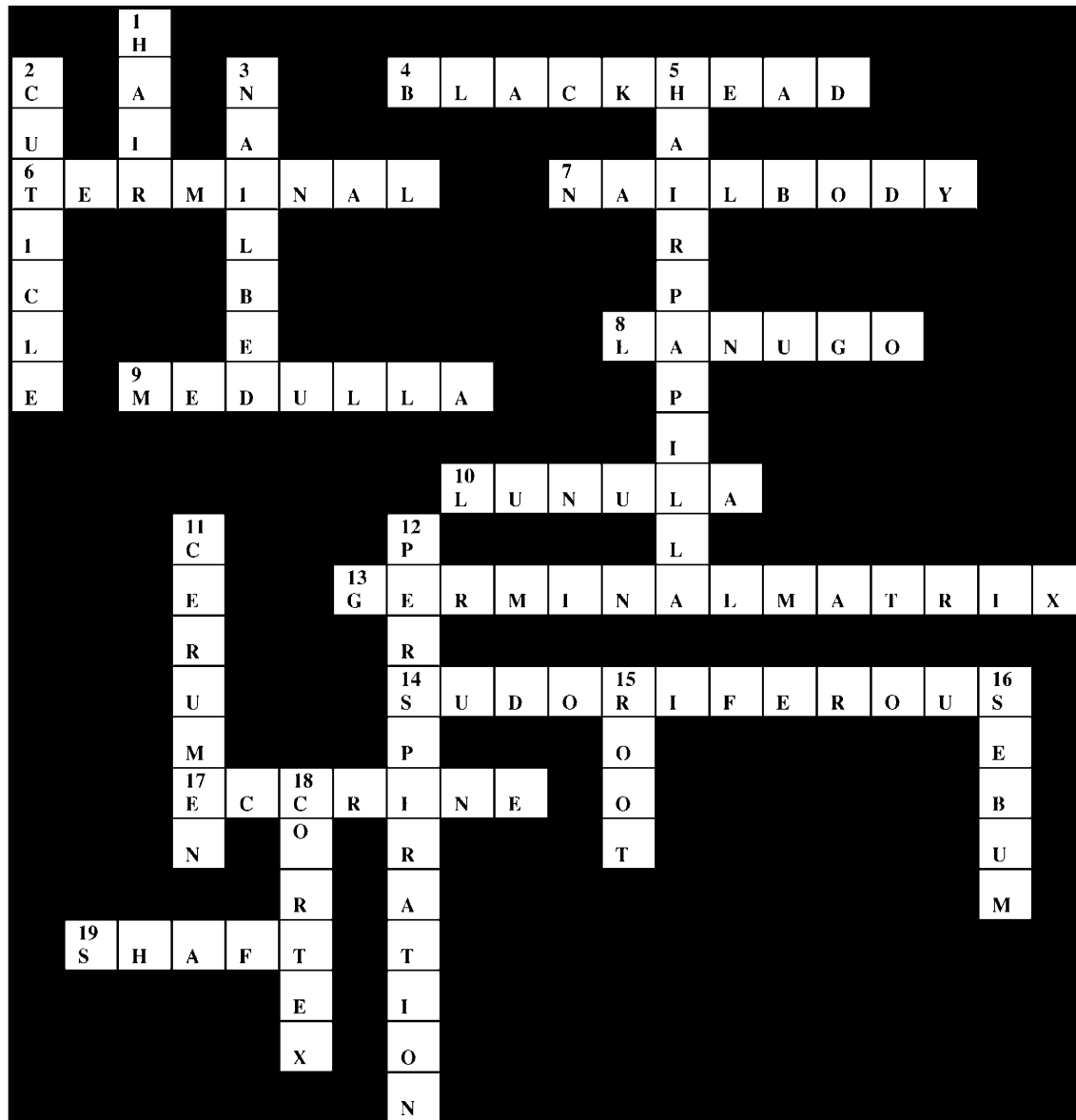
200

1. A cutaneous membrane.
2. The epidermis and dermis.
3. Dermal-epidermal junction.
4. Hypodermis or superficial fascia.
5. Keratinocytes, melanocytes, and Langerhans' cells.
6. Stratum corneum, very thin squamous cells that are dead at the skin surface.
7. The process by which cells in stratum corneum are formed from cells in deeper layers of the epidermis and are then filled with keratin and moved to the surface.
8. Stratum granulosum.
9. Stratum basale.
10. Protection.
11. Corium or true skin.
12. The dermis.
13. Skeletal and smooth muscle fibers.

201

1. Protection, temperature regulation, synthesis of important chemicals and hormones, and excretion of water and salts.
2. The pigments that acts as an effective screen to potentially harmful ultraviolet light.
3. Keratinized stratified squamous epithelial tissue.

202



203

1. The amount of pigment in the epidermis, quantity of blood circulating in the surface blood vessels, and the composition of the circulating blood.
2. Melanin.
3. A peculiar bronze cast to the skin.
4. Erythema.
5. Vesicles or vesicular eruption.

204

1. By the depth of the lesion, as well as the extent (percent of body surface area burned) of the burn.

2. By using the eleven designated areas of the body which are considered to be 9 percent of the overall body. Add up the number of areas burned and multiply by nine.
3. A second-degree burn involves the deep epidermal layers and always causes injury to the upper layers of the dermis. In deep, second-degree burns, damage to sweat glands, hair follicles, and sebaceous glands may occur, but tissue death is not complete. Blisters, severe pain, generalized swelling, and edema characterize this type of burn. Scarring is common.

205

1. Older people who are confined to bed for prolonged periods of time.
2. *Dermatosis* is a common term referring to any skin disease. *Dermatitis* is a term used to describe inflammation of the skin.
3. An acute contagious disease of staphylococcal or streptococcal origin. It manifests itself as blister-like lesions that become filled with pus and contain millions of virulent bacteria.
4. Fungi.
5. Squamous cell carcinoma, basal cell carcinoma, and malignant melanoma.
6. Squamous cell carcinoma.
7. Carbuncles.

206

1. A condition of the living animal or one of its parts that impairs the performance of a vital function.
2. Chronic.
3. Treat the symptoms, prolong life, and cure disease.
4. The patients' age, weight, sex, health, etc., and the drug-half life, route of administration, absorption rate, excretion rate, etc.

207

1. Antihistamines.
2. Pruritis and urticaria.
3. The use of antihistamines may thicken secretions and impair expectoration.
4. Seborrheic dermatitis, localized neurodermatitis, anogenital pruritis, psoriasis.
5. Very high potency, high potency, medium potency, low potency.
6. Acne vulgaris and superficial pyogenic infections .
7. C.
8. 12 to 24 months.
9. Griseofulvin and fluconazole.
10. Nystatin, gentian violet, and Tolnaflate.
11. Ketoconazole shampoo.
12. None.
13. Superficial basal cell carcinoma.
14. An Anti-hypertensive.
15. A pregnant woman.
16. A combination product containing hydrocortisone.

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. (200) Which layer of skin contains fibers that make the skin stretchable and elastic?
 - a. Dermis.
 - b. Reticular.
 - c. Papillary.
 - d. Corium.
2. (201) Which of the following substances is produced by the skin?
 - a. Melanin.
 - b. Serotonin.
 - c. Vitamin D.
 - d. Epithelium.
3. (202) On average, the hair on our heads grows about how many inches per?
 - a. 2.
 - b. 3.
 - c. 4.
 - d. 5.
4. (202) Which of the following is *not* a skin gland?
 - a. Sudoriferous.
 - b. Ceruminous.
 - c. Sebaceous.
 - d. Papillary.
5. (202) Which term is used to describe the shedding of epithelial elements from the skin surface?
 - a. Shedding.
 - b. Sloughing.
 - c. Desquamation.
 - d. Cerumenation.
6. (203) Which condition is caused by the presence of excessive quantities of bilirubin in the blood?
 - a. Jaundice.
 - b. Sunburn.
 - c. Excoriation.
 - d. Hyperpigmentation.
7. (203) Which type of skin eruption is characterized by blisters or small sacs full of fluid?
 - a. Macules.
 - b. Papules.
 - c. Vesicles.
 - d. Pustules.

8. (204) When using the “Rule of Nines” to estimate body surface area, into how many areas is the body divided?
 - a. 8.
 - b. 9.
 - c. 10.
 - d. 11.
9. (204) Which type of burn involves the deep epidermal layers of skin and causes injury to the dermis?
 - a. First degree.
 - b. Second degree.
 - c. Third degree.
 - d. Fourth degree.
10. (205) What condition is found in older people who are confined to bed for prolonged periods of time?
 - a. Impetigo.
 - b. Alopecia.
 - c. Desmosomes.
 - d. Decubitus ulcers.
11. (205) Which skin disorder is characterized by distinct white or yellow spots on nails with surrounding skin becoming red and itchy?
 - a. Eczema.
 - b. Candidia.
 - c. Tinea cruris.
 - d. Onychomycosis.
12. (206) Which term is used to describe a disease which has a slow onset and long duration?
 - a. Acute.
 - b. Chronic.
 - c. Infectious.
 - d. Congenital.
13. (206) Which pregnancy category for drugs states, “There is evidence of human fetal risk, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks”?
 - a. A.
 - b. B.
 - c. C.
 - d. D.
14. (206) Which of the following is *not* an example of drug therapy use in a non-disease state?
 - a. Immunization against diseases.
 - b. Bacteriostatic face wash for acne.
 - c. Contraceptive to prevent pregnancy.
 - d. Antibiotics to prevent infection during surgery.
15. (207) Patients with lower respiratory disorders should *not* use antihistamines because
 - a. the anticholinergic effect will depress respirations.
 - b. the sedatory effect may decrease the ability to exhale.
 - c. they may diminish mental alertness, impairing respiratory ability.
 - d. their drying effect may thicken secretions and impair expectoration.

16. (207) Which type of vehicle is preferred when applying a topical corticosteroid on an oozing lesion or in folds of the skin?
- a. Gel.
 - b. Cream.
 - c. Lotion.
 - d. Ointment.
17. (207) Occlusive dressings are used when applying topical corticosteroids because they
- a. increase skin penetration of the drug.
 - b. decrease the occurrence of fungal infections.
 - c. increase relative potency of the applied drug.
 - d. offer increased protection to the affected area.
18. (207) Which of the following is a contraindication for topical corticosteroids?
- a. Facial use.
 - b. Atopic dermatitis.
 - c. Insect bite reactions.
 - d. First and second degree burns.
19. (207) For which skin disorder is silver sulfadiazine cream indicated?
- a. Burns.
 - b. Impetigo.
 - c. Acne vulgaris.
 - d. Superficial pyogenic infections.
20. (207) What is the primary effect of most anti-fungal agents?
- a. Prevent colonization of new tissue.
 - b. Destroy fungal infections on contact.
 - c. Alter the fungus to a harmless organism.
 - d. Coat the fungus, denying oxygen to the organism.

Unit 2. The Skeletal System

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BONES are the framework of our body. They are made up of a combination of several kinds of tissue and contain blood vessels and nerves. Bones are attached to one another at joints. The combination of bones and joints, together with related connective tissues, form the skeletal system. First we'll discuss bones and joints, then conditions associated with the skeletal system, and finally the drugs used to treat these conditions.

2–1. Anatomy and Physiology of the Skeletal System

This section will take you on a guided tour through the bone portion of the skeletal system. Our tour begins with the structure and function of bones. Then, we'll look at the divisions of the skeleton and landmarks of these bones. We conclude with a discussion of the joints, to include the different types, their function and structure. So fasten your seat belts and put your seats and tray tables in their upright position, we are ready for take-off into the bone portion of the skeletal system.

208. Bone structure and function

The structure portion of this lesson briefly discusses the arrangement of the component parts of the bones. The function portion will only talk about the main function of the bones.

Bone structure

Bones are primarily composed of a bone tissue known as *osseous tissue*. Before we go any farther, I must tell you “bones are anything BUT lifeless!” It is true that the spaces between the cells of bone tissue are permeated with stony deposits of calcium, but these cells are very much alive. Bones have their very own system of blood and lymphatic vessels, and nerves. Bones are organs! In the embryo, which is the early developmental stage of a baby, most of the bones-to-be are cartilage. During the second and third months of embryonic life, bones begin to form. At this point, some bone-building cells, known as *osteoblasts*, become very active. Their first job is to manufacture a substance called *intercellular material*. This intercellular material is located between the cells, and contains large amounts of a protein known as *collagen*. Before long, with the aid of enzymes, calcium compounds are deposited with the intercellular material. There are some other cells, called *osteoclasts*, that are responsible for the process known as *resorption*. Resorption is basically the breakdown of bone. Enzymes also implement this process. Consequently, as a bone grows, alterations to its shape are the outcome of bone being added to some surfaces and resorbed from others.

The processes of bone formation and bone resorption remain active throughout life. Of course, it is more rapid at some times than others. Small children's bones are relatively pliable because they contain a larger proportion of cartilage and a smaller amount of the firm calcium salts than those of adults. Elderly people have much less of the softer tissues like cartilage, and higher proportions of calcium salts. Hence, their bones are more brittle. Bone fractures in elderly people heal with great difficulty, primarily because of this relatively high proportion of inert material and the small amount of the more vascular softer tissues.

I am sure at some time in your life you have heard the words "bone marrow." There are two different types of bone marrow:

1. *Red marrow* is found in certain parts of all bones.
2. *Yellow marrow*, the "soup bone" type, is found mainly in the central cavities of the long bones and is largely made up of fat.

Except for the joint regions, bones are covered on the outside by a membrane called the *periosteum*. The periosteum's inner layer contains osteoblasts, which are required for bone formation, not only during growth, but also in the repair of fractures. The periosteum's blood and lymph vessels play an important role in the nourishment of bone tissue. Let's not forget the nerve fibers. Nerve fibers make their presence known when you suffer a fracture, or when you receive a blow, like hitting your shin. There is also a thinner membrane called the *endosteum*. This membrane lines the marrow cavities of bone. The endosteum also has cells that aid in growth and repair of bone tissue.

Main functions of bones

Bones have quite a large number of functions, many more than we have room to discuss. Many of these functions are not at all obvious. Some of the main functions of bones are:

1. To serve as a firm framework for the entire body.
2. To protect such delicate structures as the brain and spinal cord.
3. To serve as levers, actuated by their attached muscles
4. To serve as a storehouse for calcium, which may be removed to become a part of the blood if there is not enough calcium in the diet.
5. To produce blood cells.

209. Divisions of the skeleton

The skeleton is the complete bony framework of the body (figure 2-1). It may be divided into two main groups of bones:

1. The *axial skeleton* includes the bony framework of the head and trunk.
2. The *appendicular skeleton* forms the framework for the *extremities*—more commonly known as the arms and legs.

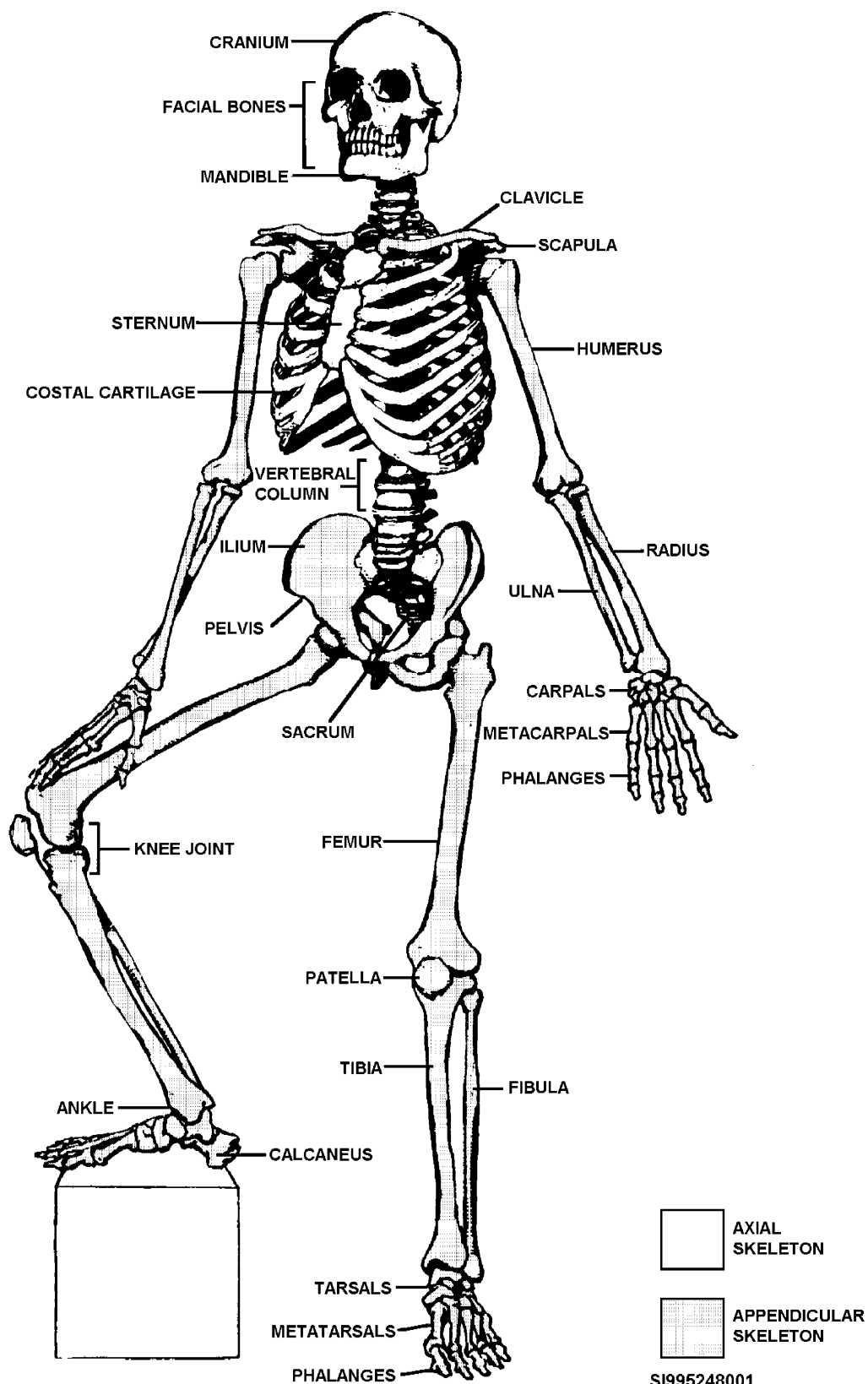


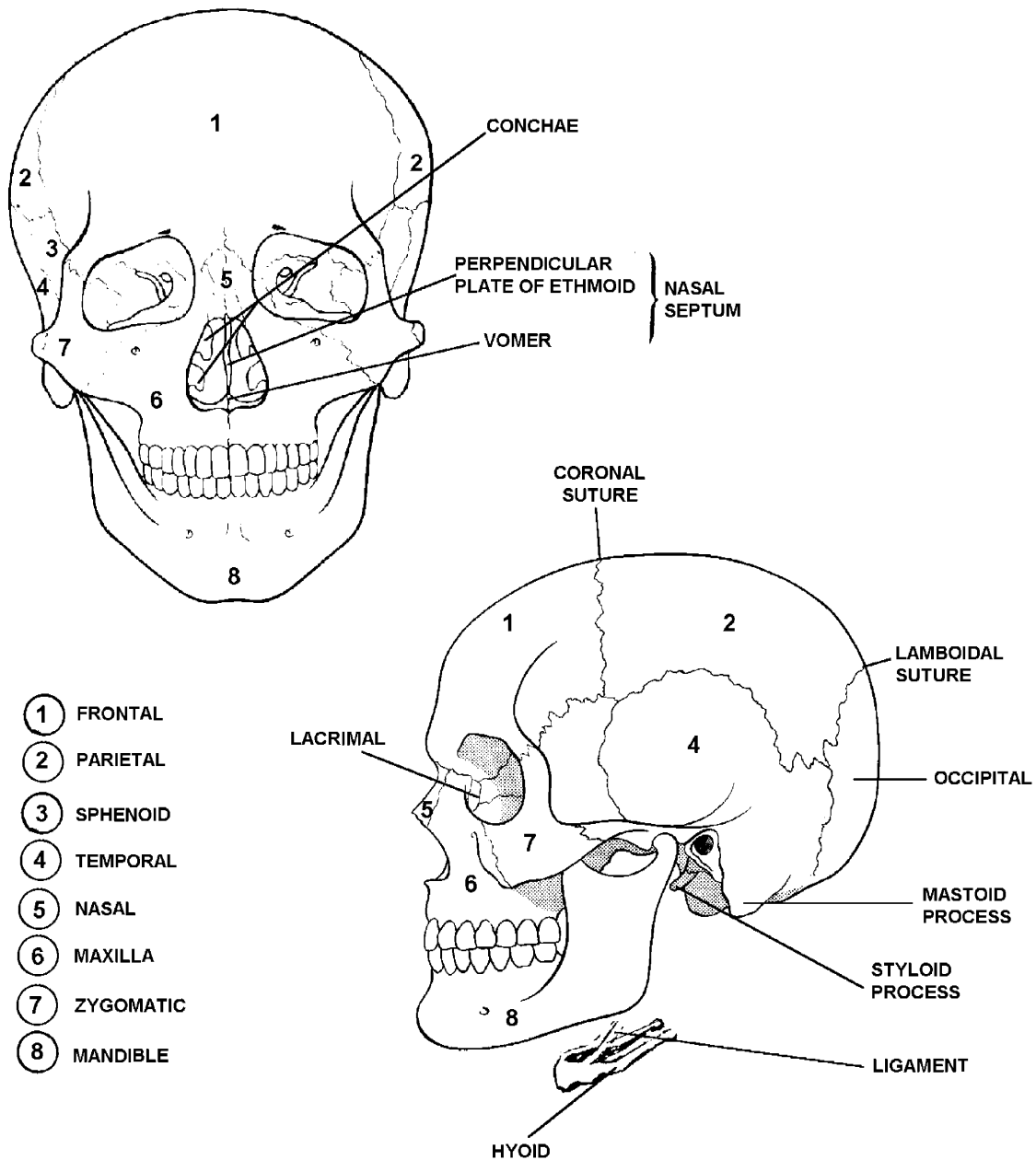
Figure 2-1. The Skeleton

The axial skeleton

Lets take a look at the framework of the head and trunk, beginning with the head.

The framework of the head

The bony framework of the head is known as the *skull*. It is subdivided into two parts: the cranium and the facial portion.



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Figure 2-2. The Skull

The cranium

The cranium is a rounded box enclosing the brain, and is made up of eight distinct cranial bones (figure 2-2).

Bone	Description
Frontal bone	Forms the forehead, the front of the skull's roof. It also helps in forming the roof over the eyes and nasal cavities. Air spaces known as the <i>frontal sinuses</i> communicate with the nasal cavities.
Ethmoid bone	Can be found between the eyes, in the orbital cavities. The upper surface of the ethmoid bone forms the roof of the nasal cavities and part of the base of the cranium. There is also a thin plate of bone extending downward forming the upper part of the nasal septum.
Occipital bone	The back and part of the base of the skull.
Parietal bones (2)	Form most of the top and side walls of the cranium.
Sphenoid bone	When viewed from above, it, looks like a bat with its wings extended. It lies at the base of the skull, in front of the temporal bones.
Temporal bones (2)	Form part of the sides and some of the base of the skull. Each of the temporal bones houses the <i>mastoid sinuses</i> in addition to the ear canal, eardrum, and the entire middle and internal ear.

The facial portion

The facial portion of the skull is made up of 14 bones:

Bone	Description
Hard palate	Roof of the mouth.
Inferior nasal conchae (2)	The two bones that extend horizontally along the lateral wall (sides) of the nasal cavities.
Jaw bone	Is also called the mandible. It is the only movable bone of the skull.
Lacrimal bones	They are about the size of a fingernail. They lie near the inside corner of the eye in the front portion of the medial wall of the orbital cavity.
Maxillae (3)	They fuse in the mid-line to form the upper jaw bone, to include the front part of the hard palate. Each maxilla has a large air space known as the maxillary sinus that communicates with the nasal cavity.
Nasal bones (2)	The two slender bones that lie side by side form the bridge of the nose.
Palatine bones	The back portion of the hard palate is formed from a pair of palatine bones.
Superior and middle conchae	These are paired bones that are part of the ethmoid bone.
Vomer	The lower portion of the nasal septum is formed by the vomer. The vomer is shaped much like the blade of a plow.
Zygomatic bones	The prominence of the cheeks is formed by these bones.

In addition to the facial bones and the bones of the cranium, there are three tiny bones (*ossicles*) in each middle ear. There is also a single U-shaped bone that lies just below the skull proper, known as the *hyoid bone*. The tongue is attached to the hyoid bone.

Many blood vessels, nerves, and other structures enter and exit through spaces made by the openings in the base of the skull. Projections and slightly raised portions of the bones allow for the attachment of muscles. Some parts have delicate structures (e.g., the part of the temporal bone that encloses the middle and internal sections of the ear). The air sinuses furnish lightness and serve as resonating chambers for the voice.

The framework of the trunk

The bones of the trunk include the *vertebral column* and the bones of the *thorax* (chest).

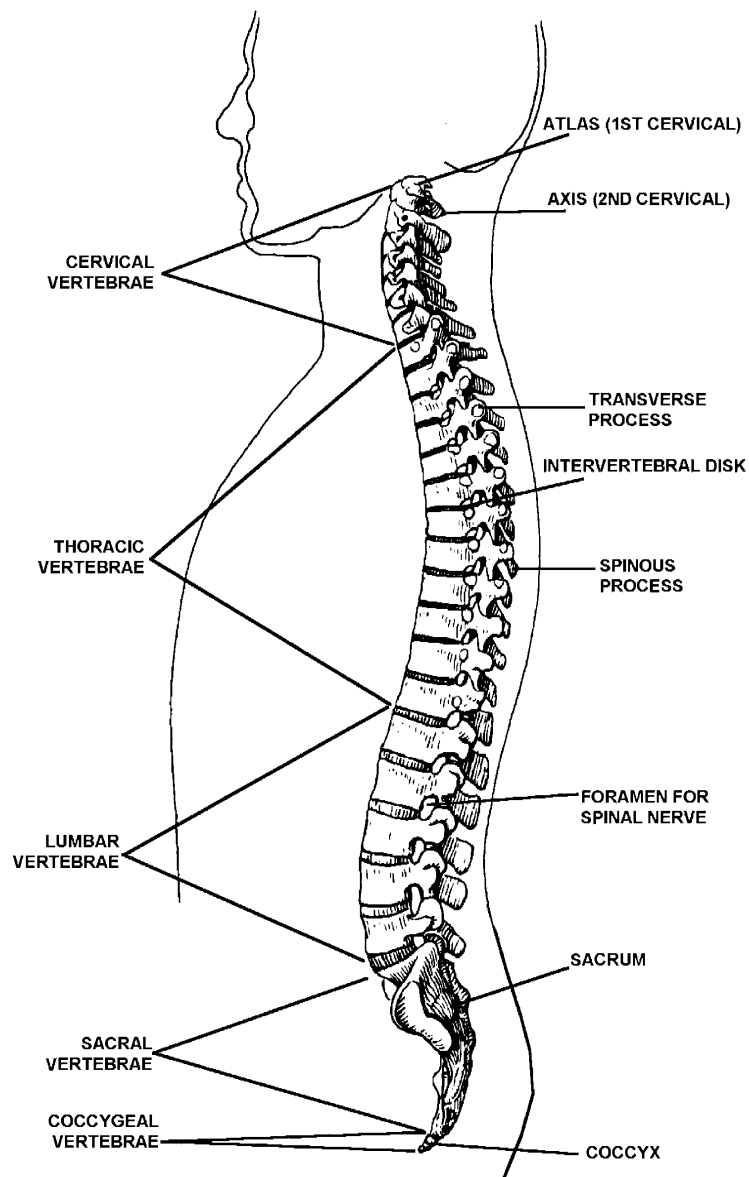
Vertebral column

The vertebral column consists of a series of irregularly shaped bones (fig. 2-3). There are 33 or 34 of these bones in children. Due to unions that occur later in life, in the lower part of the spine, there are usually only 26 separate bones in the adult vertebral column.

Each of these vertebrae, except the first two cervical vertebrae, has a drum-shaped body located anteriorly (toward the front) that serves as the weight-bearing part; disks of cartilage between the vertebral bodies provide flexibility and act as shock absorbers. In the center of each vertebra is a large hole, called the foramen, for the spinal cord. The spinous process protrudes backward from the bony arch that encircles the spinal cord and can normally be felt just under the skin of the back. The vertebrae are linked in series by ligaments (strong connective tissue bands), resulting in a bony cylinder that protects the spine.

The vertebral column's bones (2-4) are named and numbered starting at the neck and moving downward.

1. There are seven cervical vertebrae located in the neck. Two of them are specifically named. The first vertebrae, known as the atlas supports the head. When you nod your head to indicate agreement, the skull (occipital bone) rocks back and forth on the atlas. The second cervical vertebrae, known as the axis, serves as a pivot when you turn your head from side to side to indicate disagreement.
2. There are twelve thoracic vertebrae located in the thorax. The posterior ends of the ribs (12 pairs) are attached to these thoracic vertebrae.
3. There are five lumbar vertebrae located in the small of the back. These vertebrae are larger and heavier than the other vertebrae.
4. There are five separate bones in a child known as the sacral vertebrae. These vertebrae eventually fuse together to form a single bone in adults. This bone is known as the sacrum. The sacrum is wedged between the two hip bones, and serves to complete the posterior portion of the bony pelvis.
5. The tailbone bone is called the coccyx. The coccyx is made up of four or five tiny bones in children. In adulthood these bones fuse together to become a single bone.



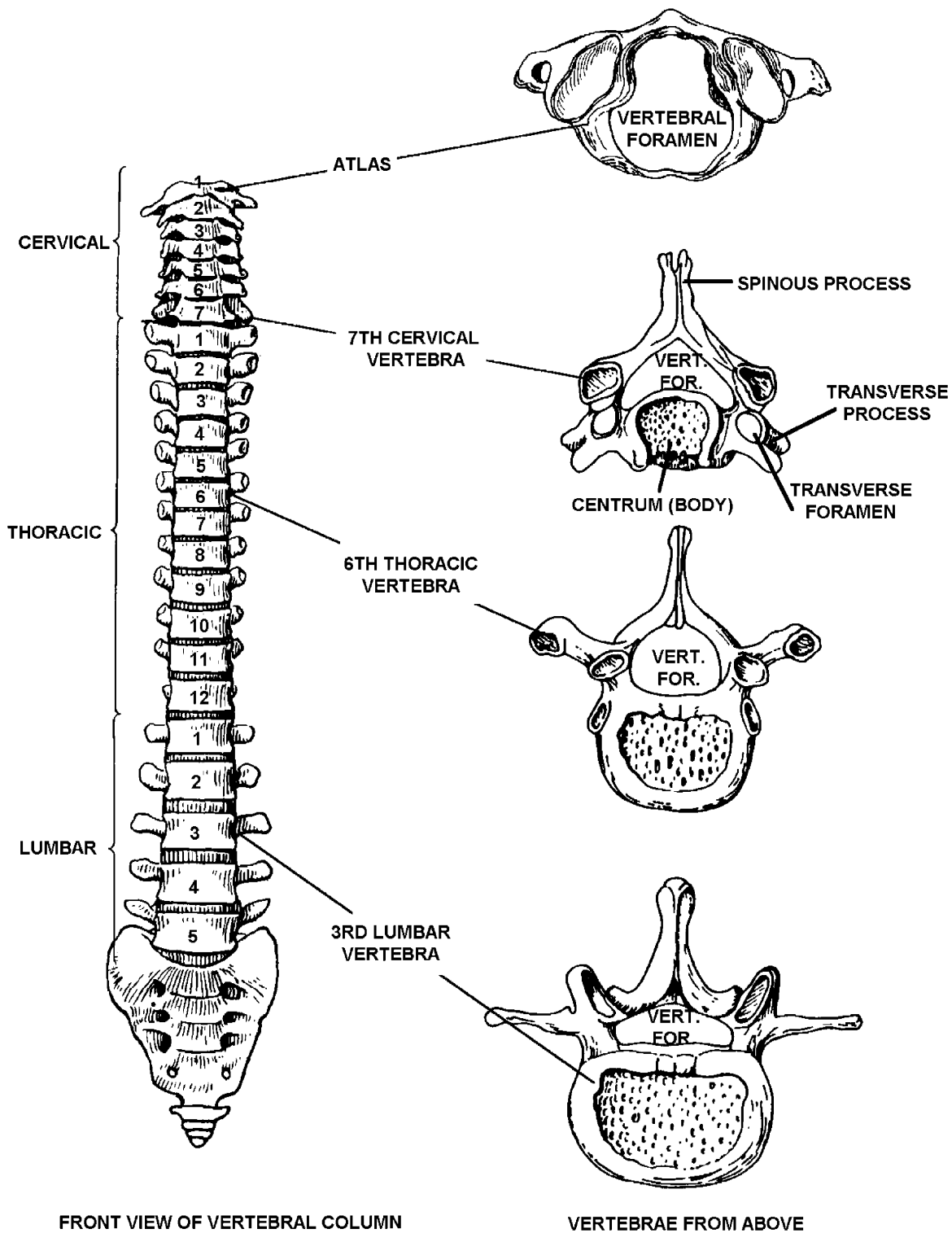
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Figure 2-3. The vertebral column (side view)

If you take a side view, you can see the four curves of the vertebral column (fig. 2-3). These four curves correspond to the four groups of vertebrae. The entire column is concave forward—the primary curve, in newborn infants. As the infant begins to assume an erect posture, secondary curves, those that are concave to the rear, may be seen. For the most part, the cervical curve appears when an infant begins to hold up its head or at about three months, and the lumbar curve appears when it starts to walk. Some of the spring and resilience essential for running and walking is provided by the curves of the vertebral column.

The bones of the thorax

The bones of the thorax form a cone-shaped cage. Twelve pairs of ribs form the bars of this cage. The sternum (breastbone) assists the ribs anteriorly. The thorax serves as protection for the heart, lungs, and other organs.



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Figure 2-4. Vertebral column (front view and above)

All 24 ribs are attached to the posterior side of the vertebral column. But there are some variations in the anterior attachment of these slender, curved bones that lead to the following classifications:

1. The first seven pairs of ribs are called true ribs. These ribs are directly attached to the sternum by individual extensions known as costal cartilages.
2. The remaining five pairs of ribs are called false ribs. The eighth, ninth, and tenth pairs of these ribs attach to the cartilage of the rib above. The last two pairs of ribs have no anterior attachment at all. They are known as floating ribs.

There are muscles, blood vessels, and nerves located in the intercostal spaces (spaces between the ribs).

The appendicular skeleton

The appendicular skeleton forms the framework for the extremities—more commonly known as the arms and legs. Let's look at the bones associated with this division of the skeleton.

The bones of the extremities

The longest bones of the body are in the framework of the extremities. Long bones have a shaft and two ends. The shaft portion of long bones contains a special hollowed-out space called the *medullary cavity*. This space is filled with yellow marrow. The ends of long bones are honeycombed with tiny spaces that contain red marrow. These bone structures are about as light and as strong as a bamboo stick. Some of the other bones of the extremities are flat, some are irregular, and still others are short. Like bones elsewhere in the body, they contain red marrow. There are two divisions of the extremities: upper and lower.

Upper extremities

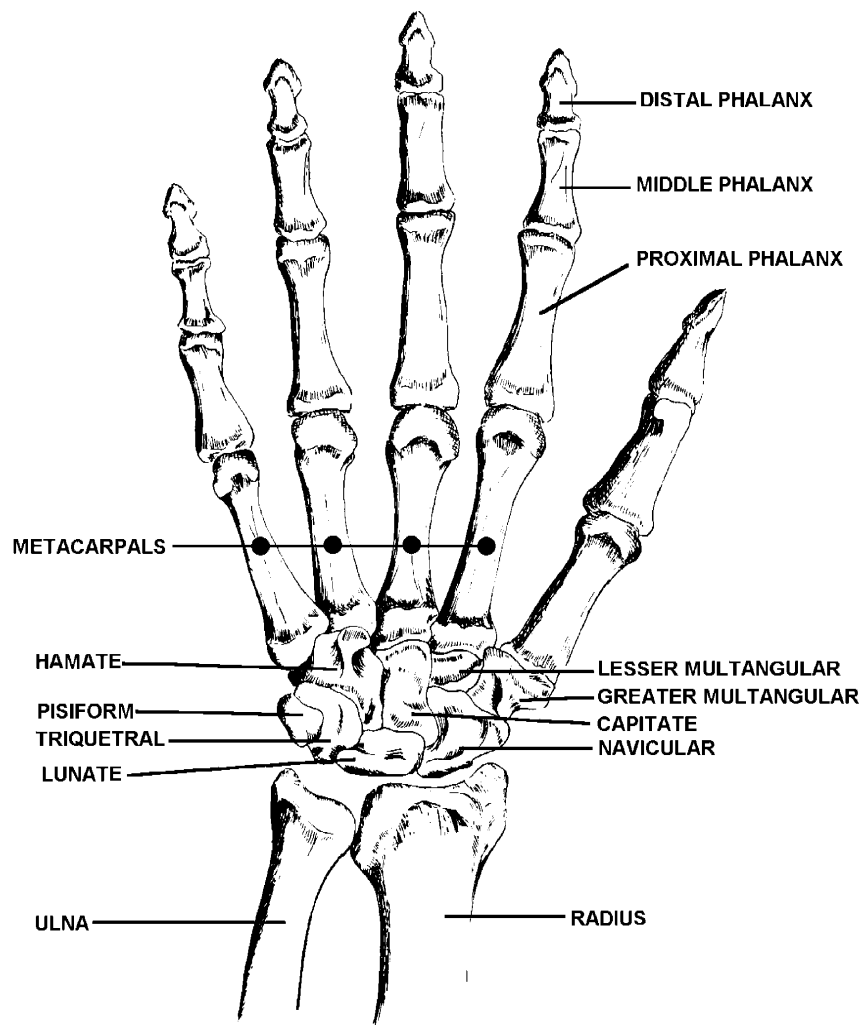
The upper extremities include the following:

1. Shoulders.
2. Arms (between the shoulders and elbows).
3. Forearms (between the elbows and wrists).
4. Wrists.
5. Hands.
6. Fingers.

The bones of the upper extremity may be divided into several groups for ease of study.

Group	Description
Arm bone (humerous)	Form the joint with the scapula and with the two forearm bones at the elbow.
Carpal bones (8)	They are in the wrist, and arranged in two rows of four each. These bones are all different from each other and each has a name of its own (see fig. 2-5).
Forearm bones (ulna)	Lies on the medial (little finger) side, and the radius, on the lateral (thumb) side. If you place your palm in an upright or forward position, the two bones are parallel. If you turn your palm downward, the lower end of the radius moves around the ulna so that the shafts of the two bones are crossed.
Metacarpal (5)	Form the framework of the body of the hand. The rounded distal ends of these bones make the knuckles.

Group	Description
Phalanges (14)	<p>Each hand has 14 of these finger bones. There are two for the thumb and three for each finger. Each of these bones is called a phalanx. They are identified as follows:</p> <ol style="list-style-type: none"> 1. The first, or <i>proximal phalanx</i>, which is attached to the metacarpal. 2. The second, or <i>middle phalanx</i>. 3. The third, or <i>distal phalanx</i>. <p>Obviously, the thumb only has a proximal and distal phalanx.</p>
Shoulder girdle	<ol style="list-style-type: none"> 1. Collar bone (clavicle) 2. Shoulder blade (scapula)



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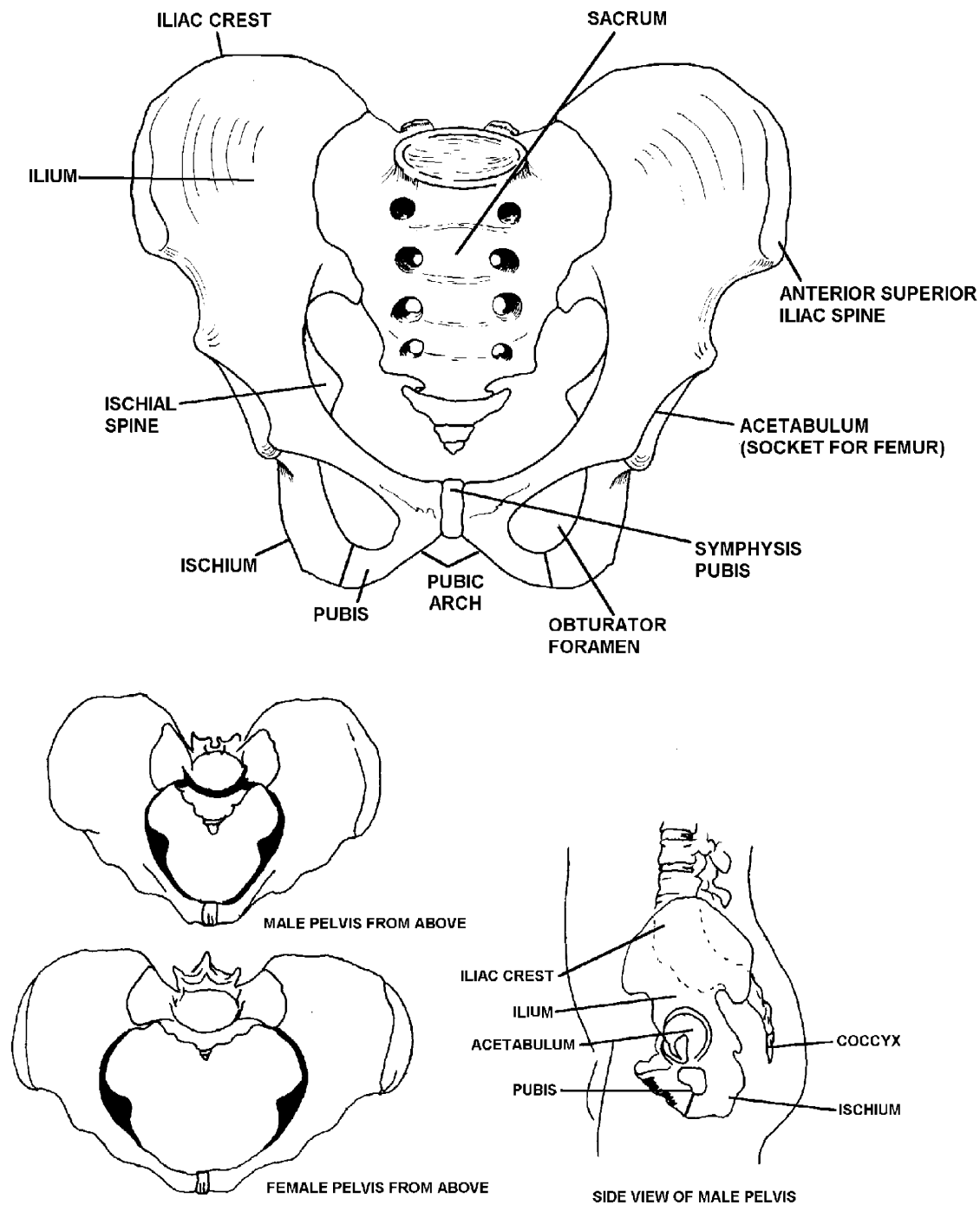
Figure 2-5. The hand (anterior view)

Lower extremities

The lower extremities include the hips (pelvic girdle), the thighs (between the hips and the knees), the legs (between the knees and the ankles), the ankles, the feet, and the toes.

The bones of the lower extremities are group together similarly to the upper extremities.

Group	Description
Foot bones	<p>The foot's structure is much like that of the hand, except that the foot supports the weight of the body, and therefore is stronger and less mobile than the hand.</p> <ol style="list-style-type: none"> 1. Tarsal bones (7) associated with the ankle and foot. The largest of these is the heel bone. It is called the <i>calcaneus</i>. 2. Metatarsal bones (5) make up the framework of the instep, and the heads of the metatarsal bones form the ball of the foot.
Leg bones	<ol style="list-style-type: none"> 1. Tibia, or shin bone, is located medially (on the big toe side), is the longer, weight-bearing bone. 2. Fibula, a slender bone located laterally (little toe side) and does not reach the knee joint, so it is not a weight-bearing bone.
Patella (kneecap)	<p>It is embedded in the tendon of the large anterior thigh muscle, the <i>quadriceps femoris</i>, where it crosses the knee joint. The patella is a <i>sesamoid bone</i>, a type of bone that develops within a tendon or a joint capsule.</p>
Pelvic girdle	<p>A strong bony ring forming the walls of a basin called the <i>pelvis</i>. The pelvic girdle (fig. 2-6) consists of two <i>hip bones</i>, that form the front and the sides of the ring, and the <i>sacrum</i> which articulates or joins with the hip bones to complete the ring at the back (posteriorly). When you talk of one hip bone it is referred to as an <i>os coxae</i>. Each hip bone starts its development in three independent parts:</p> <ol style="list-style-type: none"> 1. The <i>ilium</i>, which forms the upper flared portion. 2. The <i>ischium</i>, which is the lowest and strongest part. 3. The <i>pubis</i>, which forms the anterior part. <p>The joint formed by the anterior juncture of the two hip bones is called <i>symphysis pubis</i>. The bony pelvis supports the trunk and the organs of the lower abdomen (pelvic cavity). These organs include the urinary bladder, the internal reproductive organs, and parts of the intestine. A female's pelvis is adapted for pregnancy and childbirth; therefore, it is broader and lighter than that of the male.</p>
Thigh bone (femur)	<p>The longest and strongest bone in the body.</p>
Toe bones	<p>These toe bones, phalanges, are counterparts of those in the fingers. The great toe has two of these bones, and there are three in each of the other toes.</p>



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Figure 2-6. The pelvic girdle

210. Bone landmarks

Our bones' contour looks very similar to the topography of an interesting and varied landscape with hills and valleys. Projections often act as regions for muscle attachment. There are literally hundreds of these prominences or *processes*, with different names, of course. Lucky for you, we don't have room to list them all here, but we will discuss a few of the more important points of reference.

Landmark	Description
Acetabulum	A deep socket of the hipbone that receives the head of the femur to form the hip joint.
Acromion	Part of the scapula that forms the highest tip of the shoulder. It protrudes over the <i>glenoid cavity</i> , which is a smooth, shallow socket that articulates with the humerus to form the shoulder joint.
Greater trochanter	Part of the femur, it is a very large knob located at the top of the shaft, on the lateral side.
Iliac crest	The curved rim located along the upper border of the ilium. It can be felt near the level of the waist. There are bony projections at either end of the crest. The more prominent one is the <i>anterior superior iliac spine</i> . Each hip bone has three other iliac spines, but the anterior superior iliac spine is the most important. This landmark is often used as a reference point in diagnosis and treatment.
Ischial spine	Located at the back of the pelvic outlet. This landmark is used as a point of reference during childbirth to indicate the progress of the presenting parts (usually the baby's head) down the birth canal.
Ischial tuberosity	This large landmark is located just below the ischial spine. It helps support the weight of the trunk when one sits down.
Lateral malleolus	Is located at the lower end of the fibula, and forms the outgrowth on the outer aspect of the ankle.
Lesser trochanter	A smaller part of the femur that is located on the medial side.
Mastoid process	Part of the temporal bone that protrudes downward closely behind the external part of the ear. It houses the mastoid air cells, and also serves as a place for muscle attachment.
Medial malleolus	The downward projection at the lower end of the tibia. It forms the outgrowth on the inner aspect of the ankle.
Olecranon	Located at the upper end of the ulna, forms the point of the elbow.

The bone landmarks also include some holes in the bones. These holes are called *Foramina*. Numerous foramina allow the passage of blood vessels to and from the bone tissue and the marrow cavities. Larger foramina in the base of the skull and other locations allow for the passage of cranial nerves, blood vessels, and other structures that connect with the brain. The *foramen magnum*, located in the occipital bone, for example, is a large opening through which the spinal cord communicates with the brain. When viewed from the side, the vertebral column can be seen to have a series of *intervertebral foramina*.

These are openings through which the spinal nerves emerge as they leave the spinal cord. The body's largest foramina are found in the pelvic girdle. They are located near the front of each hip bone, one on each side of the symphysis pubis. These foramina are called the *obturator foramina*, and are partially covered by a membrane.

Fossae are valley-like depressions on a bone's surface, the singular form being *fossa*. Some Fossae are filled with muscle tissue, like the large fossae of the two scapulae. The term *groove(s)* is used to describe other depressions of narrow elongated areas. Grooves may allow for the passage of blood vessels or nerves. The grooves of the ribs, for example, contain intercostal nerves and vessels.

211. The joints

Another name for a joint is an *articulation*. Joints are areas of junction or union between two or more bones.

Types of joints

There are three main groups of joints. They are divided on the basis of the degree of movement permitted.

Joint	Description
Amphiarthroses	Slightly immovable joints.
Diarthroses	Freely moveable joints.
Synarthroses	Immovable joints

The structure of joints

Ligaments are the connective tissue bands that hold the bones together. They are found in connection with all the freely moveable joints and a large number of the less moveable joints. In some instances these ligaments completely enclose the joint, these ligaments are called *capsular ligaments*. There are other ligaments that reinforce and help to stabilize joints at various points. There is a smooth layer of gristle covering the contact surfaces of each freely moveable joint, known as *articular cartilage*. Joint spaces have a thick, colorless fluid inside called *synovial fluid*. Synovial fluid resembles uncooked egg whites.

The immovable and slightly movable joints form continuous structures where either cartilage or fibrous connective tissues fill the gaps between the bones. These areas of soft tissue are rather large in children, become smaller in adults, and ultimately may be completely filled with bone in later life. An example of joints that completely disappear, and rather early in life, are the joints between the sacral vertebrae in the lower part of the spinal column. The skull is held together by fibrous connective tissue aided by the dovetailing of somewhat irregular sawtooth type of bone edges.

Functions of the joints

The main function of the freely moveable joints is to allow for changes of position and consequently provide for motion. These movements are named in a manner to describe the nature of the change in the position of the body parts. For example, there are four types of angular movement, or movement that changes the angles between bones:

Motion	Description	Example
Abduction	Movement away from the midline of the body.	Moving the arms straight out to the side.
Adduction	Movement toward the midline of the body.	Bringing the arms back to their original position beside the body.
Extension	A straightening movement that increases the angle between bone.	Straightening of fingers to open the hand.
Flexion	A bending motion that decreases the angle between bones.	Bending of fingers to close the hand.

Circumduction is a combination of these angular movements enabling one to execute a movement. To experience circumduction for yourself, stand with your arm outstretched and draw a large imaginary circle in the air. Notice the smooth combination of flexion, abduction, extension and adduction that makes circumduction possible.

On the other hand, the twisting or turning of a bone on its own axis is called *rotation*. An example of rotation is the turning of the head from side to side as when saying “No.”

There are some special movements characteristic of the forearm and ankle:

1. Turning your palm up or forward is called *supination*.
2. Turning your palm down or backward is called *pronation*.
3. The turning of the sole inward, so it faces the opposite foot is called *inversion*.
4. Turning your sole outward, away from the body is called *eversion*.

This concludes our discussion of the anatomy and physiology of the skeletal system. After answering the self-test questions, you will move on to our next section which covers the conditions associated with the skeletal system.

Self-Test Questions

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

208. Bone structure and function

1. What is the primary tissue that bones are composed of?
2. Why do elderly people have such difficulty with the healing of bone fractures?
3. Except for the joint regions, what membrane covers the outside of bones?

209. Divisions of the skeleton

1. What are the two main groups of skeletal bones?
2. What are the two subdivisions of the skull?
3. Where is the hyoid bone located, and what is attached to this bone?
4. How many bones are in the vertebral column of a child? An adult?
5. How are vertebral column bones named and numbered?
6. How many finger bones are found in each hand?

210. Bone landmarks

1. Where is the mastoid process of the temporal bone located and what is its function?
2. What is the highest tip of the shoulder?
3. What is the most important iliac spine of the hip bone?
4. What term is used to describe holes that extend into or through bones?

211. The joints

1. What are joints?
2. Describe the three main types of joints.
3. What are ligaments?
4. What type of ligaments completely enclose the joint?
5. What is the main function of the freely moveable joints?
6. What is rotation?

2-2. Conditions Associated with the Skeletal System

There are numerous conditions associated with the skeletal system. Some are disorders of the bone and some are disorders of the joints. We discuss both kinds of disorders in this section.

212. Bone disorders

This is just a sampling of the disorders of the bone. Due to lack of space, we will not be able to discuss all the disorders of the bone or discuss the disorders in great detail.

Osteomyelitis

This is an inflammation of bone caused by *pyogenic* bacteria. Osteomyelitis may remain localized or it can spread through the bone, involving the marrow and the periosteum as well. The bacteria may reach the bone in two ways: (1) through the bloodstream or (2) by way of an injury where the skin has been broken. Prior to the advent of antibiotic drugs, bone infections were very resistant to treatment and the likelihood of successful treatment was poor. Currently, we see very few cases of osteomyelitis because many of the bloodstream infections are prevented or treated early enough so that bone infection is less common. The chance of cure is excellent if those that do appear are treated quickly.

Fractures

Almost any bone fracture can be caused by severe violence. The word “fracture” means “a break or rupture in a bone.” Fractures may be classified as follows (fig. 2-7):



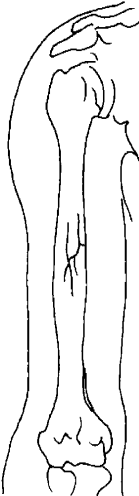

Diagram	Fracture	Description
 <p>COMMINUTED</p>	Comminuted	A fracture in which there is more than one fracture line, resulting in several fragments.
 <p>COMPOUND</p>	Compound	A fracture in which the skin and other soft tissues are torn and the bone protrudes through the skin.

Diagram	Fracture	Description
 <p>GREENSTICK</p> <p>SI995248012</p>	Greenstick	An incomplete break in which the bone splits in much the same way as a piece of green wood might split. This is a common fracture in children.
	Impacted	A fracture in which the broken ends of the bone are jammed into each other.
 <p>SIMPLE</p>	Simple	A fracture in which the break in the bone is not accompanied by a break in the skin.
	Spiral	A fracture in which the bone has been twisted apart. This type of fracture is fairly common in skiing accidents.

If it is ever necessary for you to perform any type of first aid on a person with a fracture, the number one rule is this: prevent movement of the affected parts. You need to evaluate the situation carefully, protect the area with a simple splint, and call for professional help. Victims with back injuries can escape serious spinal cord damage if they are moved *correctly* on a firm board or door. “Hands off” is the rule in these cases if a healthcare provider or ambulance can reach the scene. Cover the victim with blankets to combat shock if there is no external bleeding. Victims with bleeding should always have first aid immediately directed toward the control of hemorrhage.

Rickets

This is mainly a disease of children. An obstruction of growth and the failure of the bones to sufficiently calcify characterize rickets. Calcium and phosphorus deficiencies are the main causes of

rickets. These deficiencies may be the direct result of not having enough minerals in the diet. An indirect cause can be a deficiency of vitamin D, a fat-soluble vitamin that is necessary in order for calcium and phosphorus to be absorbed by the body. In such a case, if foods containing vitamin D are not given, the body will not be able to utilize the minerals, no matter what quantity is taken in with food. Another predisposing factor of rickets is an insufficient exposure to the sun, since the ultraviolet rays of the sun act on the skin to manufacture vitamin D. Rickets is most common among children with heavy pigmentation, and those who grow up in the gloominess of city slums.

One result of rickets is that bones don't calcify sufficiently, and they become soft and easily bent. Certain deformities can result (e.g., bowlegs).

Osteopenia and Osteoporosis

Osteopenia is reduced bone mass due to inadequate osteoid synthesis and is a major risk factor for osteoporosis. Osteoporosis is a skeletal disease characterized by low bone mass and deterioration of bone tissue, leading to enhanced bone fragility and an increase in fracture risk.

Osteoporosis has a much higher incidence in women than in men, and occurs primarily after the menopause. It is also more common in Caucasian than in Black women. Three main factors are responsible for the fragility of bone:

1. Reduced bone mass
2. Impaired repair of the microdamage caused by normal wear and tear of bone.
3. Falls.

213. Joint disorders

Joints are subject to a wide variety of disorders. Some examples are:

- Dislocations and sprains.
- Arthritis.
- Tuberculosis.
- Degenerative joint diseases.
- Gout.
- Backaches.

Dislocations and sprains

A dislocation is a derangement of the parts of the joint. A sprain is the wrenching of a joint with rupture or tearing of ligaments.

Arthritis

Arthritis is the most common type of joint disorder. The term arthritis means "inflammation of the joints." Although there are many types of arthritis, the most familiar type is rheumatoid arthritis. Swelling of the joints in the hands, feet, and other parts of the body due to inflammation and overgrowth of the synovial membrane and other joint tissues characterize this crippling arthritis.

The articular cartilage is slowly destroyed, and the joint ends develop adhesions. These adhesions cause the surfaces to stick together, so that the joints stiffen and ultimately become useless. The cause of rheumatoid arthritis is unknown at this time; however, many believe it to be a disorder of metabolism.

Tuberculosis

The tuberculosis organism can attack the joints as well as bones, resulting in a gradual destruction of parts of the bone near the joints. This organism is carried by the blood stream, most often from a point in the lungs or lymph nodes, and may cause sizable damage before being discovered. The bodies of

several vertebrae may be affected in some patients, while others may experience one hip or other single joint being diseased. Patients may complain only of difficulty walking, and diagnosing this disorder is difficult unless tests have indicated the presence of tuberculosis. This disorder is most common in children.

Degenerative joint diseases

This group of diseases normally occurs in older people. Obesity and repeated trauma can aid in their occurrence. These diseases occur most often in weight-bearing joints. Some of the various degenerative changes in the joints include the following:

1. Formation of spurs at the edges of the articular surfaces.
2. Thickening of the synovial membrane.
3. Atrophy of the cartilages.
4. Calcification of the ligaments.

Another term for these diseases is osteoarthritis.

Gout

This is another type of arthritis, and it is basically caused by a disturbance in metabolism. Uric acid is one of the products of metabolism and is normally excreted in the urine. When not enough uric acid is excreted, or there happens to be an over abundance of uric acid, the accumulated uric acid forms crystals. These crystals are deposited as masses about the joints and other parts of the body. The joints, in turn, become inflamed and extremely painful. Any joint can be affected, but the most common joint affected by gout is the great toe. Men past middle life are the most common victims of gout.

Backache

This is another common complaint made by patients. Some of the causes of backache are:

1. Diseases of the vertebrae, such as infections or tumors. Older people may have degenerative arthritis or atrophy of the bone following long illnesses.
2. Disorders of the intervertebral disks, particularly in the lower lumbar region. Patients may experience severe pain, muscle spasms, and extension of symptoms along the course of the sciatic nerve (back of thigh).
3. Abnormalities of the lower vertebrae or ligaments and other supporting structures.
4. Disorders involving organs of the pelvis or those in the retroperitoneal space (i.e., the pancreas). On rare occasions, variations in the position of the uterus may be a cause.
5. Strains on the lumbosacral (where the lumbar region joins the sacrum) or sacroiliac (where the sacrum joins the ilium of the pelvis) joints.

Self-Test Questions

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

212. Bone disorders

1. What two ways can the bacteria associated with osteomyelitis reach the bone?
2. Describe a greenstick fracture.

3. What is the main cause of rickets?

213. Joint disorders

1. Describe a dislocation.
2. What does the term “arthritis” mean?
3. How is the tuberculosis organism carried to the joints and bones?
4. List four types of degenerative joint diseases.
5. Describe gout.

2–3. Drugs Used to Treat Conditions Associated with the Skeletal System

Several types of drugs are used to treat conditions associated with the skeletal system of bones and joints. The drugs we discuss in this section are the skeletal muscle relaxants, narcotic analgesics, non-narcotic analgesics, non-steroidal anti-inflammatory agents, and anti-gout agents. Remember we will only be discussing these drugs as they apply to treating conditions associated with the skeletal system.

214. Non-narcotic analgesics

Non-narcotic analgesics do exactly as the name implies. They relieve pain without the use of narcotics. This section will be divided into two categories. First we'll discuss acetaminophen and then the class of salicylates.

Acetaminophen (APAP)

Skeletal system indications

Acetaminophen is indicated in the treatment of mild to moderate pain. It provides symptomatic relief only. Additional therapy to treat the cause of pain should be established when necessary. Acetaminophen has minimal anti-inflammatory activity and does not relieve redness, swelling, or stiffness due to arthritis. It cannot be used in place of aspirin or other salicylates or other non-steroidal anti-inflammatory agents in the treatment of rheumatoid arthritis. It may be used to relieve pain due to mild osteoarthritis. Fever reduction comes from APAP's direct action on the hypothalamus where it increases dissipation of body heat through vasodilation and sweating. APAP also inhibits prostaglandin synthesis in the CNS to relieve pain.

Oral Dosing:

1. Adults - 325 to 650 milligram (mg) every 4 to 6 hrs, or 1gram (g) 3 to 4 times/day. Do not exceed 4g / day.
2. Children - May repeat doses every 4 hours; do not exceed 5 doses in 24 hours.

The following table shows the dosing schedule for children.

Age	Dose (mg)	Age	Dose (mg)
0–3 months	40	6–8 years	320
4–11 months	80	9–10 years	400
1–< 2 years	120	11 years	480
2–3 years	160	12–14 years	640
4–5 years	240	> 14 years	650

Suppository dosing:

1. Adults – 650 mg every 4 to 6 hrs. Give no more than 4 g in 24 hours.
2. Children – the following table lists the children's dosage:

Age	Dosage
3 to 11 months	80 mg every 6 hours
1 to 3 years	80 mg every 4 hours
3 to 6 years	120 to 125 mg every 4 to 6 hours. Give ≥ 729 in 24 hours
6 to 12 years	325 mg every 4 to 6 hours. Give ≤ 2.6 g in 24 hours

Contraindications

Acetaminophen is contraindicated only in patients that have shown a sensitivity to it in the past.

Warnings

1. Severe liver damage has occurred in patients using acetaminophen and alcohol. Alcohol users should use as little acetaminophen as possible.
2. Acetaminophen is pregnancy category B. It is also excreted in breast milk with no adverse reactions occurring.

Interactions

1. Large doses or long-term administration of Barbiturates, Carbamazepine, Hydantoins, Isoniazid, and Rifampin may increase the potential hepatotoxicity of APAP. The therapeutic effects of APAP may also be decreased.
2. Propranolol and Probenecid may increase the pharmacologic effects of APAP.
3. Oral contraceptives may decrease the effectiveness of APAP
4. APAP may decrease the effectiveness of loop diuretics.

Patient information

1. Severe or recurrent pain or high or continued fever may indicate serious illness. If pain persists for > 5 days or if redness or swelling is present, consult physician.
2. Do not exceed the recommended dosage. Consult physician for use > 5 days (children), > 10 days (adults), or > 3 days for fever (adults and children).

Salicylates

The salicylates have analgesic, antipyretic and anti-inflammatory effects. Aspirin and other salicylic acid derivatives are changed to salicylic acid. They reduce fever through peripheral vasodilation, enhancing dissipation of excess body heat. The analgesic and anti-inflammatory actions are obtained through the inhibition of prostaglandins. We'll look at Aspirin and Salsalate in this class. All of the information presented is for both of these medications, unless otherwise noted.

Indications

Mild to moderate pain, fever, various inflammatory conditions such as rheumatic fever, rheumatoid arthritis and osteoarthritis.

Contraindications

Hypersensitivity to salicylates or nonsteroidal anti-inflammatory drugs (NSAIDs). Cross-sensitivity may exist between aspirin and other NSAIDs that inhibit prostaglandin synthesis. Aspirin hypersensitivity is more prevalent in those with asthma, nasal polyposis, chronic urticaria.

Salicylates are contraindicated in hemophilia, bleeding ulcers and hemorrhagic states.

Warnings

Condition	Description
Otic effects	Discontinue use if dizziness, ringing in ears (tinnitus) or impaired hearing occurs. Tinnitus probably represents blood salicylic acid levels reaching or exceeding the upper limit of the therapeutic range.
Reye's syndrome	Use of salicylates, particularly aspirin, in children or teenagers with influenza or chickenpox may be associated with development of Reye's syndrome.
Surgical patients	Avoid aspirin, if possible, for 1 week prior to surgery because of the possibility of postoperative bleeding.

Aspirin is pregnancy category D. Salsalate is category C. All salicylates are excreted in breast milk.

Interactions*Drugs affecting salicylates:*

Corticosteroids decrease the effectiveness of aspirin.

Drugs affected by salicylates:

Drug	Affect
Alcohol	The risk of GI ulceration increases when salicylates are given concomitantly.
Angiotensin converting enzyme inhibitors	Antihypertensive effectiveness of these agents may be decreased.
Anticoagulants, oral	Therapeutic aspirin has an additive effect. <ul style="list-style-type: none"> Beta-adrenergic blockers may have their antihypertensive action decreased. Heparin - Aspirin can increase bleeding risk in heparin anticoagulated patients.
Loop diuretics	May be less effective when given with salicylates.
Methotrexate	Salicylates increase drug levels, causing toxicity.
Nitroglycerin	May result in unexpected hypotension.
NSAIDs	Aspirin may decrease NSAID serum concentrations. Concomitant use offers no advantage and may significantly increase incidence of GI effects.

Drug	Affect
Probenecid	Salicylates work against the uricosuric effect.
Sulfonylureas	Salicylates may potentiate the glucose lowering effect of these drugs.
Valproic acid	Aspirin increases the pharmacological effects.

Patient information

1. May cause GI upset; take with food or after meals.
2. Take with a full glass of water (240 ml) to reduce the risk of lodging medication in the esophagus.
3. Patients allergic to tartrazine dye should avoid aspirin .
4. Notify physician if ringing in ears or persistent GI pain occurs.
5. Do not use aspirin when it has a strong vinegar-like odor.

215. Narcotic analgesics

Narcotic analgesics are classified as agonists, mixed agonist-antagonists, or partial agonists by their activity at opioid receptors.

Morphine-like *narcotic agonists* include the natural opium alkaloids (e.g., morphine and codeine), semisynthetic analogs (e.g., hydromorphone, oxymorphone, and oxycodone), and synthetic compounds (e.g., meperidine, levorphanol, and methadone).

Mixed *agonist-antagonist* drugs like nalbuphine and pentazocine have agonist activity at some receptors and antagonist activity at other receptors.

We will only be discussing narcotic analgesics and how they relate to treating conditions associated with the skeletal system. The discussion will cover the class in general and then point out specific drug peculiarities.

Narcotic agonists

Narcotic agonists encompass a group of naturally-occurring, semisynthetic, and synthetic drugs which effectively relieve pain without producing loss of consciousness. They react with five major opioid receptor sites that control analgesia, euphoria, and respiratory and physical depression at the brain stem along with spinal analgesia, sedation, and psychotomimetic effects (hallucinations). These drugs have the potential to produce physical dependence.

Indications

Relief of moderate to severe pain, preoperative medication, and as analgesic adjuncts during anesthesia.

Contraindications

Hypersensitivity to narcotics, acute bronchial asthma, and upper airway obstruction.

Warnings

The use of narcotic analgesics has many side effects. The next table lists the narcotic agonists and some of their side effects.

Drug	Constipation	Respiratory Depression	Sedation	Emesis	Dependency
Codeine	slight	slight	slight	slight	slight
Morphine	moderate	moderate	moderate	moderate	moderate

Oxycodone	moderate	moderate	moderate	moderate	moderate
Meperidine	slight	moderate	slight	N/A	moderate
Propoxyphene	N/A	slight	slight	slight	slight

All of these agents are pregnancy category C. Most of them appear in breast milk. It is recommended that nursing mother wait 4–6 hours after use before nursing.

Drug interactions

No drugs interact with the entire class. The individual interactions will be discussed with the individual drug sections.

Patient information

1. May cause drowsiness, dizziness or blurring of vision; use caution while driving or performing other tasks requiring alertness.
2. Avoid alcohol and other CNS depressants.
3. Notify physician if nausea, vomiting, or constipation becomes prominent.
4. If GI upset occurs, these agents may be taken with food.
5. Notify physician if shortness of breath or difficulty in breathing occurs.

Morphine

Morphine is the principle opium alkaloid. All other narcotic agonists are compared against it.

Administration and dosage

Morphine sulfate is less potent orally because of first-pass metabolism. Oral administration is 1/3 to 1/6 as effective as parenteral administration.

Method	Dosage
Oral	10 – 30 mg every 4 hours or as directed by a provider.
SC/IM	10 mg/70 kg every 4 hours
IV	15 mg/70 kg in 4–5 ml water for injection, administered over 4–5 minutes. Rapid IV infusion increases the incidence of adverse reactions. Do not give IV unless a narcotic antagonist is immediately available.

Meperidine

Meperidine's actions are very similar to morphine's. However, it causes less smooth-muscle spasm and less constipation than morphine.

Administration and dosage

Meperidine's dosage is different for relief of pain and preoperative sedation. We will consider only the dosage for relief of pain. Meperidine is less effective given orally than parenterally. The dosage has to be individualized to 50–150 mg IM, SC, or orally every 3–4 hours.

Drug interactions

Fatal reactions have occurred in people using meperidine concomitantly with MAO inhibitors.

Oxycodone

Oxycodone is indicated for relief of moderate to moderately severe pain. It is not indicated for use in children. The adult dose is 5mg every 6 hours as needed, individualized.

Codeine

Codeine is a narcotic analgesic that pharmacologically resembles morphine, but has milder actions. Codeine is used more for its antitussive properties than its analgesic ones. Codeine is only two-thirds effective orally as parenterally.

The usual adult dosage for analgesic use is 15 to 60 mg every 4–6 hours, not to exceed 360 mg in 24 hours.

Propoxyphene

Propoxyphene is related to methadone. Propoxyphene is only about half as potent as codeine for analgesic use. Propoxyphene is more effective when combined with other analgesics, either narcotic or non-narcotic. Propoxyphene is available in two salts—hydrochloride and napsylate. Our discussion will focus on the napsylate salt.

Administration and dosage

Propoxyphene napsylate is indicated for relief of mild to moderate pain. The standard dose is 65 mg every 4 hours, not exceeding 390 mg/day.

Drug interactions

1. Propoxyphene has an additive CNS depression effect with barbiturates.
2. Propoxyphene may increase carbamazepine levels, producing dizziness and nausea.
3. The use of cimetidine may cause CNS toxicity involving confusion, disorientation, respiratory depression, apnea, and seizures.
4. Propoxyphene may increase the actions of warfarin.

Narcotic agonist-antagonist

The narcotic agonist-antagonist analgesics are potent analgesic agents with a lower abuse potential than pure narcotic agonists. Because of their narcotic antagonist activity, these agents may help with withdrawal symptoms in patients with opiate dependence.

Indications/dosage form

Drug	Available Dosage Forms	Indication	Recommended Dose
Butorphanol	IV, IM, Nasal	Management of pain, including migraine	<ul style="list-style-type: none"> • IV: 1 mg every 3–4 hrs • IM: 2 mg every 3–4 hrs • Nasal: 2 mg (2 sprays) every 3–4 hrs
Nalbuphine	SC, IM, IV	Moderate to severe pain	10 mg/70 kg (20 mg max) every 3–6 hours
Pentazocine	Oral, IM, SC*, IV	Moderate to severe pain	<ul style="list-style-type: none"> • Oral: 50 mg every 3–4 hrs • IM, IV, SC: 30 mg every 3–4 hrs

*tissue damage may occur at injection site

Contraindications

These medications are contraindicated if a patient has shown sensitivity to any of their components.

Warnings

1. Both Pentazocine and Butorphanol are in pregnancy category C. Nalbuphine has no pregnancy category assigned and should be administered to pregnant women only when the benefits outweigh the possible hazards.

- For head injury and increased intracranial pressure, the possible respiratory depressant effects of narcotic analgesics may elevate cerebrospinal fluid pressure. This may be exaggerated in the presence of head injury, intracranial lesions, or a preexisting increase in intracranial pressure.

Drug interactions

All three of these medications may increase the respiratory and CNS depression of barbiturates.

Patient information

- May cause drowsiness; observe caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity.
- Avoid alcohol and other CNS depressants.
- Instruct patients on the proper use of the nasal spray. (Butorphanol only).

216. Nonsteroidal anti-inflammatory drugs (NSAID)

NSAIDs have analgesic, antipyretic, and anti-inflammatory actions. However, the indications for the specific agents may vary because of lack of specific testing and/or clinical-use data, as well as the toxicity of the individual NSAID. Clinically, most of these drugs are used to treat a variety of painful and/or inflammatory conditions. Mechanisms of action vary from prostiglandin suppression (pain), to inhibition of leukotrienes, enzymes, and neutrophils (inflammation). Once again, we will only be discussing these drugs as they apply to treating conditions associated with the skeletal system.

Drug	Dosing	Analgesic action:	
		Onset (hrs)	Duration (hrs)
Ibuprophen	400–800 mg 3–4 times daily	0.5	4 to 6
Indomethacin	25–50 mg 2–3 times daily	0.5	4 to 6
Nabumetone	1–2 gm once daily	-	-
Naproxen	200–500 mg twice daily	1	up to 7
Oxaprozin	1200 mg once daily	-	-
Piroxicam	20 mg daily	1	48 to 72

Indications

Indication	Ibuprophen	Piroxicam	Naproxen	Indomethacin	Nabumetone	Oxaprozin
Acute gout			X	X		
Acute Migraine			X			
Ankylosing spondylitis			X	X		
Bursitis			X	X		
Dysmenorrhea	X	X	X	X		
Fever	X		X			
Migraine Prophylaxis			X	X		
Mild to moderate pain	X		X			

Indication	Ibuprophen	Piroxicam	Naproxen	Indomethacin	Nabumetone	Oxaprozin
Osteoarthritis	X	X	X	X	X	X
Premenstrual syndrome			X			
Rheumatoid Arthritis	X	X	X	X	X	X
Tendinitis			X	X		

Contraindications

All NSAIDs are contraindicated in patients who are sensitive to aspirin.

Warnings

1. GI upset, bleeding, ulceration, and perforation can occur during chronic NSAID therapy.
2. Naproxen is pregnancy category B with nabumetone and oxaprozin being in category C. Safety for use in pregnancy has not been established.

Drug interactions

The following drugs affect NSAIDs:

1. Cimetidine – may increase or decrease NSAID effects.
2. Probenecid – increases NSAID effects, possible toxicity.
3. Salicylates – decreases effects of NSAIDs and increases side effects.

NSAIDs affect the following drugs:

Drug	Reaction
Anticoagulants	May increase prothrombine time.
ACE inhibitors	NSAIDs decrease their effects.
Beta blockers	Effects may be decreased.
Cyclosporine	Nephrotoxicity of both may be increased.
Digoxin	Digoxin levels may be increased.
Hydantoins	Increased toxic effects of phenytoin may occur.
Lithium	Lithium levels may be increased.
Loop diuretics	Diuretic effect may be decreased.
Sympathomimetics	Increased blood pressure may result.
Thiazide diuretics	Decreased anti-hypertensive effects may occur.

Patient information

Side effects of NSAIDs can cause discomfort and, rarely, more serious side effects such as GI bleeding which may result in hospitalization and even fatalities. NSAIDs are often essential in the management of arthritis and have a major role in treating pain, but they also may be commonly employed for less serious conditions. Apprise patients of potential risks.

1. Avoid aspirin and alcoholic beverages while taking medication.
2. If GI upset occurs, take with food, milk or antacids. If GI symptoms persist, notify physician.
3. May cause drowsiness, dizziness or blurred vision; patients should observe caution while driving or performing other tasks requiring alertness.

4. Notify physician if skin rash, itching, visual disturbances, weight gain, edema, black stools, or persistent headache occurs.
5. Ibuprofen (otc use): Do not take for > 3 days for fever, or 10 days for pain. If these symptoms persist, worsen or if new symptoms develop, contact a physician.

217. Anti-gout medications

If you will recall, gout is basically caused by a disturbance in metabolism. Uric acid is one of the products of metabolism and is normally excreted in the urine. When not enough uric acid is excreted, or there happens to be an over abundance of uric acid, the accumulated uric acid forms crystals. These crystals are deposited as masses about the joints and other parts of the body. The joints, in turn, become inflamed and extremely painful. Any joint can be affected, but the most common joint affected by gout is the great toe. This lesson discusses some of the medications used in the treatment of gout. These agents don't group well together, so we'll have to look at them one at a time.

Allopurinol

Indications and dosage

Allopurinol is indicated for managing gout, both long term and acute attacks. It works by inhibiting xanthine oxidase, the enzyme responsible for converting xanthine to uric acid. The average dose is 200 to 300 mg/day for mild gout and 400 to 600 mg/day for moderate to severe gout. Divide doses that are > 300 mg. The minimum effective dose is 100 to 200 mg daily; the maximum recommended dose is 800 mg/day. Allopurinol is available in 100 and 300 mg tablets.

Contraindications

Some patients have severe reactions to allopurinol. Do not try to restart these patients on this drug. Do not use allopurinol to treat asymptomatic hyperuricemia.

Warnings

Allopurinol is pregnancy category C. Use only when clearly needed. Allopurinol is excreted into breast milk and extreme caution should be used in lactating mothers. Allopurinol is rarely indicated in children.

Drug interactions

The following drugs affect allopurinol:

1. ACE inhibitors – a higher risk of hypersensitivity reactions occurs.
2. Thiazide diuretics – may increase the incidence of hypersensitivity reactions.

Allopurinol affects the following drugs:

1. Ampicillin – increased skin rash may occur.
2. Anticoagulants – anticoagulant action may be enhanced.
3. Theophyllines – possible theophylline toxicity.

Patient information

1. Allopurinol is better tolerated if taken with food or milk.
2. Drink at least 10 to 12 (8 oz.) glasses of fluids per day.
3. May produce drowsiness; observe caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity.
4. Notify physician if skin rash, painful urination, blood in the urine, irritation of the eyes, or swelling of the lips and mouth occurs.
5. Remind patients to continue drug therapy prescribed for gouty attacks since optimal benefit may be delayed for 2 to 6 weeks .

6. Urinary acidification with large doses of vitamin C may increase the possibility of kidney stone formation.

Colchicine

Indications and dosage

Relieves pain in acute gout attacks. May be used to prevent acute attacks. Used prophylactically between attacks. Oral doses for acute gouty arthritis would be an initial 1 to 1.2 mg followed by 0.5 to 1.2 mg doses every 1–2 hours. For prophylaxis, if patients have less than 1 yearly attack, the usual dose is 0.5 to 0.6 mg daily 3–4 days weekly. In patients who have more than 1 yearly attack, use the same dose every day.

Contraindications

Colchicine is contraindicated in patients with renal, cardiac, or hepatic disorders.

Warnings

1. Vomiting, diarrhea, nausea, and abdominal pain may occur, especially at maximum doses.
2. Oral colchicine is pregnancy category C and parenteral is D. Colchicine can cause fetal harm when given to a pregnant woman. It's not known if colchicine is excreted into breast milk.
3. There are no studies in the use of colchicine on children.

Drug interactions

No interactions have been reported.

Patient information

1. Notify physician if skin rash, sore throat, fever, unusual bleeding, bruising, tiredness, weakness, numbness, or tingling occurs.
2. Discontinue medication as soon as gout pain is relieved or at the first sign of nausea, vomiting, stomach pain, or diarrhea. If symptoms persist, notify physician.

Probenecid

Indications and dosage

Probenecid increases the excretion of uric acid to effectively decrease deposits. Probenecid therapy shouldn't be started during an acute attack of gout. Continue probenecid therapy if an attack starts during the therapy. Start therapy with 250 mg twice daily for 1 week and then go to 500 mg twice daily. Probenecid is available in 500 mg tablets.

Contraindications

Probenecid shouldn't be used in children under 2 years old or in patients with uric acid kidney stones. Do not start therapy during an acute attack.

Warnings

1. Probenecid may exacerbate gout attacks. Since probenecid is a sulfonamide, patients with sulfa allergies may react to probenecid.
2. Probenecid is in pregnancy category B. It has been used in pregnancy without adverse fetal effects.
3. Do not use probenecid in children under 2 years old.

Drug interactions

Salicylates inhibit the uricosuric action of probenecid.

Probenecid affects the following drugs:

Drug	Reaction
Allopurinol	A beneficial interaction, increases the uricosuric lowering effect.
Benzodiazepines	A more rapid onset and prolonged effect may occur.
NSAIDS	NSAID levels may increase causing toxicity.
Penicillamine	Effects may be increased.
Rifampin	Effects may be increased.
Sulfonamides	Effects may be increased.
Sulfonylureas	Effects may be felt longer.

Patient information

1. Avoid taking aspirin or other salicylates that antagonize the effects of probenecid.
2. May cause GI upset; may be taken with food or antacids. If nausea, vomiting, or loss of appetite persists, notify physician .
3. Drink plenty of water, at least 6 to 8 full (8 oz) glasses daily, to prevent development of kidney stones.

218. Anti-rheumatic agents

Rheumatoid arthritis (RA) can be a devastating disease, severely affecting a patient's quality of life. Nearly 1% of all adults are at risk of developing RA. Unfortunately the exact cause of this debilitating disease is unclear. Because RA is incurable, disease progression can lead to debilitating deformity and substantially affect a patient's quality of life. Therapeutic alternatives in the treatment of rheumatoid arthritis and related conditions include a diverse array of agents ranging from aspirin and similarly acting nonsteroidal anti-inflammatory agents (NSAIDs), to the slow-acting and possibly disease modifying agents such as gold compounds and penicillamine. Because of their toxicity, the slow-acting agents are generally reserved for progressive disease unresponsive to more conservative therapy. The agents we will look at in this section include:

- Hydroxychloroquine.
- Gold compounds.
- Methotrexate.
- Sulfasalazine.

Hydroxychloroquine

Hydroxychloroquine is a compound, similar to chloroquine (the anti-malarial). It's not a first line drug for RA. Hydroxychloroquine works by inhibiting antigens that cause reactions and the development of RA symptoms

Indications and dosage

Hydroxychloroquine is indicated for acute and chronic RA. Its action is slow. Patients start with a 400–600 mg per day dose for 4–12 weeks until a good response is obtained. After that, the dose can be cut in half for maintenance. NSAIDs and steroids can be used with hydroxychloroquine, mainly in the initial phase of treatment. The additional therapy can be reduced or stopped after hydroxychloroquine has been used for several weeks.

Contraindications

Any retinal or visual changes that can be attributed to hydroxychloroquine use or any hypersensitivity to this drug.

Warnings

1. Use in patients with psoriasis may precipitate a severe attack.
2. Irreversible retinal damage may occur with prolonged therapy.
3. Avoid use of hydroxychloroquine during pregnancy. Very low concentrations of hydroxychloroquine appear in breast milk.

Drug interactions

Hydroxychloroquine increases digoxin levels.

Patient information

1. May cause GI upset; take with food or milk.
2. Notify physician if any of the following occur: Blurring or other vision changes; ringing in the ears or hearing loss; fever, sore throat or unusual bleeding or bruising; unusual pigmentation (blue-black) of the skin; muscle weakness; bleaching or loss of hair; mood or mental changes.

Gold compounds

Gold suppresses or prevents, but does not cure arthritis. Its activity results in the inhibition of phagocytosis, decreasing the concentration of rheumatoid factor and immunoglobulins. This activity decreases inflammation and retards cartilage and bone destruction.

Indications and dosage

Gold compounds are indicated in active early rheumatoid arthritis not adequately controlled by other anti-inflammatory agents.

Drug	Dosage form	Dosing
Auranofin	3 mg capsule	6 mg daily in 1 or 2 doses, may increase to 9 mg daily, given in 3 doses
Aurothioglucose	50 mg/ml suspension for injection	Weekly injections, first 10 mg, second and third 25 mg, subsequent 50 mg
Gold Sodium Thiomalate	50 mg/ml injection	same as above

Contraindications

Hypersensitivity, uncontrolled diabetes mellitus, severe debilitation, history of hepatitis, marked hypertension, uncontrolled congenital heart failure (CHF), blood disorders, or any history of adverse reaction to heavy metals.

Warnings

All gold compounds are pregnancy category C. Gold crosses the placenta and is usually contraindicated in pregnant patients. Gold is also excreted into breast milk; therefore, lactating mothers should not be treated with gold compounds.

Drug interactions

Gold compounds may increase phenytoin blood levels.

Patient information

1. Notify physician of the following: itching, rash, sore mouth, indigestion, metallic taste, easy bruising or nosebleed.
2. Increased joint pain may continue 1 or 2 days after an injection and usually subsides after the first few injections.

3. Chrysiasis (gray-to-blue pigmentation) may occur, especially on photoexposed areas. Minimize exposure to sunlight or artificial ultraviolet light.
4. Observe careful oral hygiene in conjunction with therapy.
5. Warn women of childbearing potential of the risks of using gold therapy during pregnancy.

Methotrexate (MTX)

You may already be familiar with methotrexate (MTX) as an antineoplastic agent. MTX is used as a rheumatoid agent because of its effects on articular swelling and tenderness. It does not induce remission of arthritis or have any effect on bone erosion.

Indications and dosage

MTX is indicated in severe, active rheumatoid arthritis. Its use should be secondary in patients who have had poor response or are intolerant of first-line NSAIDs and at least one trial of another anti-rheumatic drug. Dosage of MTX is individualized. Initial therapy is a 7.5 mg weekly dose using 2.5 mg tablets at 12 hour intervals for 3 doses. The schedule is then adjusted to obtain an optimal response, not exceeding 20 mg per week. Therapeutic response usually begins in 3–6 weeks and patients may continue to improve for another 12 weeks. With continued use, the improvements are maintained for up to 2 years. When MTX is discontinued, the arthritis usually worsens within 3–6 weeks.

Contraindications

Pregnant and lactating women, alcoholics, persons with chronic liver disease or evidence of immunodeficiency should not use MTX.

Warnings

MTX is pregnancy category X, may cause fetal death. Because of the potential for serious adverse reactions, MTX should not be used by lactating mothers.

Drug interactions

There are no listed interactions for MTX.

Patient information

There are no specific patient instructions for MTX.

Sulfasalazine

Sulfasalazine is an anti-inflammatory drug that modulates the immune system (lymphocytes and phagocytes) and has an affinity for connective tissue. These properties make it very useful as an anti-rheumatic.

Indications and dosage

Enteric coated sulfasalazine is indicated in rheumatoid arthritis in patients who have responded inadequately to salicylates or other nonsteroidal anti-inflammatory drugs. Sulfasalazine is available in 500 mg tablets, both enteric coated and uncoated. For the RA indication, only use enteric coated sulfasalazine. Start therapy with 500 mg to 1 gm daily, increasing to 2 gms daily in divided doses.

Contraindications

This medication should not be used in children under 2 years old; patients with intestinal obstruction; hypersensitivity to sulfasalazine, salicylates, sulfonyleureas, thiazide, and loop diuretics or sunscreens with PABA.

Warnings

Sulfasalazine is pregnancy category B. Sulfonamides are excreted into breast milk.

Drug interactions

Sulfasalazine inhibits the absorption of both digoxin and folic acid, lowering those drugs' effectiveness.

Patient information

1. If sore throat, fever, pallor, purpura or jaundice occur, patients should contact their physician.
2. Instruct patients to take sulfasalazine enteric coated tablets in evenly divided doses, preferably after meals, and to swallow the tablets whole.
3. Advise patients that sulfasalazine may produce an orange-yellow discoloration of the urine or skin.
4. Instruct patients to drink plenty of water.

Self-Test Questions

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

214. Non-narcotic analgesics

1. What warning is given to alcohol users about acetaminophen?
2. What drug interaction may occur if acetaminophen is administered in combination with loop diuretics?
3. What drug interaction may occur if aspirin is administered concurrently with nitroglycerin?

215. Narcotic analgesics

1. Is the difference included? What are the three types of narcotic analgesics?
2. What narcotic analgesic are all others compared against?
3. What interaction may occur between meperidine and MAO inhibitors?
4. What injectable drug may cause tissue damage at the injection site when given subcutaneously?
5. What may happen if narcotic analgesics are administered to patients with head injuries?
6. What possible drug interaction exists between propoxyphene and cimetidine?

7. What narcotic analgesic is available in a nasal spray?

216. Nonsteroidal anti-inflammatory drugs (NSAID)

1. What are the skeletal system indications of naproxen?
2. What possible drug interaction exists between ibuprofen and digoxin?
3. What possible drug interaction exists between nabumetone and cyclosporine?

217. Anti-gout medications

1. What possible drug interaction exists between hydrochlorothiazide HCTZ and allopurinol?
2. What possible drug interaction exists between probenecid and allopurinol?
3. Why is probenecid contraindicated in patients with renal impairment?

218. Anti-rheumatic agents

1. Which anti-rheumatic agent is similar to an anti-malarial?
2. How many weeks may pass before a good response is seen when using hydroxychloroquine?
3. How do gold compounds suppress RA symptoms?
4. What are the contraindications to gold compounds?
5. How is methotrexate dosed?
6. How does sulfasalazine work?

7. What two drugs does sulfasalazine interact with? What is the interaction?

Answers to Self-Test Questions

208

1. Osseous tissue.
2. Because their bones contain a high proportion of inert material and a small amount of vascular softer tissues.
3. Periosteum.

209

1. The axial skeleton and appendicular skeleton.
2. The cranium and the facial portion.
3. It lies just below the skull proper, and the tongue is attached to the hyoid bone.
4. 33 to 34 in children, and 26 in adults.
5. From above downward, and on the basis of their location.
6. 14.

210

1. It is located closely behind the external part of the ear; it houses the mastoid air cells, and serves as a place for muscle attachment.
2. The acromion of the scapula.
3. The anterior superior iliac spine.
4. Foramina.

211

1. Areas of junction or union between two or more bones.
2. (1) The *synarthroses joints* are immovable joints, (2) the *amphiarthroses joints* are the slightly immovable joints, and (3) the *diarthroses joints* are the freely moveable joints.
3. The connective tissue bands that hold the bones together.
4. Capsular ligaments.
5. To allow for changes of position and provide for motion.
6. The twisting or turning of a bone on its own axis.

212

1. (1) Through the bloodstream; or (2) by way of an injury where the skin has been broken.
2. Incomplete breaks in which the bone splits in much the same way as a piece of green wood might.
3. Calcium and phosphorus deficiencies.

213

1. A derangement of the parts of the joint.
2. Inflammation of the joints.
3. By the blood stream.
4. (1) Formation of spurs at the edges of the articular surfaces, (2) thickening of the synovial membrane, and (3) atrophy of the cartilages, and (4) calcification of the ligaments.
5. An overabundance of uric acid forms crystals that are deposited as masses about the joints. The joints become inflamed and extremely painful.

214

1. Severe liver damage has occurred in patient(s) using acetaminophen and alcohol.
2. The effectiveness of loop diuretics is decreased.
3. Unexpected hypotension may result.

215

1. Narcotic agonists and mixed agonist-antagonists. The mixed agonist-antagonists have a lower abuse potential than pure agonists.
2. Morphine
3. Fatal reactions have occurred.
4. Pentazocine
5. The possible respiratory depressant effects of narcotic analgesics may elevate cerebrospinal fluid pressure. This may be exaggerated in the presence of head injury.
6. Increased CNS toxicity involving confusion, disorientation, respiratory depression, apnea, and seizures.
7. Butorphanol

216

1. Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, mild to moderate pain, dysmenorrhea, tendinitis, bursitis, acute gout, fever, acute migraine, migraine prophylaxis, pre-menstrual syndrome.
2. Digoxin levels may be increased.
3. Nephrotoxicity of both drugs may be increased.

217

1. The use may increase the incidence of hypersensitivity reactions.
2. It is a beneficial interaction; the uricosuric lower action may be increased.
3. Due to the formation of uric acid kidney stones.

218

1. Hydroxychloroquine.
2. 4-12 weeks
3. They inhibit phagocytosis, decreasing the concentration of rheumatoid factor and immunoglobulins.
4. Hypersensitivity, uncontrolled diabetes mellitus, severe debilitation, history of hepatitis, marked hypertension, uncontrolled CHF, blood disorders, any history of adverse reaction to heavy metals.
5. Dosage of MTX is individualized. Initial therapy is a 7.5 mg weekly dose using 2.5 mg tablets at 12 hour intervals for 3 doses. The schedule is then adjusted to obtain an optimal response, not exceeding 20 mg per week.
6. It modulates the immune system and has an affinity for connective tissue.
7. Sulfasalazine inhibits the absorption of both digoxin and folic acid, lowering those drugs effectiveness.

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.

21. (208) What type of bone marrow is found mainly in the central cavities of the long bones and is largely made up of fat?
 - a. Red marrow.
 - b. Black marrow.
 - c. White marrow.
 - d. Yellow marrow.
22. (209) Which bones in the cranium house the mastoid sinuses?
 - a. Frontal.
 - b. Occipital.
 - c. Sphenoid.
 - d. Temporal.
23. (209) What part of the human skeleton forms the framework for the extremities?
 - a. Intercostal spaces.
 - b. Coastal cartilages.
 - c. Cervical vertebrae.
 - d. Appendicular skeleton.
24. (210) The bone landmark that forms the point of the elbow is the
 - a. Mastoid process.
 - b. Acetabulum.
 - c. Acromion.
 - d. Olecranon.
25. (210) What are the holes that extend into or through bones to allow the passage of blood vessels called?
 - a. Fossae.
 - b. Foramina.
 - c. Trochanter.
 - d. Intercostal vessels.
26. (211) Which of the following is an immovable joint?
 - a. Amphiarthroses.
 - b. Synarthroses.
 - c. Capsular.
 - d. Articular.
27. (211) Which type of joint movement involves movement away from the midline of the body?
 - a. Flexion.
 - b. Extension.
 - c. Abduction.
 - d. Adduction.
28. (212) The name of the bone disorder that is an inflammation of the bone caused by pyogenic bacteria is
 - a. osteopenia.
 - b. osteoporosis.
 - c. osteoarthritis.
 - d. osteomyelitis.

-
-
29. (212) What is a bone fracture called where there is more than one fracture line, resulting in several fragments?
- Spiral fracture.
 - Greenstick fracture.
 - Comminuted fracture.
 - Compound fracture.
30. (212) What bone disorder is characterized by an obstruction of growth and the failure of the bones to sufficiently calcify?
- Rickets.
 - Scurvey.
 - Beri-beri.
 - Osteoporosis.
31. (213) What bone disorder occurs from an over abundance of uric acid?
- Gout.
 - Tuberculosis.
 - Osteoarthritis.
 - Rheumatoid arthritis.
32. (214) Which non-narcotic analgesic inhibits prostaglandin synthesis in the central nervous system to relieve pain?
- Aspirin.
 - Salsalate.
 - Propoxyphene.
 - Acetaminophen.
33. (215) Which group of narcotic analgesics relieve pain without producing a loss of consciousness?
- Agonists.
 - Antagonists.
 - Partial agonists.
 - Mixed agonist-antagonists.
34. (215) What narcotic analgesic is the principal opium alkaloid?
- Morphine.
 - Oxycodone.
 - Meperidine.
 - Propoxyphene.
35. (215) Which narcotic analgesic pharmacologically resembles morphine, but has milder actions?
- Codeine.
 - Oxycodone.
 - Meperidine.
 - Propoxyphene.
36. (216) What is the only NSAID to have an indication for premenstrual syndrome?
- Naproxen.
 - Piroxicam.
 - Nabumetone.
 - Indomethacin.

37. (216) In which pregnancy category is naproxen?
- a. A.
 - b. B.
 - c. C.
 - d. X.
38. (217) Which anti-gout medication works by the reducing xanthine oxidase?
- a. Colchicine.
 - b. Probenecid.
 - c. Allopurinol.
 - d. Penicillamine.
39. (217) Using which anti-gout medication may exacerbate gout attacks?
- a. Colchicine.
 - b. Probenecid.
 - c. Allopurinol.
 - d. Penicillamine.
40. (218) Which anti-rheumatic agent may cause retina damage or other visual impairment?
- a. Methotrexate.
 - b. Sulfasalazine.
 - c. Gold compounds.
 - d. Hydroxychloroquine.
41. (218) Which anti-rheumatic works by the inhibition of phagocytosis, decreasing the concentration of rheumatoid factor and immunoglobulins.
- a. Methotrexate.
 - b. Sulfasalazine.
 - c. Gold compounds.
 - d. Hydroxychloroquine.
42. (218) Which anti-rheumatic agent may produce an orange-yellow discoloration of the urine or skin?
- a. Methotrexate.
 - b. Sulfasalazine.
 - c. Gold compounds.
 - d. Hydroxychloroquine.

Unit 3. The Muscular System

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THERE are more than 600 muscles in the muscular system (figure 3-1), each of which is a distinct organ. Nonetheless, muscles normally act in groups in order to execute a body movement. Speaking of movement, let's move on. This unit discusses the characteristics of skeletal muscle, the attachments of these muscles, muscle movement, muscles of the head and neck, muscles of the upper extremities, muscles of the trunk, and muscles of the lower extremities. Then we will discuss conditions associated with the muscular system and the drugs used to treat those conditions.

3–1. Anatomy and Physiology of the Muscular System

There are three basic types of muscle tissue: skeletal, smooth, and cardiac. We will only discuss skeletal muscles in this unit.

219. Skeletal muscle characteristics

Skeletal muscle is muscle attached to bones. Skeletal muscles are regarded as organs because each muscle has a connective tissue framework and is supplied with blood vessels and nerves. Additionally, each muscle has specialized muscle cells that are capable of shortening or contracting.

If you were to look through a microscope, muscle cells would look long and threadlike. Hence, the name muscle fibers. These fibers are arranged in bundles, held together by connective tissue. Groups of these bundles are held together by additional connective tissue. In addition, the entire muscle is encased in a tough connective tissue sheath called the epimysium.

An important property of muscle tissue is *excitability*, or *irritability*, which is the capacity to respond to a stimulus. Muscle cells may be excited by chemical, electrical, or mechanical means. Skeletal muscles are normally excited by nerve impulses generated in the brain and spinal cord. Nerve fibers carry impulses to the muscles. Each fiber supplies from a few up to more than one hundred individual muscle cells. Endings of the motor nerve fibers are known as *myoneural junctions* or motor end plates. Stimulus received by way of the end motor plates results in a change called an *action potential* that is transmitted along the cell membrane.

The capacity of a muscle fiber to shorten and change its shape, becoming thicker, is known as *contractility*. Studies of the electron microscope reveal that the cytoplasm of each skeletal muscle fiber contains special protein threads or filaments, known as *actin* and *myosin*. These filaments slide over each other in such a manner that the muscle fiber contracts, or becomes shorter and thicker. These contraction processes need energy; consequently, working muscles require an adequate supply of oxygen and glucose. A substance known as *adenosine triphosphate* (ATP) is the immediate source of energy for muscle contraction. ATP is a temporary energy store that acts as a go-between, because it transfers the energy released during chemical reactions to the muscles and other tissues. Likewise, oxygen plays an important role in preventing the accumulation of lactic acid waste products which can cause muscle fatigue. While performing strenuous activities, a person may not be able to breathe

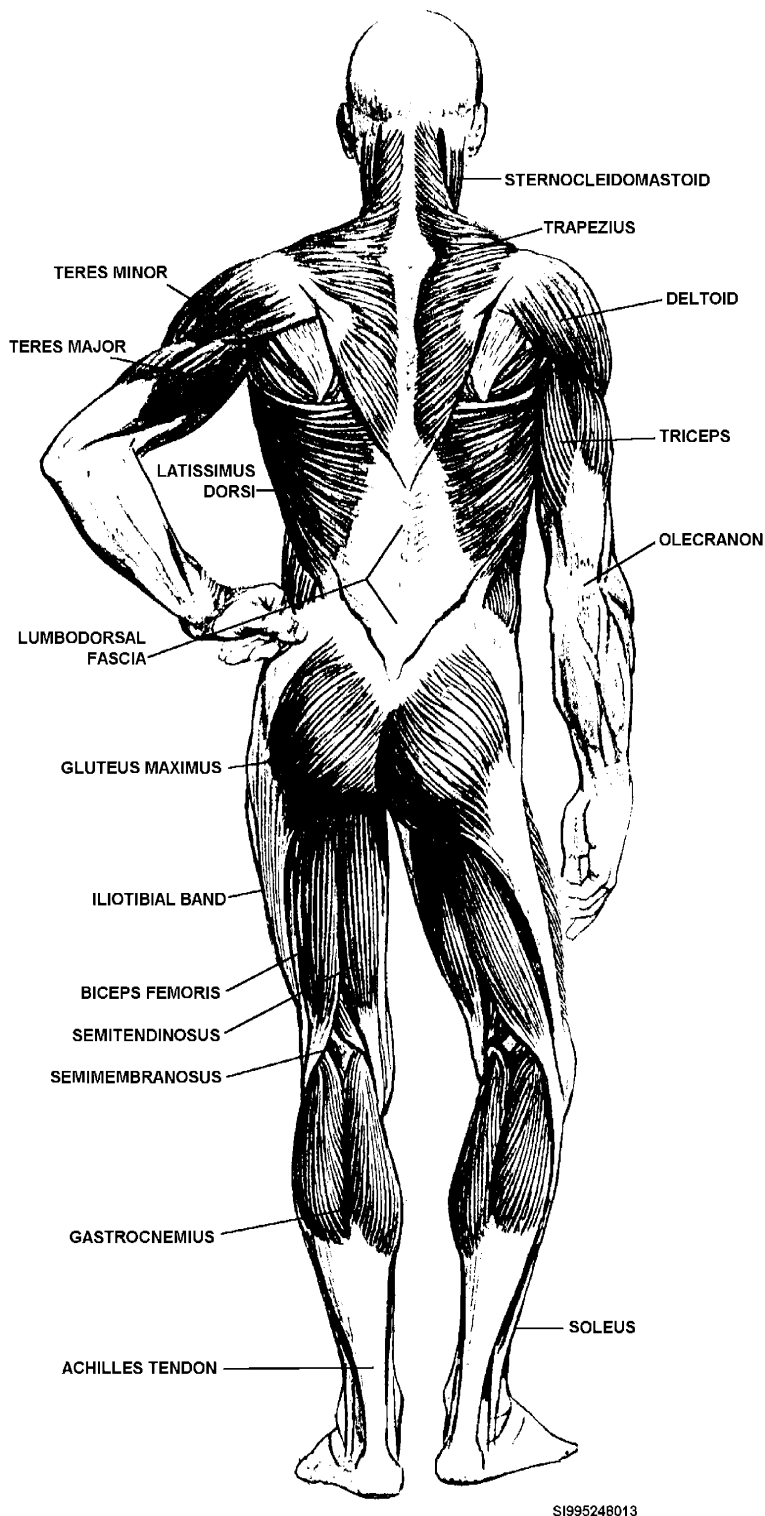


Figure 3-1. The muscles of the body, posterior view.

stopped exercising, they must continue to take in more oxygen until the debt is paid in full.

Muscle tone pertains to a partially contracted state of the muscles which is normal even though the muscles may not be in use at the time. The maintenance of this *tone* or *tonus* is caused by actions of

in oxygen fast enough to meet the needs of the hard-working muscles. If lactic acid accumulates, the person develops what is known as an *oxygen debt*. After a person has stopped exercising, they must continue to take in more oxygen until the debt is paid in full.

The capacity of a muscle fiber to shorten and change its shape, becoming thicker, is known as *contractility*. Studies of the electron microscope reveal that the cytoplasm of each skeletal muscle fiber contains special protein threads or filaments, known as *actin* and *myosin*. These filaments slide over each other in such a manner that the muscle fiber contracts, or becomes shorter and thicker. These contraction processes need energy; consequently, working muscles require an adequate supply of oxygen and glucose. A substance known as *adenosine triphosphate* (ATP) is the immediate source of energy for muscle contraction. ATP is a temporary energy store that acts as a go-between, because it transfers the energy released during chemical reactions to the muscles and other tissues. Likewise, oxygen plays an important role in preventing the accumulation of lactic acid waste products which can cause muscle fatigue. While performing strenuous activities, a person may not be able to breathe in oxygen fast enough to meet the needs of the hard-working muscles. If lactic acid accumulates, the person develops what is known as an *oxygen debt*. After a person has

the nervous system, and their effect is to keep the muscles in a constant state of readiness for action. Muscles that are not used often soon become flabby and weak, and lack tone.

Partial contractions are responsible for muscle tone. Additionally, the body also depends on two other types of contractions. The majority of muscles contract either isotonically or isometrically. Even so, most of the movements of the body involve a combination of both types of contraction.

Isotonic contractions

Isotonic contractions are contractions where the tone or tension within the muscle remains the same, but the muscle as a whole shortens, causing movement. Examples of isotonic contractions are lifting weights, walking, running, or any other activity in which muscles become shorter and thicker (forming bulges).

Isometric contractions

Isometric contractions are contractions where there is no change in muscle length, but there is a notable increase in muscle tension. If you push against a brick wall, for example, there is no movement, but you can sense the increased tension within your arm muscles.

Skeletal muscle attachments and movement

The majority of muscles have two or more attachments to the skeleton. Let's discuss how the muscles are attached and move.

Skeletal muscle attachments

In some cases, connective tissue within the muscle ties directly to the periosteum of the bone. In other instances, the connective tissue sheath and partitions within the muscle all extend to form specialized structures that assist in attaching the muscle to the bone. These extensions may take the form of a cord, in which case it is known as a *tendon*. In other instances, a broad sheet may attach muscles to bones, or to other muscles. This broad sheet is known as an *aponeurosis*.

No matter what the nature of the muscle attachment, the purpose remains unchanged—to furnish a means of harnessing the power of the muscle contractions. Each muscle has at least two attachments, one that is more freely moveable than the other. The less moveable attachment is known as the *origin*; and the attachment to the part of the body that the muscle puts into action is called the *insertion*. As a muscle contracts, it pulls on both points of attachment. This brings the more movable insertion closer to the origin and thereby causes movement of the body part.

Muscle movement

As we mentioned earlier, the human body contains over 600 skeletal muscles. These skeletal muscles make up between 35 and 40 percent of our body weight. Many of the skeletal muscles are arranged in pairs. Movement may be initiated by one muscle or a set of muscles called the *prime mover*. If an opposite movement must be made, another muscle or set of muscles, described as *antagonist*, take over. This is how body movements are coordinated, and a large number of complicated movements are done without the necessity of planning in advance the method of performing them. Initially, however, any new, complicated movement must be learned. Think of a child learning to walk or write. Now consider the number of muscles a child uses unnecessarily or forgets to use when the situation calls for them.

220. Muscles of the body

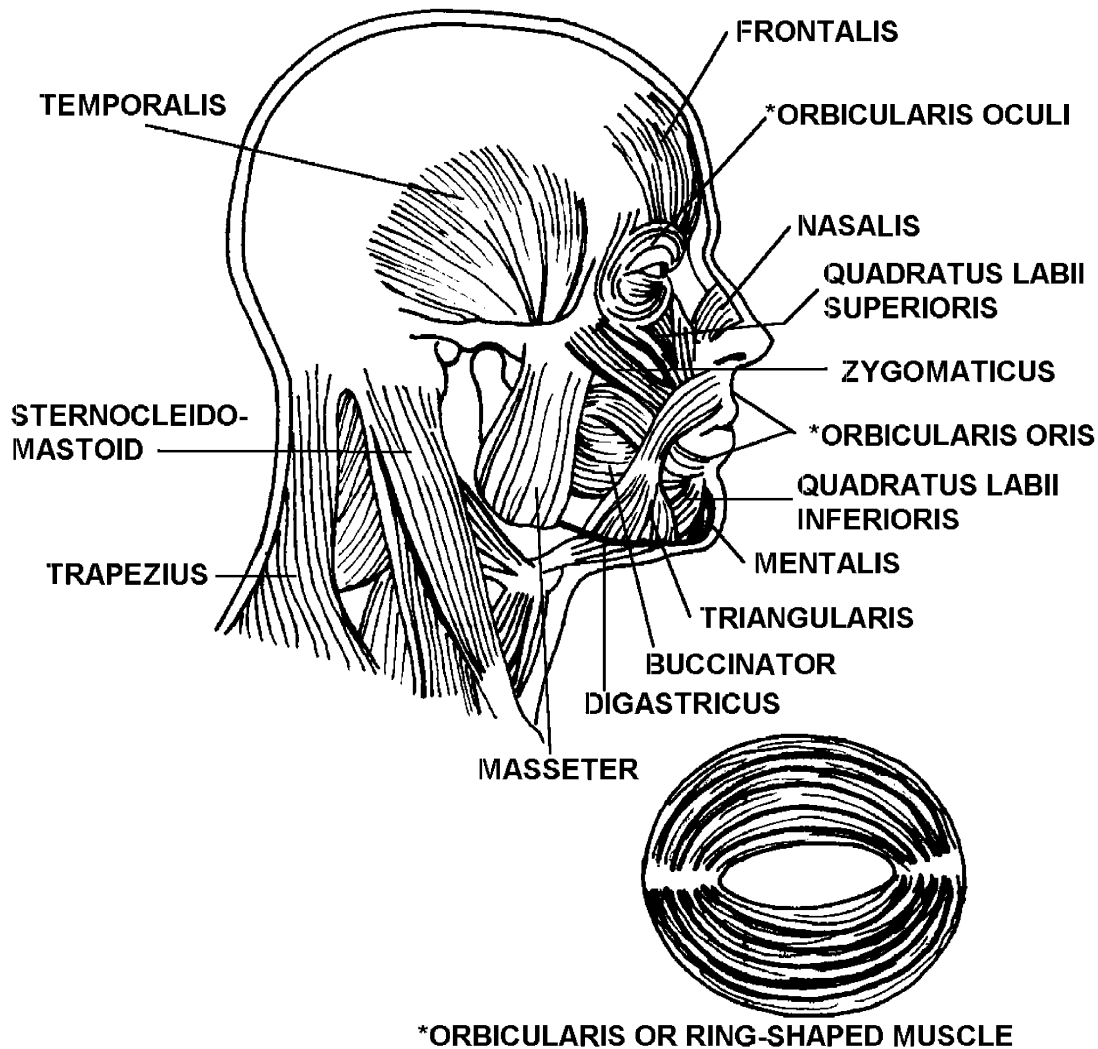
This lesson discusses all the muscles of the body to include:

- Muscles of the head and neck.
- Muscles of the upper extremities.
- Muscles of the trunk.

- Muscles of the lower extremities.

Muscles of the head and neck

The muscles of the head and neck are shown in figure 3-2. Muscles that produce the most facial expressions surround the eyes, nose, and mouth. Large muscles of mastication stretch from the upper skull to the lower jaw. These powerful muscles produce chewing movements. The neck muscles connect the skull to trunk of the body, rotating the head or bending the neck. Let's take a more in-depth look at these muscles.



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Figure 3-2. Muscles of the Head.

Muscles of the head

The main muscles of the head are those of facial expression and of mastication (chewing).

The ring-shaped muscles located around the eyes and the lips are the muscles of facial expression. These muscles are known as the *orbicularis muscles* due to their shape (think of “orbit”). The muscle that surrounds each eye is called the *orbicularis oculi*, and the muscle of the lips is called the

orbicularis oris. Of course, these muscles are all furnished with antagonists. For example, the lifter of the upper eyelid, known as the *levator palpebrae superioris*, is the antagonist for the *orbicularis oculi*.

The *buccinator* is one of the largest muscles of expression, and forms the fleshy part of the cheek. You use this muscle to whistle or blow and it is sometimes referred to as the trumpeter's muscle. Try to think of other muscles of facial expression. One example is the antagonists of the *orbicularis oris* that produces a smile, a sneer, or a grimace. There are also quite a few scalp muscles used to lift the eyebrows or otherwise draw together to form a frown.

Muscles of mastication are broken down into four pairs, all of which insert on the mandible and move it. The largest pair is the *temporal muscles*, located above and near the ear, and the muscles at the angle of the jaw, known as the *masseter muscles*.

The tongue contains two groups of muscles. One group, known as the *intrinsic muscles*, is located entirely within the tongue. The other group, the *extrinsic muscles*, originate outside the tongue. These muscles are responsible for the tongue's flexibility and ability to perform so many functions. Think about the intricate tongue motions involved when speaking, chewing, and swallowing.

Muscles of the neck

The muscles of the neck tend to be ribbon-like and extend up and down or diagonally (obliquely) in several layers and in a very complex manner. The ones you hear of most often are the *sternocleidomastoid muscles*. Sometimes they are called the *sternomastoids*. These are very strong muscles, extending from the sternum upward, across either side of the neck, to the mastoid process. Operating simultaneously, they bring the head forward on the chest (flexion). Working alone, each muscle tilts and rotates the head so as to carry the face toward the opposite side. When a person's head is abnormally fixed in this position, they are said to have *torticollis* (wryneck). This condition may be caused by injury or spasm of the muscle. A portion of the trapezius muscle (discussed later in this lesson) is located in the back of the neck where it aids in holding the head upright (extension). The other large deep muscles are the main extensors of the head and neck.

Muscles of the upper extremities

This group of muscles controls the movements of the shoulder, arm, forearm and hand.

Shoulder and arm movement

Shoulder position depends to a large part on the degree of contraction of the *trapezius muscles*. Each trapezius fans out like a pointed cape down the back of the neck and over the back of the shoulder to insert on the scapula (shoulder blade). The trapezius muscles provide the means for raising your shoulder and pulling your shoulders back. The upper portion of the trapezius can also extend the head and turn it from side to side.

The muscles originating from the vertebral spines in the middle and lower back, and covering the lower half of the thoracic region, are known as the *latissimus dorsi muscles*. The fibers of each of these muscles converge to a tendon that inserts on the humerus. The *latissimus dorsi* forcefully extends the arm, bringing it down powerfully as in swimming.

The large *pectoralis major muscle* is located on the front of the body, on either side of the chest. This muscle arises from the sternum, upper ribs, and clavicle, and forms the anterior "wall" of the arm pit or axilla. It inserts on the upper part of the humerus. The *pectoralis major* flexes and adducts the arm, pulling it across the chest.

The *serratus anterior* is located on the side of the chest, below the axilla. It originates on the upper eight or nine ribs on the side and front of the thorax, and inserts in the scapula on the side towards the vertebrae. The *serratus anterior* muscle moves the scapula forward, for example, when you push something. It also helps raise the arm above the horizontal level.

The muscle covering the shoulder joint and responsible for the roundness of the upper part of the arm just below the shoulder is called the *deltoid muscle*. This area is frequently used as a site for injections. It arises from the shoulder girdle (clavicle and scapula), and converges to insert on the lateral side of the humerus. Contraction of the deltoid muscle abducts the arm, raising it laterally to the horizontal position.

Forearm and hand movement

Young children often display their *biceps brachii* as proof of their strength. This muscle inserts on the radius and serves to flex the forearm. It is a supinator of the hand.

The muscle located on the back of the arm, and inserted into the olecranon of the ulna, is called the *triceps brachii*. This muscle, also called the boxer's muscle, straightens the elbow when a blow is delivered. The *triceps brachii* is also important in pushing because it converts the arm and forearm into a sturdy rod.

The majority of the muscles that move the hand and fingers originate from the radius and ulna. Some of them insert on the carpal bones of the wrist, others have long tendons that cross the wrist and insert on bones of the hand and the fingers. The *flexor carpi* and the *extensor carpi* muscles are responsible for many movements of the hand. The several *flexor digitorum* and *extensor digitorum* muscles produce finger movements. Special groups of muscles in the fleshy parts of the hand are responsible for the intricate movements that may be performed with the thumb and fingers. One of the most useful endowments given to humans is the thumb, its position and freedom of movement.

Muscles of the trunk

The trunk muscles include the muscles used for respiration, those of the abdomen and pelvis, and also those in the deep part of the back.

Muscles of respiration

The diaphragm is the most important muscle involved in the act of breathing. The diaphragm is a dome-shaped muscle that forms the partition between the thoracic cavity above and the abdominal cavity below. The central dome-shaped portion is pulled downward as the diaphragm contracts, thereby enlarging the thoracic cavity from top to bottom. The external *intercostal muscles* fill the spaces between, and are attached to, the ribs. This enlarges the thoracic cavity from side to side and front to back. Use figure 3-3 during discussion of the muscles of respiration.

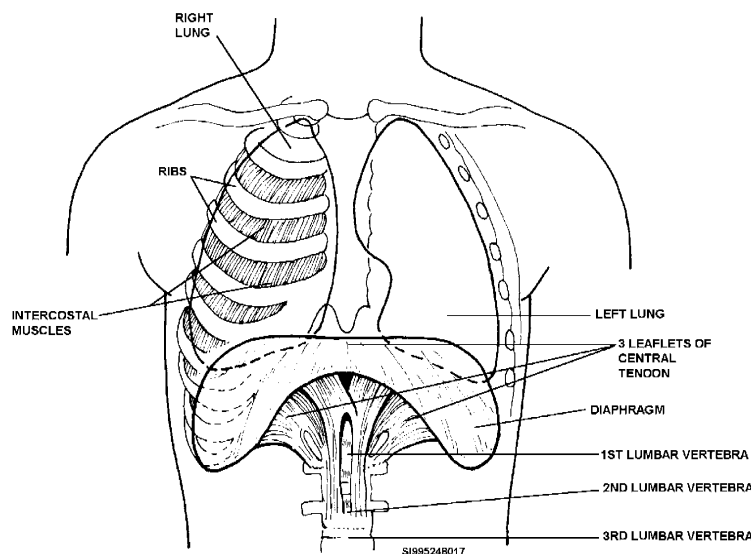


Figure 3-3. Respiratory muscles

Abdomen and pelvis muscles

There are three main muscles arranged in layers on the front and side (anterolateral) walls of the abdomen:

1. *External oblique* (on the outside).
2. *Internal oblique* (in the middle).
3. *Transversus abdominis* (is the innermost layer).

These three muscles have fibers that run in different directions. These layers are “glued” together forming a total effect like that of a piece of plywood. The result is a very strong abdominal wall.

A fourth muscle, the long, narrow *rectus abdominis*, closes the front of the abdomen. The rectus abdominis originates in the pubis and ends at the ribs. It is girdled by connective tissue layers from the other three muscles.

There are a number of functions of the abdominal muscles besides protecting the underlying organs:

1. Assist indirectly with the process of respiration, relaxing when the diaphragm contracts and vice versa.
2. Help in expelling substances from the body by compressing the abdominal cavity and increasing the pressure within the cavity (e.g., when coughing or vomiting and during childbirth).
3. Help in bending the trunk forward and sideways.

The *perineum* (pelvic floor) has its own form of diaphragm. It is shaped similarly to a shallow dish. The principal muscle of this pelvic diaphragm is the *levator ani*. The *levator ani* acts on the rectum and consequently aids in defecation.

Deep back muscles

These muscles act on the vertebral column itself. The deep muscles of the back are thick vertical masses that lie under the trapezius and latissimus dorsi (see figure 3-1). The *sacrospinalis* is the longest of these muscles. It helps to maintain the vertebral column in the erect position.

Muscles of the lower extremities

The muscles of the lower extremities are among the longest and strongest in the body. They are specialized for locomotion and balance.

Thigh and leg movement

The fleshy part of the buttocks is formed by the *gluteus maximus*, and is relatively large in humans due to its performance when a person is standing erect. The gluteus maximus extends the thigh and is very important in walking and running. The gluteus maximus partially covers the *gluteus medius*. The gluteus medius serves to abduct the thigh.

Originating in the ilium and the bodies of the lumbar vertebrae is the *iliopsoas muscle*. It crosses the front of the hip joint to insert on the femur. This muscle is a powerful flexor of the thigh and also aids in keeping the trunk from falling backward when a person is standing erect.

In the medial part of the thigh, you will find the *adductor* muscles. These muscles originate from the pubis and ischium and insert on the femur. These are very strong muscles. They are used to press your thighs together; for example, when you grasp a saddle between your knees when riding a horse, you are using your adductor muscles.

The long, narrow muscle originating at the iliac spine, winding downward and inward across the entire thigh, and ending on the upper medial surface of the tibia, is called the *sartorius*. This muscle is often referred to as the tailor’s muscle because it is used in crossing the leg, in the manner of tailors, who in days gone by sat cross-legged on the floor.

The *quadriceps femoris* cover the front and sides of the femur. This large muscle has four heads of origin (one from the ilium and three from the femur). All four heads have a common tendon of insertion on the tibia. This is the tendon that encloses the knee cap or patella. The *quadriceps femoris* is used when extending the leg, like you do to kick a ball.

In the posterior part of the thigh you will find the hamstring muscles. The tendons of the hamstring muscles may be felt behind the knee as they descend to insert on the tibia and fibula. The hamstring muscles are used to flex the leg on the thigh (e.g., when you kneel).

Foot movement

The chief muscle of the calf of the leg is the *gastrocnemius*. It is sometimes referred to as the toe dancer's muscle due to its necessity in standing on tiptoes. It ends near the heel in a prominent cord known as the "Achilles tendon." The Achilles tendon then attaches to the *calcaneus* (heel bone). The Achilles tendon is the largest tendon in the body.

The *tibialis anterior* is another muscle that acts on the foot. It is located on the front of the leg. The tibialis anterior performs the opposite function of the gastrocnemius. Most noticeable when you walk on your heels, it is used to raise the rest of the foot off the ground (dorsiflexion). In addition, the tibialis anterior is responsible for inversion of the foot. The muscle for eversion of the foot is the *peroneus longus*. It is located on the lateral side of the foot.

The *flexor digitorum* are sets of muscles in the toes. Some originate at the tarsus and at the posterior surface of the tibia, passing through the sole to the toes. Others originate from both the tarsus and anterior surface of the fibula, passing over the top of the foot to the toes.

221. Functions of the muscles

There is an overwhelming amount of knowledge available about muscle functions. We will touch briefly on this subject, discussing only the basic principles.

Skeletal muscles contract only if stimulated

Skeletal muscles do not have the quality of automation inherent in cardiac and visceral muscles. It is true that nerve impulses are the natural stimuli for skeletal muscles, but electrical and some other artificial stimuli, such as heat or injury, can also activate them. Skeletal muscles become functionless masses when deprived of nerve impulses. Consequently, try thinking of a skeletal muscle and its motor nerve as a physiological unit. They are always functioning together and one is useless without the other.

Skeletal muscle contractions may be any of several types

Skeletal muscle contractions may be any of the following types of muscle contractions:

Tonic contraction

A tonic contraction is a constant, partial contraction. At any given time, a small number of the total fibers in a muscle contract, producing a tautness of the muscle rather than a recognizable contraction and movement. Different groups of fibers scattered throughout the muscle contract in relays. Tone, or tonic contraction, is typical of normal individuals while they are awake. Tonic contraction is very important for maintaining posture. To illustrate the necessity of tonic contraction, let's look at an example: When someone loses consciousness, their muscles lose their tone and they collapse in a heap, unable to maintain a sitting or standing posture. *Flaccid muscles* are muscles with less tone than normal, and *spastic muscles* are those with more than normal tone. Tone is maintained by impulses over stretch reflex arcs. *Muscle spindles* and *neurotendinous end-organs* are specialized sensory (stretch) receptors. They are able to detect the degree of stretch (in a muscle) or at the junction of a muscle with its tendon. These receptors allow regulation of tone at a reflex level. Inhibiting the passage of impulses from these sensory end-organs by cutting the reflex arc results in loss of muscle tonus.

Isotonic contraction

Iso means same, and *tonic* means tone, pressure, or tension. This type of contraction is one in which the tone or tension within a muscle stays the same, but the length of the muscle changes, shortening to produce movement.

Isometric contraction

In this type of contraction, the muscle length stays the same, but the muscle tension increases. To experience isometric contraction, place your hand on a wall, now push your arms against the wall. Do you feel the tension increase in your arm muscles? Isometric contractions “tighten” a muscle; they do not produce movement or do any type of work. Conversely, isotonic contractions produce movement and do work. A large number of muscles can contract either isotonically or isometrically, and most body movements are a combination of the two.

Twitch contraction

This contraction is a quick, jerky contraction in response to a single stimulus. The muscle does not shorten at the instant of stimulation, but a fraction of a second later. It also reaches a peak of shortening and then slowly resumes its former length. These three phases of contraction are known as the *latent*, *contraction*, and *relaxation phases*.

The twitch, in its entirety, normally lasts less than 1/10 of a second. Twitch contractions in the body are very rare.

Tetanic contraction (tetanus)

This contraction is a more sustained contraction than a twitch. A series of stimuli bombarding the muscle in rapid succession produces this muscle contraction. For example, approximately 30 stimuli per second evoke a tetanic contraction in a frog’s gastrocnemius muscle. The rate varies for different muscles and different conditions. Normal movements are produced by incomplete tetanic contractions.

Treppe (staircase phenomenon)

Treppe is a progressive increase in strength of a muscle contraction with repeated maximal stimuli. To state this more clearly, a muscle contracts more forcefully after it has contracted a few times than when it first contracts. Athletes practice this principle when they warm up. It is presumed that this practice relates partly to the rise in temperature of active muscles and partly to their accumulation of metabolic products. Muscles will respond to a considerable number of successive stimuli with maximal contractions after the first few stimuli. As time goes by, the muscle will respond with less and less strong contractions. The relaxation phase gradually becomes shorter and disappears entirely. *Contracture* is a term used to describe a muscle staying partially contracted, which is an abnormal state of prolonged contraction.

In time, repeated stimulation of a muscle will lessen its irritability and contractility, and may possibly result in muscle fatigue. Muscle fatigue is a condition in which the muscle does not respond to even the strongest stimuli. However, complete muscle fatigue very seldom occurs in the body.

Fibrillation

This is an abnormal type of contraction where individual fibers contract *asynchronously*. Asynchronously means the failure of events to occur in time with each other as they usually do. This produces a flutter of the muscle but no effective movement.

Convulsions

Convulsions are abnormal-uncoordinated tetanic contractions of varying groups of muscles.

Skeletal muscles (organs) contract according to the graded strength principle

Skeletal muscles do not contract according to the all-or-none principle, like the individual muscle cells that compose them. Skeletal muscles contract with different degrees of strength at different times.

Graded strength contractions may be explained by several generalizations.

1. The strength of skeletal muscle contractions bears a direct relationship to the initial length of its fibers, their metabolic condition, and the number of them contracting.
2. When a muscle is somewhat stretched at the moment when contraction begins, the force of its contraction increases.
3. Oxygen and energy supplies are the leading metabolic conditions that influence contraction.

When adequate amounts of these essentials are present, a muscle may contract with greater force than possible without these essentials or with deficient amounts. The more muscle fibers contracting simultaneously, the stronger the contraction of a muscle. The number of muscle fibers contracting depends on how many motor units are activated. In turn, this depends on the intensity and frequency of stimulation. Overall, the more intense and frequent a stimulus, the more motor units contract. Consequently, the more fibers that are activated, the stronger the contraction. Contraction strength also relates to previous contraction. Remember our discussion of the warm-up principle?

The force of a contraction is also influenced by the size of the load imposed on the muscle. The heavier the load, within certain limits, the stronger the contraction. When you lift a pencil, in comparison to lifting a book, you can feel your arm muscles contract more strongly with the book.

Skeletal muscles produce movements by pulling on bones

Most of our muscles span at least one joint and attach to both articulating bones. Therefore, when they contract, their shortening puts a pull on both bones. This pull moves one of the bones at the joint and draws it toward the other bone. The pull is somewhat like the pull on marionette strings that moves a puppet's parts.

In case you are pondering why both bones don't move, since both bones are pulled on by the contracting muscle, one of them is normally stabilized by isometric contractions of other muscles, or by certain features of its own that make it less mobile.

Bones serve as levers, and joints serve as fulcrums of these levers

A *lever* is any rigid bar free to turn about a fixed point called its *fulcrum*. Contracting muscles apply a pulling force on a bone lever at the point of a muscle's attachment to the bone. This causes the bone (known as the *insertion bone*) to move about its joint fulcrum. Do you remember when we discussed skeletal muscles and their motor nerve acting as a functional unit? Now, we can add bones and joints to this unit and call the physiological unit for movement a neuromusculoskeletal unit. Injury or disease of any of the parts of this unit (nerve, muscle, bone, or joint) can cause abnormal movements or complete loss of movement. Poliomyelitis, multiple sclerosis, and hemiplegia, for example, all involve the neural part of the units. In comparison, muscular dystrophy affects the muscle portion and arthritis the skeletal portion.

Muscles that move a part usually do not lie over that part

Muscles, for the most part, lie proximal to the part moved. Therefore, muscles that move the lower arm lie proximal to it in the upper arm. Applying that same principle, where do you expect to find the muscles that move the hand? The lower leg? Or the upper arm?

Skeletal muscles almost always act in groups rather than singularly

The majority of movements are created by the coordinated action of several muscles. Some of the muscles in the group relax and other contract. In identifying each muscle's special function in the group, you use the following classifications:

Group	Description
Antagonists	Muscles that relax while the prime mover is contracting to produce movement. One exception is the contraction of the antagonist at the same time as the prime mover when some part of the body needs to be held rigid, like the knee joint when standing.
Prime movers	Muscle or muscles whose contraction actually produces the movement.
Synergists	Muscles that contract at the same time as the prime mover. This may aid the prime mover in producing its movement, or it may stabilize a part of the body—hold it still—so that the prime mover produces a more effective movement.

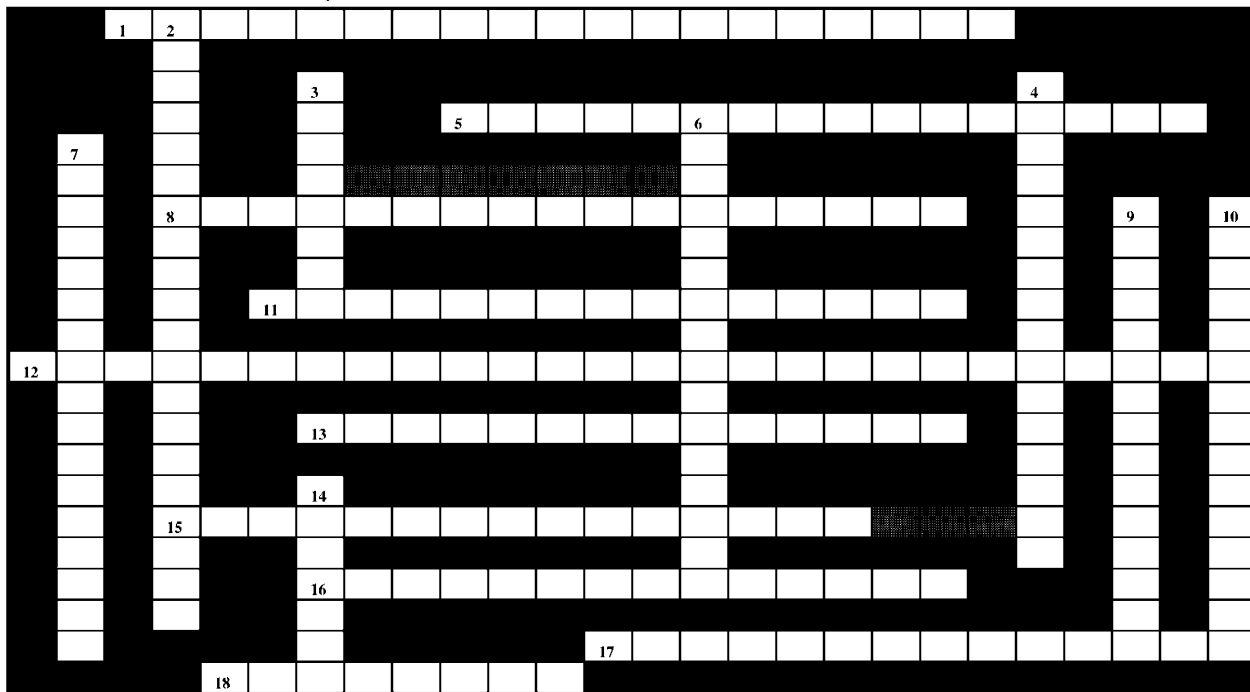
Self-Test Questions

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

219. Skeletal muscle characteristics

1. Why are skeletal muscles looked upon as organs?
2. Define contractility.
3. What is oxygen debt?
4. What is muscle tone, and how is it maintained?
5. Give an example of isometric and isotonic contractions?
6. Define tendon.
7. Define aponeurosis.
8. Define muscle origin.
9. Define muscle insertion.

220. Muscles of the body



<i>ACROSS</i>	<i>DOWN</i>
1. Muscle of the neck; heard of most frequently.	2. Innermost muscle layer along the anterolateral walls of the abdomen.
5. Moves the scapula forward when one is pushing something.	3. Muscle of mastication located at the angle of the jaw.
8. Muscle surrounding the eye.	4. Muscle surrounding each eye.
11. Muscle of the lips.	6. Leg muscle that acts on the foot and is located on the front of the leg.
12. The lifter of the upper eyelid, and antagonist for the orbicularis oculi.	7. Large muscle that covers the front and sides of the femur and has four heads of origin.
13. Largest tendon in the body.	9. Produces finger movements (in conjunction with extensor digitorum muscles).
15. The middle muscle of the abdomen.	10. Closes the front of the abdomen and originates in the pubis and ends at the ribs.
16. Muscle located on the back of the arm, and inserted into the olecranon of the ulna.	14. Muscle covering the shoulder joint and responsible for the roundness of the upper part of the arm just below the shoulder.
17. The fleshy part of the buttocks.	
18. Located in the medial part of thigh, these muscles originate from the pubis and ischium and insert on the femur.	

221. Functions of the muscles

1. What happens to skeletal muscles when they are deprived of nerve impulses?
2. Describe a tonic contraction.
3. What is the difference between a flaccid muscle and a spastic muscle?
4. What type of muscle contraction is one in which the tone or tension within a muscle stays the same, but the length of the muscle changes, shortening, to produce movement?
5. What type of contraction would you experience as you place your hand on a wall and push?
6. List the three phases of twitch contraction.
7. What type of muscle contraction occurs when increasingly stronger twitch contractions occur in response to constant-strength stimuli, and is repeated at a rate of about once or twice a second?
8. Define asynchronously.
9. Describe a convulsion.
10. What are the main metabolic conditions influencing muscle contraction?
11. Why don't both bones move when pulled on by a contracting muscle?
12. What are "prime movers?"

3-2. Muscular System Disorders and Drug Therapy

There are many disorders of the muscular system, and there is not enough room to list all of them here. So we will discuss some of the more common conditions associated with the muscular system.

The main drugs used to treat conditions associated with the muscular system are skeletal muscle relaxants. But where would we be without liniments and rubs? These are aromatic compounds that somehow make our sore muscles feel better. We will discuss the relaxants and liniment and rubs, but we will also re-hash a little of NSAIDs and analgesics we talked about in the skeletal unit.

222. Muscular disorders

This lesson covers atrophy, strains, sprains, muscular dystrophy, myasthenia gravis, fibromyositis, bursitis, and flatfoot—just a sampling of the numerous muscular disorders.

Atrophy

Atrophy is a wasting away or decrease in size of a bodily organ, tissue, or part owing to disease, injury, or lack of use. Muscular atrophy is a wasting or decrease in the size of a muscle when it cannot be used. This happens frequently when an extremity (leg or arm) must be put in a cast following a fracture.

Strains and sprains

Strains and sprains are typical injuries that frequently affect muscles. Severe and excessive exertion may cause detachment of muscles from bones or tearing of some of the muscle cells. Sprains may involve damage to other structures besides the ligaments, mostly blood vessels, nerves, and muscles. The majority of pain and swelling associated with a sprain can be stopped by immediately applying ice packs. Ice packs will constrict some of the smaller blood vessels and decrease internal bleeding.

Muscular dystrophy and myasthenia gravis

These two diseases affect the muscles, and their cause and cure are not yet known. They continue to be a major topic of intensive research. Muscular dystrophy surfaces most often in male children. The term muscular dystrophy refers to a group of progressive muscle disorders caused by a defect in one or more genes that control muscle function, and is characterized by gradual irreversible wasting of skeletal muscle. The end result is complete helplessness. *Myasthenia gravis* is characterized by chronic muscular fatigue usually brought on by the slightest exertion. This disease affects adults and begins with the muscles of the head. One of the most common, early symptoms of this disease is *ptosis*, a drooping of the eyelids.

Fibromyositis

Muscular pain is called *myalgia*. *Myositis* is a term indicating the actual inflammation of muscle tissue. Inflammation of connective tissues, especially those connected with muscles and joints, is called *fibrositis*. A combination disorder of all these is called *fibromyositis*. This disorder is commonly referred to as rheumatism, lumbago, or charleyhorse. Fibromyositis may present itself as acute with severe pain on motion, or it may be a chronic disorder. The combination of heat, massage, and rest, in some instances, will relieve the symptoms.

Bursitis

Bursitis, as the name implies, is inflammation of a *bursa*. A bursa is a cavity or sac filled with synovial fluid. A bursa's purpose is to minimize friction. Some bursae are closely related to muscles, while others communicate with joints. Bursae, occasionally, develop spontaneously in response to prolonged friction.

Bursitis may be extremely painful, cause swelling and limitation of motion. The following disorders are some examples of bursitis:

Disorder	Description
Housemaid's knee	The bursa in front of the patella is inflamed. This type of bursitis is found in people who must be on their knees a great deal.
Ischial bursitis	This type of bursitis is located in the lower portion of the hipbone and is common in people who must sit a great deal, such as taxicab drivers and truckers.
Student's elbow	The bursa over the point of the elbow (olecranon) is inflamed due to long hours of leaning on the elbow while studying.
Subdeltoid bursitis	This is located in the shoulder region. It is a fairly common and unpleasant type of bursitis. In some cases, patients must be given injections of local anesthetics to relieve the pain.

Flatfoot

This is a very common disorder of the muscular system. People who are flatfooted have a breakdown of the normally raised portion of the sole of their foot (arch). This breakdown results in the entire sole of the foot resting on the ground. Flatfoot may be congenital, in which case it normally does not cause a person too much trouble. On the other hand, flatfoot may be the result of a progressive weakening of the muscles that support the arch of the foot. Usually, this condition is accompanied by a great deal of pain. In these instances, flatfoot is thought to be caused by incorrect use of the muscles that support the arch of the foot, such as toeing out when walking. It may also be caused by a lack of exercise. Walking with the toes pointed straight forward, in properly fitted shoes, may be the key to avoiding flatfoot and other painful foot disorders. Certain exercises, under the supervision of a trained person, may be helpful in strengthening the muscles that help maintain the foot arches.

223. Skeletal muscle relaxants

Muscles get injured; tiny tears appear from violent jerking and twisting caused by falls, automobile accidents, shoveling 3 feet of snow in North Dakota, or any of the disorders earlier mentioned. The muscle then is sore, tight, and tense. We've learned that even the strongest analgesic only temporarily masks pain. Sometimes to fix the problem in the muscle, we must get it to relax. For this problem we have the skeletal muscle relaxants. In this section will discuss carisoprodol, cyclobenzaprine, methocarbamol, and baclofen.

Indications and dosage

Skeletal muscle relaxants are used in addition to rest and physical therapy for relief of muscle spasm. Associated with acute painful musculoskeletal conditions, baclofen is different in that it is specifically indicated only for spasticity resulting from multiple sclerosis. All of the relaxants have CNS depressant properties. In fact, that's mainly how they work. All of these meds work at the brain stem and spinal cord interfering with neurotransmissions and synapse firing. There is no direct action on muscles. The dosage for each of these is identified in the following table:

Drug	Dosage form	Dosing
Baclofen	10,20 mg tablets 10 mg/5 and 20 ml	40–80 mg daily, divided into 3 doses see manufacturer's specifics
Carisoprodol	350 mg tablet	350 mg 3–4 times daily
Cyclobenzaprine	10 mg tablet	20–40 mg daily in 3–4 divided doses
Methocarbamol	500, 750 mg tablets 100 mg/ml injection	750 – 1000 mg 4 times daily IV, IM only. Not more than 3 gm daily

Contraindications

These agents are contraindicated in patients who are taking monoamine oxidase inhibitors currently, or are within 14 days from last using them. Patients with arrhythmia or in the acute recovery phase of myocardial infarction should not use these drugs. Baclofen should not be used in the treatment of muscle spasm resulting from rheumatic disorders, stroke, cerebral palsy or Parkinson's disease.

Warnings

1. Cyclobenzaprine is the only one of the four that has been tested in pregnant women. It is category B. It isn't known if any of these drugs are excreted into breast milk.
2. The use of these drugs in children under 12 has not been tested.

Drug interactions

Carisoprodol or methocarbamol interact with all other CNS depressants. All of the listed interactions are for cyclobenzaprine. Cyclobenzaprine in related to the tri-cyclic antidepressants (TCA). All interactions that apply to TCAs apply to cyclobenzaprine.

Drug	Interaction
Anticholinergics	The anticholinergic effects may be enhanced.
Barbiturates	Central and respiratory depressant effects may be additive.
Cimetidine	Anticholinergic symptoms (e.g., severe dry mouth, urinary retention, blurred vision) have been associated when cimetidine therapy is initiated.
Clonidine	Dangerous elevation in blood pressure and hypertensive crisis has occurred.
Levodopa	Hypertensive episodes have occurred.
MAOIs	Should not be given. Combinations can produce seizures, sweating, coma, hyperexcitability, hyperthermia, tachycardia, tachypnea, headache, mydriasis, flushing, confusion, hypotension, disseminated intravascular coagulation and death. At least 7 to 10 days should elapse between MAOI discontinuation and TCA institution.

Patient information

1. May take with food or meals if GI upset occurs .
2. May cause drowsiness or dizziness. Patients should observe caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity. Avoid alcohol and other CNS depressants.
3. If dizziness (postural hypotension) occurs, avoid sudden changes in posture; use caution when climbing stairs, etc.
4. May cause dry mouth (cyclobenzaprine only)
5. Urine may darken to brown, black, or green. (methocarbamol only)
6. Notify physician if skin rash, itching, fever, or nasal congestion occurs. (methocarbamol only)
7. May cause frequent urge to urinate or painful urination, constipation, nausea, headache, insomnia, or confusion. Notify physician if these effects persist (baclofen only).

224. Rubs and liniments, analgesics and NSAIDs

Rubs and liniments

Here, we'll talk just about what are known as *counterirritants*. Counterirritation is a novel idea. We intentionally irritate, or induce a mild inflammation of the skin, to relieve pain elsewhere. There are a

few different theories on how this irritation of skin works to relieve muscle pain. The basic premise is that pain is only as bad as it is perceived to be, and the perception of other sensations caused by the counterirritant or its applications, such as massage, warmth, or redness, causes the sufferer to disregard the sensation of pain. Another idea suggests that stimulation of sensory nerve endings in the skin may have a reflex effect on the nerve axons, resulting in vasodilation. The vasodilation produces an increase in the blood flow to the muscles by changing the thermal gradient that extends from the skin to the deeper structures. Lastly, the idea that these counterirritants may overload the portion of the brain that interprets pain stimuli has been kicked around. The intensity of response depends on the irritant used, its concentration, the solvent in which it is dissolved, and the duration of its contact with the skin.

Counterirritants are grouped into four classes based on potency. They are:

Group	Characteristics	Ingredients
A	Induces redness and irritation (potency = group D, greater than B and C)	<ul style="list-style-type: none"> • Ammonia water • Methyl salicylate • Turpentine oil
B	Produces cooling sensation	<ul style="list-style-type: none"> • Camphor • Menthol
C	Causes vasodilation	<ul style="list-style-type: none"> • Histamine dihydrochloride • Methyl nicotinate
D	Incites irritation without causing redness (equal potency to group A)	<ul style="list-style-type: none"> • Capsicum

Most of the preparations found in this area are combinations of ingredients from one or more categories. For example, Ben Gay[®] is a mixture of menthol and methyl salicylate. A product called Arthricare[®] contains Methyl nicotinate and capsicum.

No doubt, the use of counterirritants in relieving pain has a strong psychologic effect. These agents may even exert a placebo effect through their pleasant aroma and the sensations of warmth or coolness that they produce on the skin.

Indications

These products are used to relieve pain from muscle aches, neuralgia, rheumatism, arthritis, sprains, and similar conditions when the skin is intact.

Contraindications

An allergy to any component.

Warnings

For external use only. Avoid contact with eyes and mucous membranes.

Drug interactions

Counterirritants may increase the effects of anticoagulants.

Patient information

Increased irritation, redness, or blistering may occur if an occlusive dressing is applied over these medications. Patients may lightly wrap areas where these agents are applied with gauze or elastic bandages.

Analgesics and NSAIDs

We discussed, indepth, how the analgesics and non-steroidal anti-inflammatory agents were used in the skeletal system. You need to remember that those same actions can be used in the muscular system as well. The analgesia works in the CNS and will mask the pain. Anti-inflammatory drugs will exhibit their effects just as well on muscle tissue.

Self-Test Questions

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

222. Muscular disorders

1. What is muscular atrophy?
2. What disease refers to a group of progressive muscle disorders caused by a defect in one or more genes that controls muscle function, characterized by gradual irreversible wasting of skeletal muscle?
3. What is an early symptom of myasthenia gravis?
4. Name the disorder that is a combination of myalgia, myositis, and fibrositis?
5. What is a “bursa” and what is its purpose?
6. What muscular disorder is characterized as a break down of the normally raised portion of the sole of the foot (arch)?

223. Skeletal muscle relaxants

1. In what system of the human body do skeletal muscle relaxants act in to produce their muscle relaxant effects?
2. How is baclofen different from the other skeletal muscle relaxants discussed in this section?
3. What impact does methocarbamol have on urine?

224.

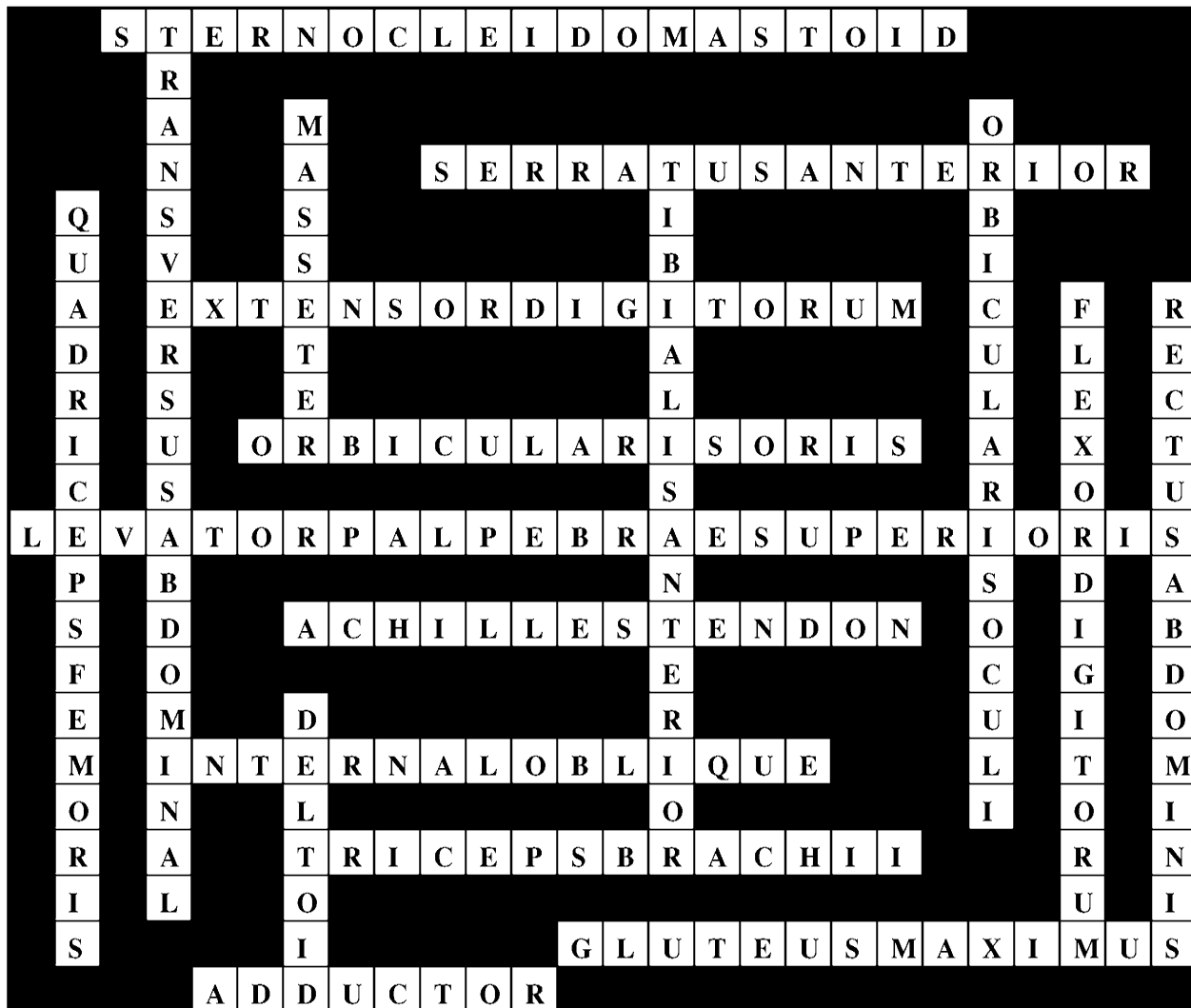
1. What is the main premise of counterirritation?
2. How are counterirritants grouped?
3. How do counterirritants provide a placebo effect?
4. What effect would an occlusive bandage have when applied on a counterirritant?

Answers to Self-Test Questions

219

1. Each muscle has a connective tissue framework and is supplied with blood vessels and nerves. And, each muscle has specialized muscle cells which are capable of shortening or contracting.
2. Capacity of a muscle fiber to undergo shortening and to change its shape, becoming thicker.
3. A person may not be able to breathe in oxygen fast enough, while performing strenuous activities, to meet the needs of the hard-working muscles, resulting in an accumulation of lactic acid.
4. It is a partially contracted state of the muscles which is normal even though the muscles may not be in use at the time. Maintenance is caused by actions of the nervous system, and their effect is to keep the muscles in a constant state of readiness for action.
5. Isotonic—lifting weights, walking, running, or any other activity in which muscles become shorter and thicker. Isometric—pushing against a brick wall.
6. The connective tissue sheath and partitions within the muscle all extend to form specialized structures that assist in attaching the muscle to the bone. When these extensions take the form of a cord they are called a tendon.
7. A broad sheet that attaches muscles to bones, or to other muscles. This broad sheet is known as an aponeurosis.
8. The less moveable attachment of a muscle.
9. The attachment of a muscle to the part of the body that the muscle puts into action.

220



221

1. They become functionless.
2. It is a constant, partial contraction. It keeps muscles taut, different groups of fibers are contracting in a relay, and it is very important in maintaining posture.
3. Flaccid muscles are muscles with less tone than normal; spastic muscles are those with more than normal tone.
4. Isotonic contraction.
5. Isometric contraction.
6. The latent phase, the contraction phase, and the relaxation phase.
7. Treppe or staircase phenomenon.
8. The failure of events to occur in time with each other as they usually do.
9. An abnormal-uncoordinated tetanic contraction of varying groups of muscles.
10. Oxygen and food supply.
11. Because one of them is normally stabilized by isometric contractions of other muscles or by certain features of its own that make it less mobile.
12. Muscle or muscles whose contraction actually produces the movement.

222

1. A wasting or decrease in the size of a muscle when it cannot be used.
2. Muscular dystrophy.
3. Ptosis, a drooping of the eyelids.
4. Fibromyositis.
5. A cavity or sac filled with synovial fluid whose purpose is to minimize friction.
6. Flatfoot.

223

1. Central nervous system (CNS).
2. It is only specifically indicated for spasticity resulting from multiple sclerosis.
3. Methocarbamol may discolor your urine (brown, black, or green).

224

1. Pain is only as bad as it is perceived to be.
2. Counterirritants are grouped into 4 categories by potency.
3. Through their pleasant aroma and warming/cooling feeling.
4. Increased irritation, redness, or blistering may occur.

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.

43. (219) The capacity of a muscle fiber to shorten and change its shape is known as?
 - a. irritability.
 - b. excitability.
 - c. contractility.
 - d. action potential.
44. (219) What type of muscle contraction is denoted by no change in muscle length, but a notable increase in muscle tension?
 - a. Actin.
 - b. Myosin.
 - c. Isotonic.
 - d. Isometric.
45. (219) The term for an extension that connects a muscle to a bone that is formed like a cord is
 - a. aponeurosis.
 - b. contractor.
 - c. insertion.
 - d. tendon.
46. (220) The fleshy part of the cheek is formed by the
 - a. orbicularis oris.
 - b. buccinator.
 - c. temporal.
 - d. masseter.
47. (220) Which of the following muscles forms the innermost layer of the abdomen wall?
 - a. Intercostal.
 - b. Internal oblique.
 - c. External oblique.
 - d. Transversus abdominus.
48. (220) Which muscle forms the fleshy part of the buttocks?
 - a. Gluteus maximus.
 - b. Gluteus minimus.
 - c. Sacrospinalos.
 - d. Iliopsoas.
49. (220) The chief muscle of the calf of the leg is the
 - a. gastrocnemius.
 - b. tibialis anterior.
 - c. peroneus longus.
 - d. flexor digitorum.
50. (221) When individual muscle fibers contract asynchronously, the type of contractions that results is
 - a. convulsion.
 - b. fibrillation.
 - c. twitch.
 - d. tetanic.

51. (221) Normally, where do muscles lie in relation to the body parts that they move?
- a. On top.
 - b. Under.
 - c. Distal
 - d. Proximal.
52. (222) What muscular disorder is characterized by chronic muscular fatigue brought on by the slightest exertion?
- a. Muscular dystrophy.
 - b. Myasthenia gravis.
 - c. Fibromyostis.
 - d. Myalgia.
53. (223) Which muscle relaxant is specifically indicated for spasticity resulting from multiple sclerosis?
- a. Baclofen.
 - b. Carisoprodol.
 - c. Methocarbamol.
 - d. Cyclobenzaprine.
54. (223) Which muscle relaxant may darken urine to brown, black, or green?
- a. Baclofen.
 - b. Carisoprodol.
 - c. Methocarbamol.
 - d. Cyclobenzaprine.
55. (224) Another term for rubs and liniments is
- a. balms.
 - b. massages.
 - c. analgesics.
 - d. counterirritants.
56. (224) What criteria is used to group rubs and linaments?
- a. Potency.
 - b. Indication.
 - c. Ingredients.
 - d. Characteristics.

Student Notes

Unit 4. The Circulatory System

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THE circulatory system is a group of organs that transport blood and the substances it carries to and from all parts of the body. In humans, the circulatory system consists of vessels (arteries and veins) that carry the blood, and a muscular pump, the heart, that drives the blood. This unit discusses the anatomy and physiology of the circulatory system, the conditions associated with the circulatory system, and the drugs used to treat conditions associated with the circulatory system.

4-1. Anatomy and Physiology of the Circulatory System

For the purpose of our discussion here, we will touch on three major parts of the circulatory system: the blood, heart, and blood vessels and blood circulation.

225. The blood

Sometimes blood is classified as a tissue, because nearly half of it is made up of cells. However, blood differs from other connective tissues since its cells are not fixed in position.

Blood is a thick (viscous) fluid varying in color from bright scarlet to dark red. Its color varies depending on how much oxygen it is carrying; the more oxygen, the darker the red. The amount of circulating blood differs with the size of the person. The average adult male, weighing 154 pounds, has approximately five and one-fourth quarts (5 liters) of blood in his body.

The purpose of blood

Blood is of fundamental importance in the maintenance of a stable internal environment (homeostasis). The circulating blood in our body serves the body in two ways: transportation and protection.

Transportation

Oxygen, from air that is breathed in, diffuses into the blood through the thin lung membranes and is carried to all the tissues of the body. A waste product of cell metabolism, carbon dioxide, is carried from the tissues to the lungs where it is breathed out.

Blood transports food and other needed substances to the cells. These materials enter the blood from the digestive system or they may be released from body stores.

Blood transports waste products from the cells to the sites from which they are released. The kidney removes excess water, minerals, and urea from protein metabolism. It also maintains the acid-base balance of the blood. The liver removes bile pigments and drugs. Blood also carries the secretions,

known as hormones, from their site of origin to the organs to be regulated. Blood transports heat, generated in the muscles, to other parts of the body, aiding in the regulation of body temperature.

Protection

Blood carries those substances that are among the body's defenders against pathogens. Other blood constituents are concerned with immunity to disease. The blood also acts to maintain a stable internal environment.

Blood constituents

The liquid element of blood is *plasma*.

The *formed elements* are cells and products of cells. Another term for the formed elements is *corpuscles*. They are grouped as follows:

1. *Erythrocytes* are the red blood cells. (Remember *erythro* means red)
2. *Leukocytes* are the white blood cells. (Remember *leuko* means white)
3. *Platelets* are cell fragments that initiate the clotting of blood. Another term used for platelets is *thrombocytes*.

Plasma

Plasma makes up over 50 percent of the total volume of blood. The plasma itself is 90 percent water with many different substances dissolved or suspended in the water, making up the other 10 percent. Plasma's content varies somewhat because the blood carries substances to and from organs for their use. Nevertheless, the body tends to maintain a fairly constant level of the various substances. As an example, the level of glucose, a simple sugar, is maintained at a remarkably constant level of about one-tenth of 1 percent solution.

The next largest percentage of material in plasma, after water, is *protein*. Proteins are the principal constituents of protoplasm and are essential to the growth and rebuilding of body tissues. These proteins are:

Protein	Description
Albumin	The most abundant protein in plasma. It is manufactured in the liver.
Amino acids	They have been absorbed by the capillaries of the intestinal villi. These are properly described as the main building blocks of protein.
Antibodies	They combat infection.
Blood clotting factors	A balance of procoagulants and anticoagulants.
Complement	A system of enzymes made of several proteins that use antibodies in their fight against pathogens.

There are also nutrients found in the plasma. One group of nutrients is given the collective name of *carbohydrates*. The principal form of carbohydrate found in the plasma is glucose. Glucose is stored mainly in the liver and released as needed to supply energy.

Lipids include fats and constitute a small percentage of blood plasma. They may be stored as fats for reserve energy or carried to the cells as a source of energy.

Mineral salts in the plasma occur mainly as chloride, carbonate, or phosphate salts of sodium, potassium, calcium, and magnesium. They have a variety of functions, to include:

1. Formation of bone (calcium and phosphorus).
2. Production of hormones by certain glands (iodine for the production of thyroid hormone).

3. Transportation of the gases, oxygen and carbon dioxide (iron).
4. Maintenance of acid-base balance (sodium and potassium carbonates and phosphates).
5. Small quantities of other elements aid in maintaining homeostasis. There are many other materials, such as waste products and hormones that are transported in the plasma.

Formed elements

We will look in more detail at each of the formed elements:

- Erythrocytes.
- Leukocytes.
- Platelets.

Erythrocytes

The red cells, erythrocytes, are tiny disk-shaped bodies with a central area that is thinner than the edges. Erythrocytes are different from other cells in that the mature form found in the circulating blood does not have a nucleus. These cells live a much shorter time than most other cells of the body. Some cells in the body may last a lifetime. One purpose of the erythrocytes is to carry oxygen from the lungs to the tissues. This is accomplished by the *hemoglobin*. Hemoglobin is a protein, containing iron. It combines with oxygen, and this gives blood its characteristic red color. The more oxygen carried by the hemoglobin, the brighter the red color of the blood. Consequently, the blood that goes from the lungs, through the arteries, to the tissues is a bright red. This is due to its greater supply of oxygen. Conversely, the blood that returns from the tissues, by way of the veins, and back to the lungs is a much darker red, because it has given up much of its oxygen. Hemoglobin that has given up its oxygen is able to carry hydrogen ions. In this way, hemoglobin plays an important role in acid-base balance. The erythrocytes also carry a small amount of carbon dioxide from the tissues to the lungs for elimination when we exhale.

Carbon monoxide is a gas that can combine with hemoglobin to form a stable compound. It displaces oxygen that is usually carried by the hemoglobin and reduces the oxygen-carrying ability of the blood. Carbon monoxide can be produced by incomplete burning of various fuels, such as gasoline, coal, wood, and other carbon-containing materials. It also occurs in automobile exhaust fumes, and cigarette smoke.

Leukocytes

The white blood cells, or leukocytes, are very different from the erythrocytes in appearance, quantity, and function. The leukocytes contain nuclei of varying shapes and sizes, and the cells themselves are shaped like balls. Leukocytes are outnumbered by erythrocytes by 700 to 1, numbering but 5,000 to 10,000 per cubic millimeter of blood. The erythrocytes have a definite color; however, the leukocytes tend to be colorless. There are many different kinds of leukocytes, but for now it is sufficient to know that the most important function of leukocytes is to destroy certain pathogens. When pathogens enter the tissues, as through a wound, the white blood cells are attracted to that area. They leave the blood vessels and proceed to the area of infection. There they engulf the invaders by a process called *phagocytosis*. If the pathogens are extremely strong or numerous, they may destroy the leukocytes. A collection of dead and living bacteria, together with dead as well as living leukocytes, forms *pus*. A collection of pus localized in one area is known as an *abscess*.

Platelets (thrombocytes)

The blood platelets (thrombocytes) are the smallest of all the formed elements. These tiny structures are not cells in themselves, but fragments of cells. The number of platelets in the circulating blood has been estimated at 200,000 to 400,000 per cubic millimeter. We could not last very long, if it were not for the platelets. The slightest cut could prove to be fatal. The platelets are essential to coagulation (blood clotting), and without them we would bleed to death. When blood is shed and comes in contact with any tissue other than that which normally carries blood, the platelets immediately disintegrate

and release a chemical that reacts with a protein called *fibrinogen*. Fibrinogen is manufactured in the liver and circulates in the plasma. Fibrinogen, changes from a liquid to a solid mass known as *fibrin*, which forms the clot.

Blood clotting

Coagulation, or blood clotting, is a protective device that prevents blood loss when a blood vessel is ruptured by an injury. There are numerous substances involved in the clotting process; some are called *anticoagulants*, which prevent clotting, and others called *procoagulants*, which promote clotting. The balance between these two groups of substances determines whether or not blood will coagulate. Usually, the anticoagulant activity prevails, and blood does not clot. But, when a blood vessel is injured, that activity of the procoagulants becomes greater, and a clot develops.

In essence, the clotting process occurs in these essential steps:

1. The injured tissues release *thromboplastin*, a substance that triggers the clotting mechanism.
2. Thromboplastin reacts with certain protein factors and calcium ions to form *prothrombin* activator that, in turn, reacts with calcium ions to convert prothrombin to *thrombin*.
3. In turn, thrombin converts soluble fibrinogen into insoluble fibrin. *Fibrin* is a network of threads that entrap red blood cells and platelets to form a clot.

Several methods are used to measure the body's ability to coagulate blood. We will discuss those later in this lesson.

Blood types and transfusions

Blood groups

If, for some reason, the amount of blood in the body is severely reduced, through excessive bleeding (*hemorrhage*) or through disease, the body cells suffer from lack of oxygen and food. The obvious measure to take in such an emergency is to inject blood from another person into the veins of a patient. This procedure is called a *transfusion*.

One person's plasma may contain substances, known as *antibodies*, that can damage the red cells of another person. The donor's red cells may become clumped or held together in bunches, a process known as *agglutination*, by the antibodies in the patient's plasma. Other times the red blood cells may rupture and release their hemoglobin. These cells are said to be *hemolyzed*, and this condition can be very serious.

For the most part, the types of proteins (antigens) on the red cell membranes determine these reactions. There are numerous types of these proteins, but only two groups are particularly likely to cause a transfusion reaction. These are the so-called A and B antigens, and the Rh factor. Four blood types involving the A and B antigens have been recognized: A, B, AB, and O. These letters indicate the type of antigen present on the red cells, with O indicating that neither A nor B antigen is present. It is these antigens on the donor's red cells that react with the antibodies in a patient's plasma and cause the transfusion reaction.

Blood serum that contains antibodies that can agglutinate and destroy red cells that have A antigen on the surface is called *anti-A serum*. And blood serum with antibodies that can destroy red cells with B antigen on the surface are called *anti-B serum*. These serums are used to determine blood type.

Rh factor

Approximately 85 percent of the population has another antigen called the *Rh factor*. These individuals are said to be *Rh positive*. The other 15 percent of the population lack this protein and are said to be *Rh negative*. If Rh-positive blood is given to an Rh-negative person, the person may become sensitized to the protein in the Rh positive blood. This person's blood may then produce antibodies to the "foreign" Rh positive antigens and destroy the cells. A mother who is Rh negative may become sensitized by proteins from an Rh positive baby (this factor having been inherited from

the father), should these proteins enter the mother's circulation during childbirth. During a subsequent pregnancy with an Rh positive fetus, some of the antibodies may pass from the mother's blood into the blood of the fetus and thereby cause destruction of red cells. This results in a condition called *erythroblastosis fetalis*. The infant may be born dead (stillborn). If the infant is born alive, replacement transfusions with Rh-negative blood should begin at once.

Blood derivatives

Blood is capable of being broken down into its various components, and the substances derived from it may be used for a variety of purposes. One of the more common of these processes is to separate the blood plasma from the formed elements. This is accomplished by means of a *centrifuge*. A centrifuge is a machine that spins a quantity of blood around in a circle at high speed. Imagine a weight tied to the end of a string, and think of spinning the weight around in a circle. That is basically how a centrifuge works. Centrifugal force tends to pull the weight outward. When a container of blood is spun rapidly, that same force "pulls" all the formed elements of the blood into a clump at the bottom of the container, separating them from the plasma, which can simply be drained off.

Blood plasma is a very useful substance. It can be given as an emergency measure to combat shock and to replace blood volume. The water can be removed, leaving the solids that can be stored in the dry state for a considerable length of time. Later, sterile distilled water may be added in order to reconstitute the plasma. It can then be given to an injured person, for example, in situations where blood typing and the use of whole blood is not possible (on battlefields or in mass disasters). Because the red blood cells have been removed, there can be no incompatibility problems; plasma can be given to anyone. Plasma that has been separated from the cellular elements can be further separated by either chemical means or by freezing.

Fresh plasma may be frozen and saved. Plasma that was frozen when it was less than 6 hours old contains most of the factors needed for clotting, and may be given when there is a special need for these factors.

Another blood derivative is called *serum*. If you have ever removed a blood clot, you have observed a watery fluid that remains. This watery fluid is serum, and it is nothing more than plasma that had its fibrinogen removed through the process of clotting. Serum can be derived from the blood of specially treated animals and then injected into humans in order to produce immunity to certain diseases.

White blood cells can be separated from a donor's blood by a machine that removes the white blood cells and returns the plasma and red cells to the donor. This procedure is called *plasmapheresis*. These white cells may be given to a patient who has bone marrow depression.

Blood tests

Many different types of tests may be made on the blood. You may be exposed to some conversation involving pharmacy care and blood tests. This section gives you a brief overview of blood tests.

Hematocrit

The *hematocrit* is the volume percentage of red blood cells in whole blood. It is also called PCV, for *packed cell volume*.

The hematocrit is expressed as volume of red cells per unit volume (100 mL) of whole blood. For example, if the laboratory report states that a person's hematocrit is "38," that means there are 38 mL of red cells per 100 mL of whole blood, or 38 percent of the whole blood is red cells. For males, the normal range is 42 to 50 mL per 100 mL of blood. The range is somewhat lower for females, it is 36 to 40 mL per 100 mL. These normal ranges may vary depending on the method used and the interpretation of the results by an individual laboratory. Hematocrit values below or above these figures point to an abnormality requiring further study.

Complete blood count (CBC)

Normally, automatic counters are used to count the blood cells. But, if necessary, a hemocytometer may be used. The normal blood count is as follows:

1. Red blood cell count varies from 4.5 to 5.5 million cells per cubic millimeter of blood.
2. White blood cell count varies from 5,000 to 10,000 cells per cubic millimeter of blood.

Patients with leukopenia have a white count below 5,000. It is characteristic of a few infections such as malaria and measles, and also of certain disorders of the blood-forming organs.

Leukocytosis means that the patient's white blood count is in excess of 10,000 per cubic millimeter of blood. It is especially characteristic of most infections. It may also occur after hemorrhage and in gout and uremia as a result of kidney disease.

Hemoglobin

It is important to know that a person has an adequate amount of hemoglobin so that the tissues are assured a sufficient supply of oxygen. This is determined by means of a *hemometer*, also known as a *hemoglobinometer*. These devices vary in design, but generally the principle is that a comparison is made between the blood and a standard color scale. The normal hemoglobin concentration ranges from 14 to 17 grams per 100 mL of blood for males, and, as with the hematocrit, the values are slightly lower for females, ranging from 12 to 15 grams per 100 mL of blood. A decrease in hemoglobin is a factor in anemia.

Blood chemistry

Batteries of tests on blood serum are often done by machine. One, the sequential multiple analyzer (SMA), provides for the running of some 12 or more tests per minute. Tests for electrolytes such as sodium, potassium, chloride, and bicarbonate, plus enzyme tests such as those for alkaline *phosphatase* and *transaminase*, may be included in this battery of tests. Others of importance include blood urea nitrogen (BUN), blood sugar, cholesterol, and triglyceride evaluations. All of these may also be done manually using test tubes containing various chemicals that yield color changes or other kinds of determinants.

Many of these blood serum tests help in evaluating disorders that may involve such vital organs as the heart, kidneys, liver, and pancreas. For example, the presence of more than the normal amount of glucose (sugar) dissolved in the blood is called *hyperglycemia* and is found most frequently in unregulated diabetic persons. Sometimes several evaluations of sugar content are done following the administration of a known amount of glucose. This procedure is called the *glucose tolerance test* and usually is given along with another test which determines the amount of sugar in the urine. This combination of tests can indicate faulty cell metabolism.

Clotting time

Nature prevents excessive loss of blood from small vessels by the formation of a clot. Preceding surgery and under some other circumstances, it is important to know that the time required for coagulation to take place is not too long. Since clotting is a rather complex process involving many elements, a delay may be due to a number of different factors, including lack of certain hormone-like substances, calcium salts, and vitamin K.

The various clotting factors are designated by Roman numerals, I through XIII. Factor I is fibrinogen, factor II is prothrombin, factor III is thromboplastin, and factor IV is assigned to calcium ions. The amounts of all thirteen factors may be determined and evaluated on a percentage basis, aiding in the diagnosis and treatment of some bleeding disorders.

Platelet Count

A count of the thrombocytes is done occasionally, but it is difficult to do accurately. Normal counts are said to vary from 200,000 to 400,000 per cubic millimeter. However, counts as low as 100,000

per cubic millimeter may not indicate an abnormality. In some severe hemorrhagic disorders, the counts have been known to go as low as 10,000 per cubic millimeter.

226. The heart

In the next two lessons, we shall investigate the manner in which the blood acquires its food and oxygen to be delivered to the cells and disposes of the waste products of cell metabolism. As you read this lesson refer to figure 4-1 for visuals.

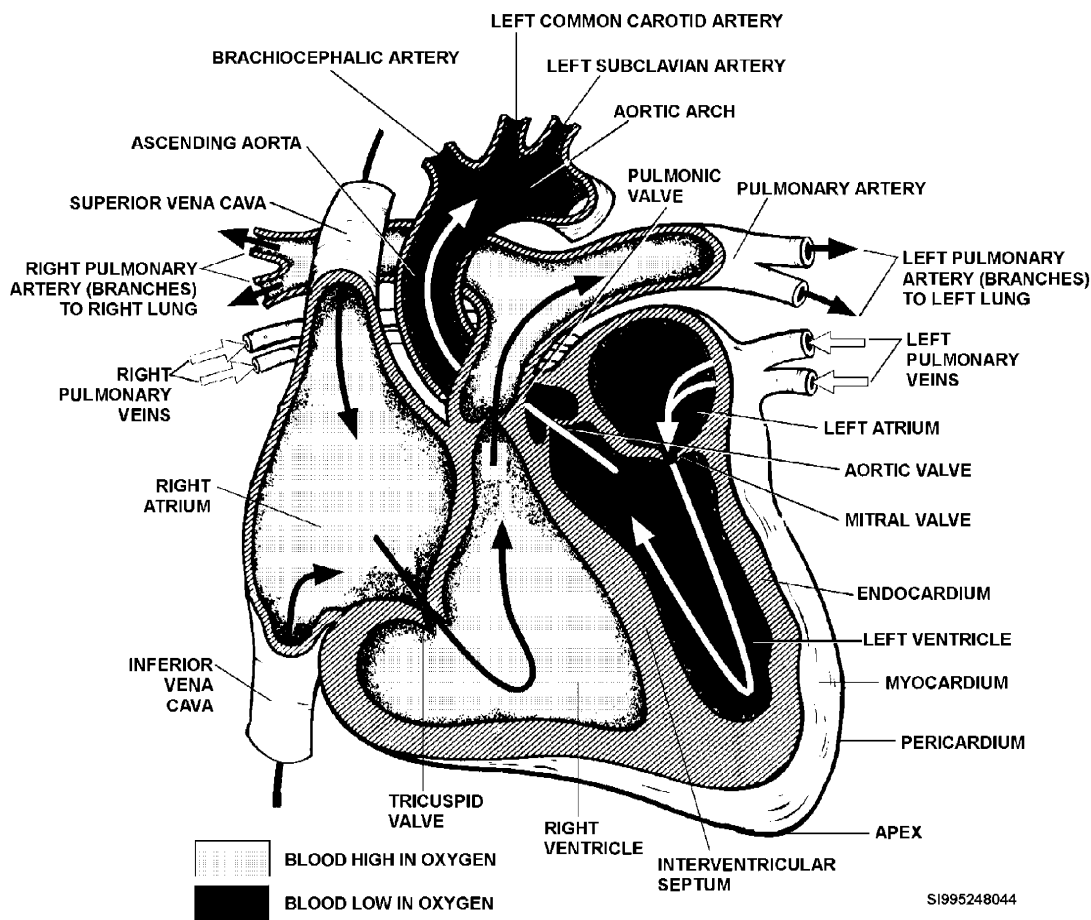


Figure 4-1. The heart and great vessels

Circulation and the heart

The continuous one-way movement of the blood is known as its circulation. The fact that blood circulates throughout the body implies that there must be some sort of propelling mechanism. The prime mover in this case is the heart; and we shall have a look at the heart before going into the circulatory vessels in any detail.

The heart is a muscular pump that drives the blood through the blood vessels. This organ is slightly bigger than a fist and is located between the lungs in the center and a bit to the left of the midline of the body. The strokes (contractions) of this pump average about 72 per minute and are carried on unceasingly for the whole of a lifetime.

The importance of the heart has been recognized for centuries. The fact that its rate of beating is affected by emotions may be responsible for the very frequent references to the heart in song and poetry. However, the vital functions of the heart and its disorders are of more practical importance to us at this time.

Heart structure

Heart wall layers

The heart is a hollow organ with walls that are formed with three different layers. Just as a warm coat might have a smooth lining, a thick and bulky interlining and an outer layer of fabric, the heart wall has three tissue layers:

1. *Endocardium* is a very smooth layer of cells. This membrane lines the interior of the heart. The valves of the heart are formed by folds of this material with reinforcement.
2. *Myocardium* is the muscle of the heart and is the thickest layer.
3. *Pericardium* forms the outermost layer of the heart wall as well as serving as the lining of the pericardial sac that encloses the heart.

Health care providers often refer to the right heart and the left heart. This is because the human heart is really a double pump. The two sides are completely separated from each other by a partition called the *septum*. The upper part of this partition is called the *interatrial septum*, while the larger lower portion is called the *interventricular septum*. This septum is largely myocardium.

Chambers of the heart

On either side of the heart there are two chambers, one of which is a receiving chamber and the other a pumping chamber:

1. The *right atrium* is a thin-walled chamber that receives the blood returning from the body tissues. This blood, which is low in oxygen is carried in the *veins*.
2. The *right ventricle* pumps the venous blood received from the right atrium, and sends it to the lungs.
3. The *left atrium* receives blood high in oxygen content as it returns from the lungs.
4. The *left ventricle* has the thickest walls of all and it pumps oxygenated blood to all parts of the body. This blood goes through the *arteries*.

Valves

We've talked about the fact that blood is being pumped in and out at the same time through contractions. What is there to keep the blood from trying to flow in the wrong direction? The heart has valves that serve as directional traffic cops. The valves, which are all one-way, are located at the entrance and the exit of each ventricle. The valves at the entrances are the *atrioventricular valves*, while the exit valves are *semilunar valves*. "Semilunar" means "resembling a half-moon." Each valve has a specific name. Each valve is identified in the following table:

Valve	Description
Aortic semilunar	Is located between the left ventricle and the aorta. Following contraction of the left ventricle, the aortic valve closes to prevent the flow of blood back from the aorta into the ventricle.
Left atrioventricular	Usually referred to as the <i>mitral valve</i> , it has two rather heavy flaps, or cusps, that permit blood to flow freely from the left atrium into the left ventricle. However, the flaps close when the left ventricle begins to contract, preventing blood from returning to the left atrium and ensuring the onward flow of blood into the <i>aorta</i> .

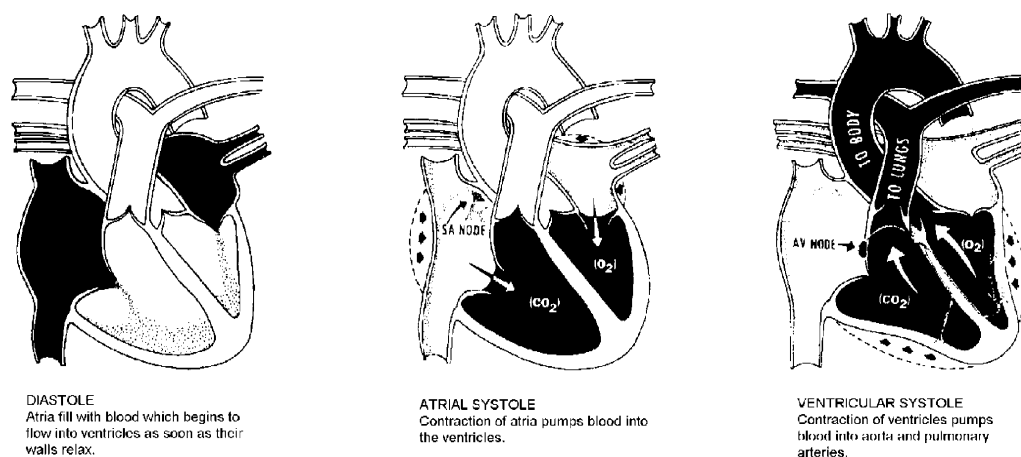
Pulmonary semilunar	Is located between the right ventricle and the pulmonary artery that leads to the lungs. When the right ventricle has finished emptying itself, the valve closes to prevent blood on its way to the lungs from returning to the ventricle.
Right atrioventricular	Also known as the <i>tricuspid valve</i> , it has three cusps or flaps that open and close. When this valve is open, blood flows freely from the right atrium into the right ventricle. However, when the right ventricle begins to contract, the valve closes so that blood cannot return to the right atrium. This ensures onward flow into the pulmonary artery.

Blood supply to the myocardium

Although blood flows through the heart chambers, only the endocardium comes into contact with this vital fluid. Therefore, the myocardium must have its own blood vessels to provide oxygen and nourishment and to remove waste products. The arteries that supply blood to the muscle of the heart are called the right and left *coronary arteries*. These arteries are the first branches of the aorta. They arise just above the aortic semilunar valve. After passing through capillaries in the myocardium, blood drains into the cardiac veins and finally into the coronary venous sinus for the return trip to the right atrium.

How the heart works

Although the right and the left sides of the heart are separated from each other, they work together (fig. 4-2). The blood is squeezed through the chambers by a contraction of heart muscle beginning in the thin walled upper chambers, the atria, and followed by a contraction of the thick muscle of the lower chambers, the ventricles. This active phase is called *systole*, and in each case it is followed by a short resting period known as *diastole*. The contraction of the walls of the atria is completed at the time the contraction of the ventricles begins. So, the resting phase (diastole) begins in the atria at the same time as the contraction (systole) begins in the ventricles. When the ventricles have emptied, the atria (which meanwhile have been filling with blood) contract while the ventricles relax and again fill with blood. Then the ventricular systole begins.



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Figure 4-2. Pumping cycle of the heart

Cardiac muscle tissue has several unique properties. One of these is due to the interconnection of the muscle fibers. The fibers are interwoven so that the stimulation that causes the contraction of one

fiber results in the contraction of the whole group. This plays an important role in the process of conduction and the working of the heart muscle.

Another property of heart muscle is its ability to adjust contraction strength to the amount of blood received. When the heart chamber is filled and the wall is stretched (within limits), the strength of the contraction is greater when the heart is emptying. When less blood enters the heart, the contraction is weaker than when the heart is filling. When more blood enters the heart, as occurs during exercise, it contracts with great strength to push the larger volume of blood out into the blood vessels.

Control of the heartbeat

If the nerves that supply voluntary muscles are cut, these muscles cease to function; they are completely paralyzed. However, if the nerves that supply the heart are severed, the heart will continue to beat. The reason for this is that although the heart is under the control of the nervous system, heart muscle itself is capable of contracting rhythmically, independent of outside control. Despite this, the impulses from the nervous system are required to cause a rapid enough beat to maintain circulation effectively. Without nerve connection, the heart rate might be less than 40 beats per minute instead of the usual 70 to 90 beats per minute.

The conduction system

Specialized masses of tissue in the heart wall form the conduction system of the heart, regulating the order of events. Two of these are called *nodes*, while the third is a branching structure called the *atrioventricular bundle*. The *sinoatrial (SA) node* is located in the upper wall of the right atrium and acts as a pacemaker. The second node is called the *atrioventricular (AV) node* and is located in the septum at the junction between the interatrial portion and the interventricular part. The atrioventricular bundle, also known as the *bundle of His*, is located in the interventricular septum with branches extending to all parts of the ventricle walls. The order in which the impulses travel is:

1. The beginning of the heartbeat is in the sinoatrial node, the pacemaker.
2. The excitation (contraction) wave travels throughout the muscle of each atrium, causing these muscles to contract.
3. The atrioventricular node is stimulated. The relatively slower conduction through this node allows the atrial contraction to fill the ventricle.
4. The excitation wave travels rapidly through the bundle of His and throughout the ventricular walls. The entire musculature of the ventricles contracts practically all at once.

Sounds and murmurs

The normal heart sounds are usually described by the two syllables “lubb” and “dupp.” The first is a longer and lower-pitched sound that occurs during the ventricular systole. It is probably caused by a combination of sounds including the closure of the atrioventricular valves. The second, or dupp, sound is shorter and sharper. It occurs during the beginning of ventricular relaxation, and is due in large part to the sudden closure of the semilunar valves. Abnormal sounds are called *murmurs* and are usually due to faulty action of the valves. If, for example, the valves fail to close tightly and blood leaks back, a murmur is heard. Another condition giving rise to an abnormal sound is the narrowing (stenosis) of a valve orifice. The many conditions that can cause an abnormal heart sound may be due to congenital defects, to disease, or to physiologic variations.

Heartrate

The terms used to describe heartrate are discussed in the following table:

Term	Description
Bradycardia	Means the heart rate is relatively slow. During rest and sleep the heart may beat less than the normal 60 to 80 beats per minute, but usually not below 50 beats per minute.

Premature beats	Also called <i>extrasystoles</i> , cause an arrhythmia that may occur in normal persons. These are beats that come in before the expected normal beats. Caffeine, nicotine or psychological stresses may initiate these beats. They are also common in heart disease.
Sinus arrhythmia	Is a regular variation in heart rate due to changes in the rate and depth of breathing, a normal phenomenon.
Tachycardia	Refers to a heart rate over 100 beats per minute.

Preventing ailments of the heart

Although there may not be complete agreement on any set of rules for preventing or at least delaying the onset of heart disease, many authorities might concur on the following:

1. Proper nutrition, including all the basic food elements, will aid in maintaining all tissues, including those of the heart, in their optimal condition. The avoidance of eating more than is necessary, in order to prevent obesity, will be better for the heart.
2. Infections should be avoided as much as possible. Mild infections should be cared for to prevent serious complications from developing.
3. Dental care should include the treatment of abscesses and the cleaning and filling of decayed teeth.
4. Temperate habits and adequate rest are desirable.
5. People who wish to avoid heart disease need to avoid excesses in the use of tobacco, of alcohol, and of food. On the basis of numerous studies, it appears that the smoker is ten times more likely to die of coronary heart disease than is the nonsmoker.
6. Emotional upsets and psychological upheavals are not conducive to maintaining a healthy heart.
7. Playing too hard is just as damaging as working too hard.
8. Regular physical examinations may be useful, particularly in older persons and in those who have had symptoms that might suggest the presence of disease.
9. Appropriate exercise programs are an important part of prevention as well as of the treatment of heart disease. Regular exercise programs, with gradual increases in the length and difficulty of activity, have been found to be most helpful. To begin with, simple walking may be most effective, followed by such activities as swimming, bicycling, and jogging. Aerobic dancing or other vigorous exercises, in which the person increases the heart rate and oxygen demand as well as getting recreation, are now used in some physical therapy programs.

Heart studies

The *stethoscope* is a relatively simple instrument used for conveying sounds from within the patient's body to the ear of the examiner. Experienced listeners can gain much information using this device. The *electrocardiograph (EKG)* is used for making records of the changes in the electric currents produced by the contracting heart muscle. It is valuable in detecting certain myocardial injuries.

The *fluoroscope*, which is an instrument for examining deep structures with x-rays, may be used to note heart action as well as for observing the size and relationships of some of the thoracic organs. It may be used in conjunction with *catheterization* of the heart. In this procedure, an extremely thin tube (a catheter) is passed through the veins of the right arm or the right groin, and then into the right side of the heart. During the passage of this tube the fluoroscope is used for observing the route taken by the catheter, and samples of blood are removed through the tube. Finally, the tube is passed all the way through the pulmonary valve and into the large lung arteries. Further samples of blood, removed for testing, are obtained along the way, while pressure readings being taken.

Ultrasound is acoustic energy generated at a frequency above the range of sensitivity of the human ear. In *echocardiography*, also known as ultrasound cardiography, the high frequency sound vibrations are sent into the heart through the chest wall, then recorded upon return. Cardiac structures return the echoes, giving information about the size and shape of the structures. Movement of the echoes is traced on an electronic instrument called an oscilloscope, and recorded on film (the same principle is employed by submarines to detect ships).

Pacemakers

Electric battery-operated pacemakers supply impulses to regulate the heart beat, and are implanted under the skin in operations performed on many thousands of individuals. The site of implantation is usually in the left chest area. Electrode catheters attached to the pacemaker are then passed into the heart and anchored to the chest wall. The frequency of battery pack replacement varies with the type of pacemaker. This rather simple device has saved many people whose hearts cannot beat effectively alone. In an emergency, a similar stimulus can be supplied to the heart muscle through electrodes placed externally on the chest wall.

Heart surgery

Coronary bypass surgery to relieve varying degrees of obstruction in the coronary arteries is a common and often successful treatment. The damaged or obstructed coronary arteries are removed and replaced with healthy segments of blood vessels from the patient's body. Usually parts of the saphenous vein (a superficial vein in the leg) are used. Sometimes as many as six or seven segments are required to replace seriously damaged coronary vessels. The mortality rate in this operation is low. Some patients are able to return to a nearly normal lifestyle following recovery from the surgery.

Diseased valves may become so deformed and scarred from endocarditis they are ineffective and often obstructive. In some cases, a special small knife can be inserted into the heart chamber and the valve can be cut so that it no longer obstructs the blood flow. The valve may even become partially functional. In other cases there may be so much damage that replacement is the only resort. Substitute valves made of plastic materials have proven to be a lifesaving measure for many patients.

Both of these procedures sound pretty complicated; they are! Sometimes, physicians can locate the blockage in arteries and insert a balloon-tipped catheter into the artery. Once the catheter is in the narrowed passage, the balloon tip is inflated and the artery is pushed open. This "balloon angioplasty" procedure has become extremely popular due to its minimal invasiveness.

227. Blood vessels and circulation

Blood vessels, together with the four chambers of the heart, form a closed system for the flow of blood. Only if there is an injury to some part of the wall of this system does any blood escape. The circulatory system will be easy to understand now that we know what the blood does and where it is supposed to go. If you keep one eye on the figures in this lesson and the other on the text, as the vessels are described, a picture of the system as a whole will gradually emerge.

On the basis of function, blood vessels may be divided into three groups:

Group	Description
Arteries	Carry blood from the ventricles (pumping chambers) of the heart out to the capillaries in organs and other parts of the body.
Capillaries	Allow exchanges between the blood and the body cells, or between the blood and the air in the lung tissues. The capillaries connect the smallest arteries (arterioles) and the smallest veins (venules).
Veins	Drain capillaries in the tissues and the organs, and return the blood to the heart.

Arteries and veins both may be subdivided into two groups or circuits—pulmonary and systemic.

Pulmonary vessels are related to the lungs. They include the pulmonary artery and its branches to the capillaries in the lungs, as well as the veins that drain those capillaries. The pulmonary arteries carry blood low in oxygen from the right ventricle, while the pulmonary veins carry blood high in oxygen from the lungs into the left atrium. An interesting note, the pulmonary arteries and veins are the only arteries and veins in the body with reversed roles. The pulmonary artery carries deoxygenated blood away from the heart (to the lungs) and the pulmonary vein carries oxygenated blood back to the heart (fig. 4-3).

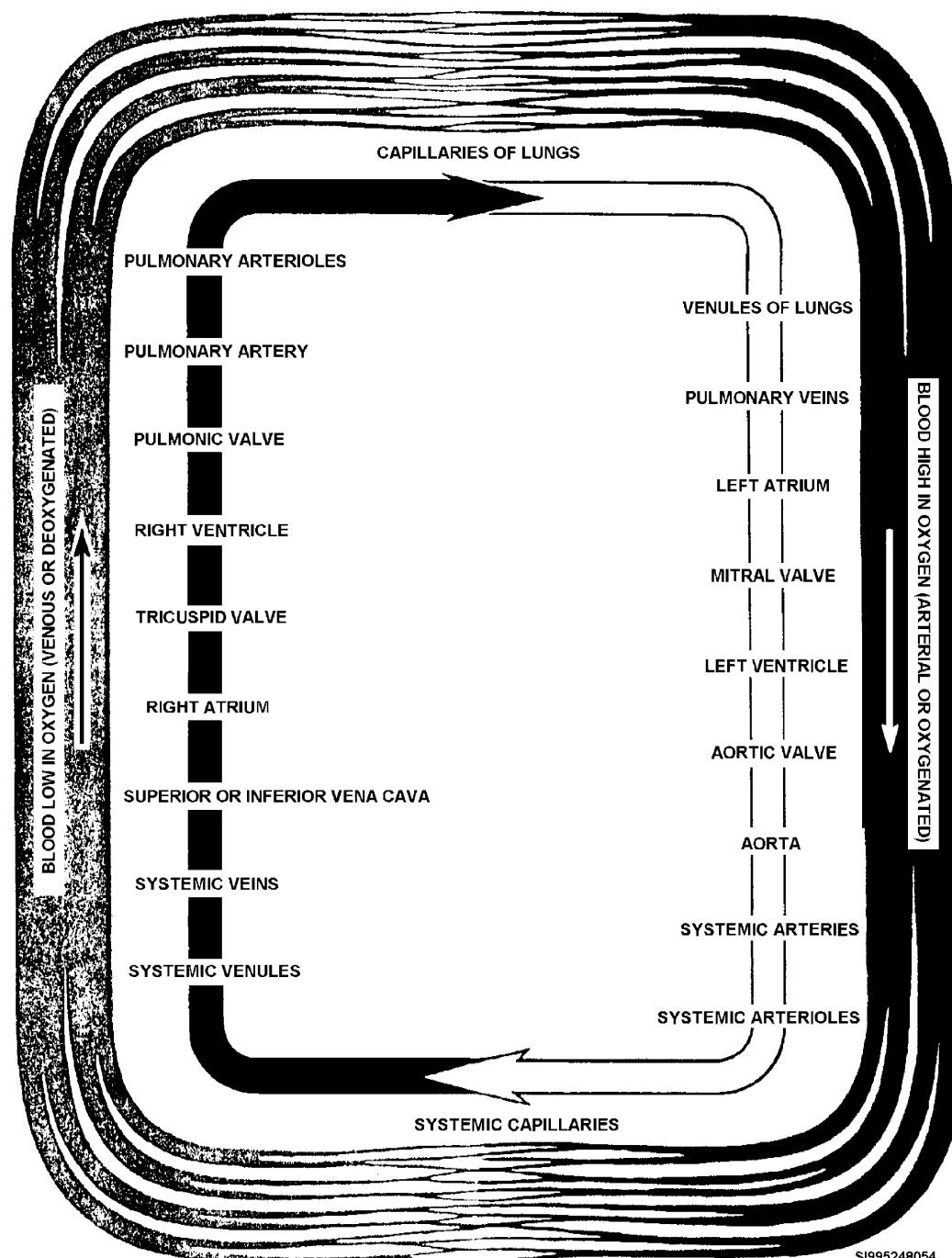


Figure 4-3. Closed system of blood flow.

Systemic arteries and veins are related to the rest of the body. This circuit is concerned with supplying food and oxygen to all the tissues of the body and carrying away waste materials from the tissues for disposal.

Blood vessels

Artery walls

The arteries have thick walls because they receive the pumping drive from the ventricles of the heart. There are three coats (tunics) which resemble the three tissue layers of the heart. The innermost coat (membrane) of *endothelium* forms a smooth surface over which the blood may easily move. The second, more bulky layer is made of *involuntary muscle* combined with elastic connective tissue. An outer tunic is made of a supporting *connective tissue*.

The largest artery, the *aorta*, is about 1 inch in diameter and has the thickest wall because it receives blood under the highest pressure from the left ventricle. The smallest subdivisions of arteries, the *arterioles*, have thinner walls in which there is very little connective tissue but relatively more smooth muscle.

Capillary walls

The microscopic branches of these tiny connecting vessels have the thinnest walls of any vessels: one cell layer. The capillary walls are transparent and are made of smooth plate-like cells that continue from the lining of the arteries. Because of the thinness of these walls, exchanges between the blood and the body cells are possible. The capillary boundaries are the most important center of activity for the entire circulatory system. Their function is explained later in this unit.

Walls of veins

The union of capillaries forms the smallest veins, called venules. Their walls are only slightly thicker than those of the capillaries. As the veins become larger, the walls become thicker. However, veins have much thinner walls than those of comparable arteries because the blood within them is under much lower pressure. Although there are three layers of tissue in the walls of the larger veins, as in the artery walls, the middle tunic is relatively thin in vein walls. Therefore, veins are easily collapsed, and slight pressure on the vein by a tumor or some other mass may interfere with the return blood flow. Most veins are equipped with one-way valves that permit the blood to flow in only one direction. They are most numerous in the veins of the extremities.

Deep veins

The deep veins tend to parallel arteries and usually have the same names as the corresponding arteries (fig.4-4). Examples of these include the *femoral* and the *iliac* vessels of the lower part of the body and the *brachial*, the *axillary*, and the *subclavian* vessels of the upper extremities. However, exceptions are found in the veins of the head and the neck. The *jugular veins* drain the areas supplied by the carotid arteries. Two *brachiocephalic* (innominate) *veins* are formed, one on each side, by the union of the subclavian and the jugular veins. (Remember that there is only one brachiocephalic artery.)

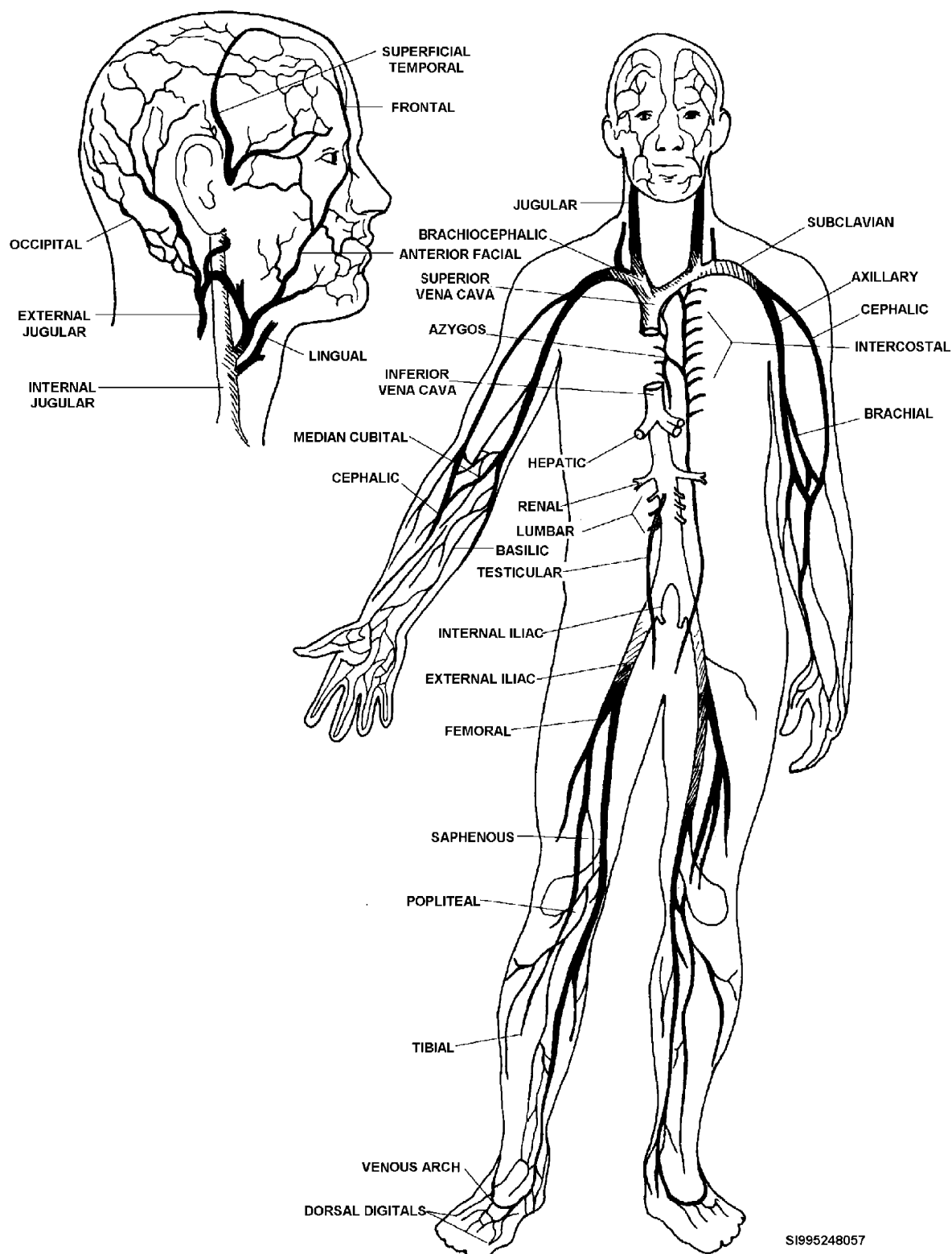
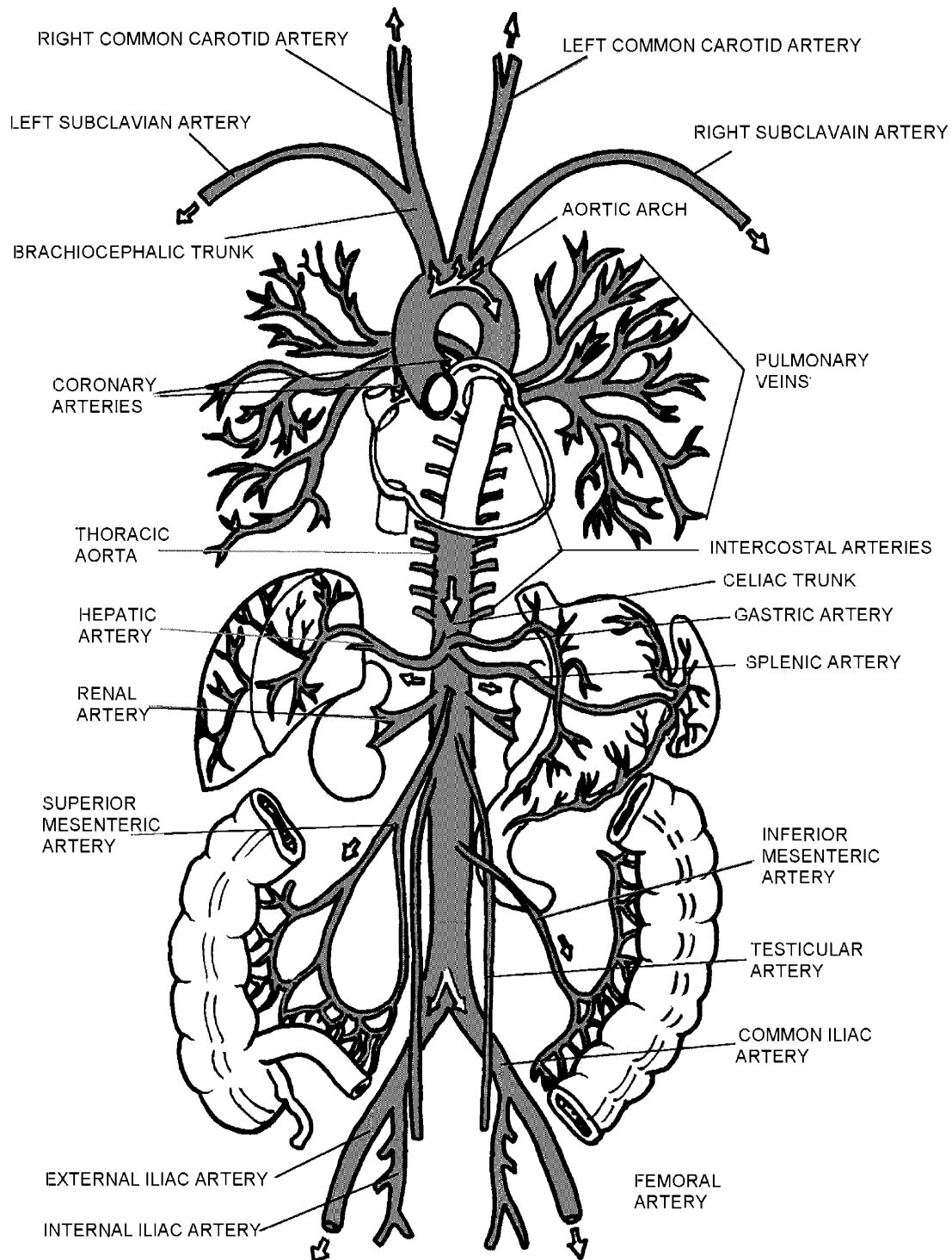


Figure 4-4. Principal veins

Systemic arteries

The Aorta and Its Parts



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Figure 4-5. The aorta and its branches.

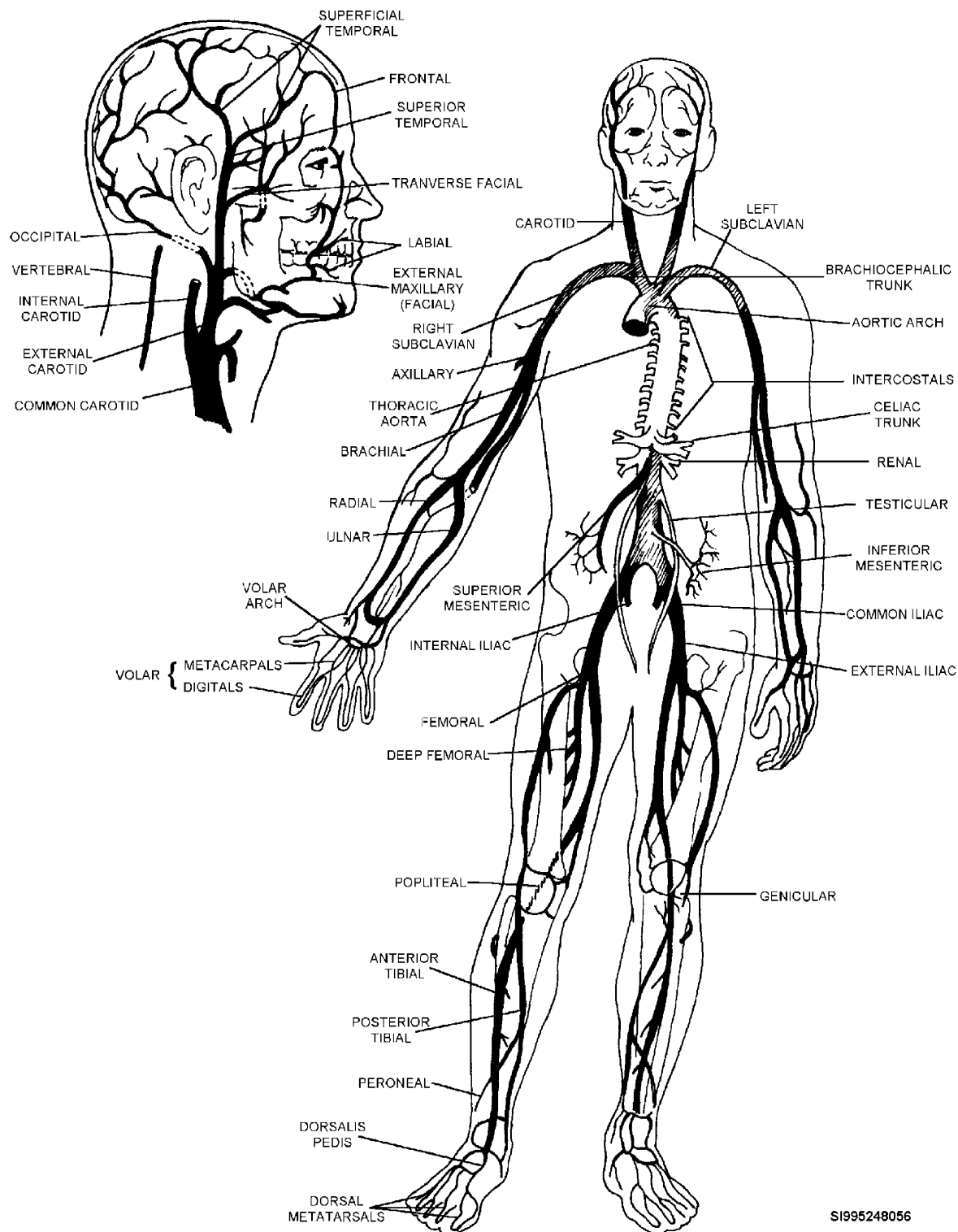


Figure 4-6. Principal arteries

The aorta is by far the largest artery of the body. It extends upward and to the right from the left ventricle. Then it curves backward and to the left. It continues down behind the heart just in front of the vertebral column, through the diaphragm, and into the abdomen (figs. 4-5 and 4-6). In figure 4-5

the arrows indicate the flow of blood. The pulmonary veins carry oxygenated blood from the lungs to the left atrium of the heart. The aorta is one continuous artery divided into four sections:

1. Ascending aorta.
2. Aortic arch.
3. Thoracic aorta.
4. Abdominal aorta.

Ascending aorta

The first, or ascending, part of the aorta has two branches called the left and right *coronary arteries* which supply the heart muscle. These form a crown around the base of the heart and give off branches to all parts of the myocardium. This section is near the heart and inside the pericardial sac.

Aortic arch

The arch of the aorta, located immediately beyond the ascending aorta, curves from the right to the left, and also extends backward. It gives off three large branches—brachiocephalic trunk, left common carotid artery, and left subclavian artery. The *brachiocephalic trunk* is a short artery formerly called the innominate. After extending upward somewhat less than 2 inches (5 cm), it divides into the right subclavian artery, which supplies the right upper extremity (arm), and the right common carotid artery, which supplies the right side of the head and the neck. The *left common carotid artery* extends upward from the highest part of the aortic arch. It supplies the left side of the neck and the head. The *left subclavian artery* extends under the left collar bone (clavicle) and supplies the left upper extremity. This is the last branch of the aortic arch.

Thoracic Aorta

The third part of the aorta supplies branches to the chest wall, to the esophagus, and to the bronchi (the treelike subdivisions of the trachea—windpipe) and their subdivisions in the lungs. It lies just in front of the vertebral column behind the heart and in the space behind the pleura. There are usually nine to ten pairs of *intercostal arteries* that extend between the ribs, sending branches to the muscles and other structures of the chest wall.

Abdominal Aorta

The abdominal aorta is the longest section of the aorta, spanning the abdominal cavity. As in the case of the thoracic aorta, there are unpaired branches extending forward and paired arteries extending toward the side. The unpaired vessels are large arteries that supply the abdominal viscera. The most important of these visceral branches are the celiac trunk, superior mesenteric artery, and inferior mesenteric artery.

The *celiac trunk* is a short artery about 1/2 inch (1.25 cm) long that subdivides into three branches, namely, the *left gastric* to the stomach, the *splenic* to the spleen, and the *hepatic artery* which carries oxygenated blood to the liver. The *superior mesenteric artery* is the largest of these branches, and carries blood to most of the small intestine as well as to the first half of the large intestine. The much smaller *inferior mesenteric artery* is located below the superior mesenteric and near the end of the abdominal aorta, and supplies the last half of the large intestine.

The lateral (paired) branches of the abdominal aorta include the following right and left divisions:

Arteries	Description
Lumbar	There are four pairs of these arteries. They extend into the musculature of the abdominal wall.
Ovarian	Found in the female, and testicular arteries in the male (formerly called the spermatic arteries), they supply the sex glands.

Arteries	Description
Phrenic	Supply the diaphragm.
Renal	Largest in this group, carry blood to the kidneys.
Suprarenal	Supply the adrenal (suprarenal) glands

Capillaries

The microscopic branches of these tiny connecting vessels have the thinnest walls of any vessels—one cell layer. The capillary walls are transparent and are made of smooth plate-like cells that branch off the lining of the arteries. Because of the thinness of these walls, exchanges between the blood and the body cells are possible. The capillary boundaries are the most important center of activity for the entire circulatory system.

In a general way, the circulating blood might be compared to a train that travels around the country, loading and unloading freight in each of the cities that it serves. For example, as blood flows through capillaries surrounding the air sacs in the lungs, it picks up oxygen and unloads carbon dioxide. Later, when this oxygenated blood is pumped to capillaries in other parts of the body, it unloads the oxygen and picks up the carbon dioxide as well as other substances resulting from cellular activities in the areas being served.

Although the heart, arteries, and veins are all essential parts of the circulatory system, the microscopic capillaries are of fundamental importance. It is only through these thin-walled vessels that exchanges can take place. However, you can't forget that all living cells are immersed in a slightly salty liquid called tissue fluid. This fluid serves as a "middleman" between the capillary membrane and the neighboring cells. As water, oxygen, and other materials necessary for cellular activity pass through the capillary walls, they enter the tissue fluid. Then these substances make their way (by diffusion) to the cells. At the same time, coming from the cells and moving in the opposite direction, are carbon dioxide and other end products of cell metabolism. These substances enter the capillary and are carried away by the bloodstream, to reach other organs or to be eliminated from the body.

Venous sinuses

The word "sinus" means "a space" or "a hollow." The sinusoids (the word means "like a sinus") found in the liver, the spleen, the thyroid gland, and other structures are channels within the tissues of the organ. Larger channels that do not have the usual tubular structure of the veins also may drain deoxygenated blood. They are known as *venous sinuses*. An important example of a venous sinus is the *coronary sinus*, which receives most of the blood from the veins of the heart wall. It lies between the left atrium and left ventricle on the under (inferior) surface of the heart. It empties directly into the right atrium along with the two venae cavae.

Other important venous sinuses are located inside the skull. They are the *cranial venous sinuses* that drain the veins that come from all over the brain.

The portal system

The portal system of veins includes those veins that drain blood from capillaries in the spleen, stomach, pancreas, and intestine. In general, these veins have the same names as the arteries that carry blood to organs. These veins deliver blood to the portal vein for a detour through the liver. The largest tributary of the portal vein is the *superior mesenteric vein*. It is joined by the *splenic vein* just under the liver. Other tributaries of the portal circulation are the *gastric*, the *pancreatic*, and the *inferior mesenteric veins*.

Upon entering the liver, the portal vein divides and subdivides into ever-smaller branches. Eventually, the portal blood flows into a vast network of capillary-like vessels called sinusoids. Since this portal blood has already passed through capillaries in other organs, its oxygen content is low.

The purpose of the portal system of veins is to transport blood from the digestive organs and spleen to the liver sinusoids so the liver cells can carry out their functions. For example, when food is digested, most of the end products are absorbed from the small intestine into the bloodstream and transported to the liver by the portal system. In the liver, these nutrients are processed, stored, and released as needed into the general circulation. Remember, back in volume 1 of this course, the *first pass* effect? This is it!

Pulse and blood pressure

Pulse

The ventricles pump blood into the arteries regularly about 70 to 80 times a minute. The force of ventricular contraction starts a wave of increased pressure, which begins at the heart and travels along the arteries. This wave is called the *pulse*. It can be felt in the arteries that are relatively close to the surface, particularly if the vessel can be pressed down against a bone. At the wrist the radial artery passes over the bone on the thumb side of the forearm, and the pulse is most commonly obtained here. Other vessels sometimes used for obtaining the pulse include the carotid artery in the neck and the dorsalis pedis on the top of the foot.

Normally, the pulse rate is the same as the heart rate. Only if a heartbeat is abnormally weak, or if the artery is obstructed, may the beat not be detected as a pulse. In checking the pulse of another person, it is important to use the second or third fingers. If you use your thumb, you may find that you are getting your own pulse. When taking a pulse, it is important to gauge the strength as well as the regularity and the rate.

Various factors may influence the pulse rate. Some of these are:

1. The pulse is somewhat faster in smaller people and usually is slightly faster in women than in men.
2. In a newborn infant, the rate may be from 120 to 140 beats per minute. As the child grows, the rate tends to become slower. Muscular activity influences the pulse rate. During sleep the pulse may slow down to 60 a minute, while during strenuous exercise the rate may go up to well over 100 a minute. If a person is in good condition, the pulse does not remain rapid despite a continuation of exercise.
3. Emotional disturbances may increase the pulse rate.
4. In many infections, the pulse rate increases with the increase in temperature.
5. An excessive amount of secretion from the thyroid gland may cause a rapid pulse. The pulse rate may serve as a partial guide for the person who must take thyroid extract.

Blood pressure

Since the pressure inside the blood vessels varies with the condition of the heart and the arteries as well as with other factors, the measurement of blood pressure together with careful interpretation may prove a valuable guide in the care and evaluation of a person's health. The pressure decreases as the blood flows from arteries into capillaries and finally into veins. Ordinarily, measurements are made of arterial pressure only. The instrument used is called a *sphygmomanometer*. The two measurements made are of systolic pressure and diastolic pressure. The *systolic pressure*, which occurs during heart muscle contraction and averages around 120, expressed in millimeters of mercury (mm Hg). The *diastolic pressure*, which occurs during relaxation of the heart muscle, averages around 80 mm Hg.

The sphygmomanometer is essentially a graduated column of mercury connected to an inflatable cuff. The cuff is wrapped around the patient's upper arm and is inflated with air until the brachial artery is compressed and the blood flow cut off. Then, listening with a stethoscope, the health care provider or nurse slowly lets air out of the cuff until the first pulsations are heard. At this point the pressure in the cuff is equal to the systolic pressure; and this pressure is read off the mercury column. Then, more air

is let out until a characteristic muffled sound indicates the point at which the diastolic pressure is to be read. Considerable practice is required to ensure an accurate reading.

Self-Test Questions

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

225. The blood

1. What determines the color of blood?
2. What is the liquid element of blood?
3. What is the most abundant protein in plasma?
4. What is the principal form of carbohydrate found in the plasma?
5. List the functions of mineral salts in plasma.
6. How do erythrocytes differ from other cells?
7. What are procoagulants?
8. What are the four blood types involving A and B antigens?
9. What does the blood test "hematocrit" measure?
10. What is leukocytosis?

226. The heart

1. How large is the heart and where is it located?

2. What is the thickest layer of the heart?
3. Which chamber of the heart receives blood returning from body tissues?
4. What type of artery supplies blood to the muscle of the heart?
5. Define bradycardia.
6. Define tachycardia.
7. What term is used to describe regular variation in heart rate due to changes in the rate and depth of breathing?

227. Blood vessels and circulation

1. Based on function, what are the three groups of blood vessels?
2. What group of blood vessels carries blood from the ventricles (pumping chambers) of the heart out to the capillaries in organs and other parts of the body?
3. What is the largest artery of the body?
4. Which veins are included in the portal system of veins?
5. What is the purpose of the portal system of veins?
6. What term describes the force of ventricular contraction starting a wave of increased pressure, beginning at the heart and traveling along the arteries?
7. What two measurements are made when taking a blood pressure?

4-2. Conditions Associated with the Circulatory System

The circulatory system is involved in many different diseases. Some people suffer from blood disorders, others suffer from disorders of the heart, and still others from disorders of their blood vessels and circulation. This section discusses some disorders within each of these three groups of disorders.

228. Blood disorders

Abnormalities of the blood are dependent on several factors, and may be divided into three groups—*anemia*, *neoplastic diseases*, and *hemorrhagic disorders*.

Anemias

Anemia may be defined as a general condition in which there is a reduction in the hemoglobin or red blood cell mass with impaired delivery of oxygen. Excessive loss or destruction of red blood cells or impaired production of red cells or hemoglobin may cause anemia. Anemia can occur with hemorrhage or with conditions that cause hemolysis, the rupture of red cells, impaired production of red cells or hemoglobin. Both nutritional deficiencies and suppression of bone marrow can cause anemia.

Anemias caused by excessive loss or destruction of red blood cells

The excessive loss of red cells occurs with hemorrhage. Hemorrhage may be sudden and acute, or gradual and chronic.

As stated earlier, the average adult has five and one-fourth quarts of blood. If a person loses as much as two quarts suddenly, death usually results. On the other hand, if the loss is gradual, over a period of days to weeks, the body can withstand the loss of as much as four to five quarts. If the cause of the chronic blood loss, such as bleeding ulcers, excessive menstrual flow, and bleeding hemorrhoids (piles) can be corrected, the body is normally able to restore the blood back to normal. This process can take up to six months. Until the blood returns to normal, anemia may be present.

Hemolytic anemia

Hemolytic anemia is anemia caused by the excessive destruction of red blood cells. Usually, the spleen destroys the older red blood cells. Occasionally, this destruction proceeds at an accelerated pace, resulting in anemia. More commonly, infections and infestations are the cause of blood cell loss. The action of the malarial organism is an example. When an infected mosquito bites an individual, the malarial parasite is injected into the bloodstream. Each parasite enters a red cell, there it multiplies until the red cell bursts, destroying that cell. The parasite is now freed and can attack other red cells in the same manner, resulting in anemia. Some bacteria, particularly streptococci, cause hemolysis, and consequently a hemolytic anemia.

Sickle cell anemia

Some inherited diseases involve the production of abnormal hemoglobin and may also result in hemolytic anemia. Hemoglobin, in normal adult cells, is of the A type and is designated HbA. In the inherited disease, *sickle cell anemia*, seen almost exclusively in persons of African-American descent, the hemoglobin in many of the red cells is abnormal so that the red cells may have a sickle shape. These sickled cells (fig. 4-7) are very fragile and tend to break easily. Due to their odd shape, they also tend to become tangled in masses that can block smaller blood vessels. If this obstruction occurs, there can be severe joint swelling and pain, especially in the fingers and toes, and there may also be abdominal pain. This development is called *sickle cell crisis*.

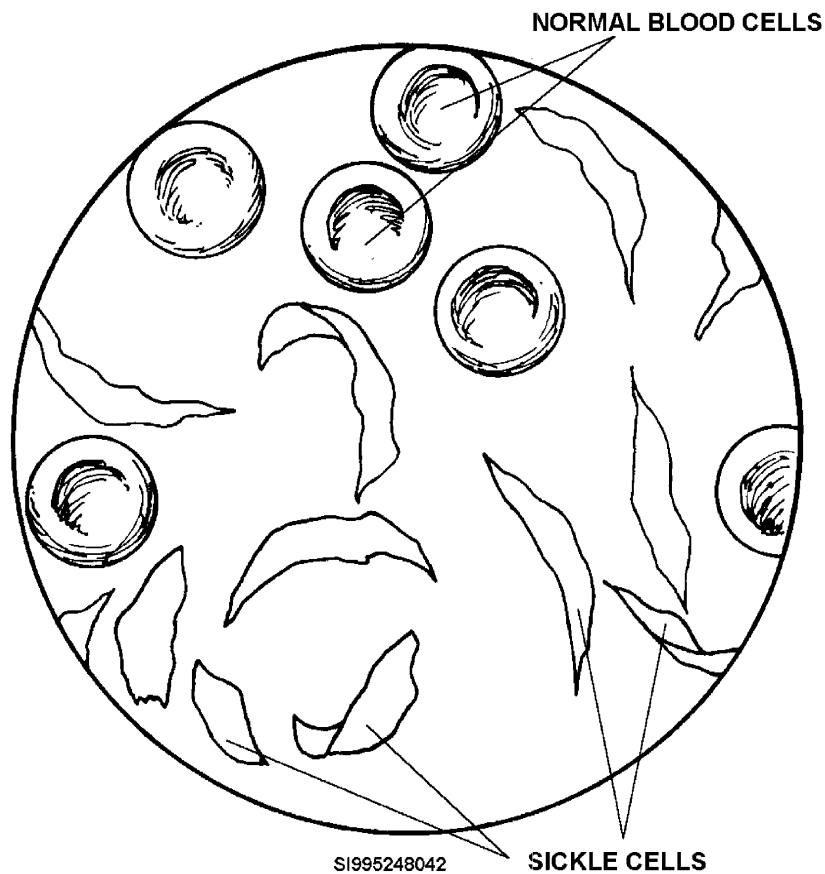


Figure 4-7. Sickling of cells

In the United States, about 8 percent of persons of African-American descent have one of the genes for the abnormal hemoglobin and are said to have the *sickle cell trait*. The clinical disease only appears when the involved gene is transmitted from both parents. About 1 percent of Americans of African-American descent have *sickle cell disease*.

Anemia caused by impaired production of red cells or hemoglobin

Many factors interfere with normal red cell production. Some are the result of nutrient deficiency; they are called *nutritional anemias*. This condition can arise from a deficiency of a specific nutrient in the diet, from the inability to absorb the nutrient, or from drugs that interfere with the body's use of the nutrient.

Iron deficiency anemia

Iron deficiency anemia is the most common nutritional anemia. Iron is an essential constituent of hemoglobin. Usually, the normal diet provides enough to meet the needs of the adult male but may be insufficient when there is an increased demand for iron. As an example, children, women of childbearing age, pregnant women, and persons who lose iron because of chronic hemorrhage may need additional iron.

Pernicious anemia

Pernicious anemia is characterized by a deficiency of vitamin B₁₂, a substance essential for the proper formation of red blood cells. Initially, the cause is a permanent deficiency of a factor in the gastric juice that is responsible for the absorption of vitamin B₁₂ from the intestine. When cases of pernicious anemia are neglected it can bring about conditions of deterioration in the nervous system. This can lead to difficulty in walking, weakness, and stiffness of the extremities, mental changes, and permanent damage to the spinal cord. When treatment is initiated early, to include vitamin B₁₂ injections and attention to a prescribed diet, there is an excellent outlook. However, this treatment must be continued for the rest of the patient's life, if they are to remain in good health.

Aplastic anemia

Bone marrow suppression or failure may cause a decrease in the production of red blood cells. Aplastic anemia is one type of bone marrow failure disease, and may be caused by a variety of physical and chemical agents. Both chemical substances and physical agents can injure the bone marrow. These substances and agents include:

Chemical Substances	Physical Agents
<ul style="list-style-type: none"> • Arsenic • Benzene • Chloramphenicol (in some persons) • Gold compounds • Nitrogen mustard 	<ul style="list-style-type: none"> • Radioactive phosphorus • Radium • X-rays • Atomic radiation

Damaged bone marrow fails to produce either red or white cells; therefore the anemia is accompanied by leukopenia. Removing the toxic agent, followed by blood transfusions until the marrow is able to resume its activity, can lead to recovery.

Additionally, bone marrow can fail to produce red blood cells when abnormal cells, such as cancer cells, crowd out normal marrow cells. For example, in one type of leukopenia, the bone marrow is filled with abnormal blood cells, destroying the other cells in the marrow, resulting in a severe anemia.

Neoplastic blood diseases

This group of blood diseases is characterized by a tremendous increase in the number of white cells, due to cancer of the tissues that produce these cells.

Neoplasms are new growths of abnormal cells or tissues, and neoplastic diseases can be cancerous. They include the *leukemias*, a group of diseases characterized by an increase in the number of abnormal white blood cells. Hemorrhagic disorders are characterized by an abnormal tendency of the body to bleed, which is caused by a breakdown in the body's clotting mechanism.]

Remember, we said that the white cells have two main sources: red marrow, also called *myeloid tissue*, and lymphoid tissue. If this mass reproduction of white cells stems from a tumor of the marrow, the condition is called *myelogenous leukemia*. When the cancer stems from the lymphoid tissue, so that most of the abnormal cells are lymphocytes, the condition is called *lymphocytic leukemia*.

Currently, the cause of leukemia is unknown. Both inherent factors and various environmental agents have been implicated. Among the latter are chemicals such as benzene, excessive exposure to x-rays or to radioactive substances, and viruses.

Patients with leukemia exhibit the general symptoms of anemia. Additionally, patients have a tendency to bleed easily. The spleen is greatly enlarged, and several other organs may be enlarged due to the accumulation of white cells within them. X-ray treatments in conjunction with drugs are given to patients with leukemia. However, due to the malignant character of the disease, it still may prove fatal. As new methods of chemotherapy are developed the outlook improves greatly. Many patients survive for years.

Hemorrhagic disorders

All hemorrhagic diseases have a disruption of the coagulation process that causes abnormal bleeding.

Hemophilia

A very rare, hemorrhagic disorder is a disease known as hemophilia. Hemophilia is the title given to a group of inherited disorders characterized by a deficiency in certain clotting factors. The results of having this disease include the possibility of serious abnormal bleeding from a simple cut or bruise. The deficient clotting factors are available in concentrated form for treatment in case of injury, in preparation for surgery, and for the painful bleeding into joints that often occurs.

Purpura

Purpura is another type of bleeding disease. In this disease, hemorrhages occur at the skin and mucous membranes. The abnormal bleeding associated with purpura may be due to a deficiency of platelets or to abnormalities of blood vessel walls. There are most likely a number of reasons for the deficiency of platelets. Drug-induced bone marrow suppression, or cancer of the bone marrow may lead to purpura.

Disseminated intravascular coagulation (DIC)

DIC is a serious disorder of clotting, where there is excessive coagulation. DIC may occur in cases of tissue damage associated with massive burns, trauma, certain acute infections, cancer, and some disorders of childbirth. During the process of DIC, platelets and various clotting factors are used up faster than they can be produced, resulting in serious hemorrhaging.

Blood transfusions

The transfer of whole human blood from a healthy individual to another patient is often a lifesaving process. Blood transfusions may be used for any condition where there is insufficient blood or blood cells to perform the functions of the blood adequately. Some examples are:

1. The treatment of hemorrhage from serious mechanical injuries, such as cuts or other wounds or from disorders that may be accompanied by internal hemorrhage.
2. The treatment of anemia from bleeding ulcers, tubercular lungs with blood loss, and other disorders in which there may be internal bleeding. “Anemia” here means “an insufficiency of blood.”
3. The treatment of *erythroblastosis fetalis*.
4. In cases of blood poisoning (*septic shock*), pneumonias, and kidney disease.
5. For patients receiving chemotherapy for cancer, and those who are on dialysis because of kidney failure.
6. As a preoperative procedure, or during an operation that causes considerable blood loss or that is performed on a patient in a weakened condition.
7. After operations as an aid in combating anemia and shock, and as an aid in the recovery process.

229. Heart disorders

There are many ways of classifying heart disease. The three layers of the heart wall—lining, muscle, and surface—form the basis for one grouping of heart pathology. This group includes endocarditis, myocarditis, and pericarditis. Endocarditis means “inflammation of the lining of the heart cavities,” but it most commonly refers to valvular disease. Myocarditis means inflammation of heart muscle. Pericarditis refers to disease of the serous membrane on the heart surface, as well as membrane lining the pericardial sac.

Another more generally used classification of heart disease is based on causative factors, such as, congenital, rheumatic, coronary, and degenerative heart disease. *Congenital* heart disease is present at birth. *Rheumatic* heart disease begins with an attack of rheumatic fever in childhood or in youth. *Coronary* heart disease involves the walls of the blood vessels that supply the muscle of the heart. *Degenerative* heart disease is due to deterioration of the heart tissues, frequently the result of disorders of long duration such as high blood pressure.

Ischemic heart disease is a term referring to coronary heart disease or degenerative heart disease in which there is a deficiency in blood supply to the heart muscle causing necrosis, or death, of the heart muscle.

Congenital heart disease

This category of heart disease includes certain abnormalities that have been present since birth, and which usually represent a failure of normal development.

The most common congenital heart defects are holes in the septum or partition between the left and right sides of the heart. Blood flow from one side of the heart to the other results in a mixture of venous and arterial blood being pumped to the tissues. This defect may be in either the atrial or ventricular septum.

The circulation of the fetus differs in several respects from that of the child after birth, one difference being that the lungs are not used until the child is born. Prior to birth the unused lungs are bypassed by a blood vessel that normally closes of its own accord once the lungs are in use. Sometimes, however, the vessel fails to close, with the result that much of the blood is detoured around the lungs instead of through them; and therefore the blood does not receive enough oxygen.

Another congenital heart defect is an obstruction or narrowing of the pulmonary artery which prevents the blood from passing in sufficient quantity from the right ventricle to the lungs.

In recent years, many of these congenital defects have been remedied by heart surgery, one of the more spectacular advances in modern medicine.

Rheumatic fever

Streptococcal infections are indirectly responsible for rheumatic fever and rheumatic heart disease. The toxin produced by the streptococci causes an immune reaction that may be followed some 2 to 4 weeks later by rheumatic fever with marked swelling of the joints. Then the antibodies formed to combat the toxin attack the heart valves, producing a condition known as rheumatic endocarditis. The heart valves, particularly the mitral valve, become inflamed. The normally flexible valve cusps thicken and harden so that the opening becomes permanently narrowed (mitral stenosis). This condition prevents an adequate flow of blood from the left atrium into the left ventricle, with a resulting pulmonary congestion, an important characteristic of mitral heart disease. The incidence of rheumatic fever and, hence, of rheumatic heart disease is being drastically reduced owing to the more prompt and effective antibiotic and other medical treatment of the streptococcal infections.

Coronary heart disease

The heart muscle receives its own blood supply through the coronary arteries. A common cause of sudden death, or at least disability, from heart disease is *coronary occlusion*, that is, closure of one or more branches of the coronary arteries. Such interference with the blood supply will result in damage to the myocardium. The degree of injury sustained depends upon a number of factors, including the size of the artery that is involved and whether the occlusion is gradual or sudden.

Arteries of the heart as well as the rest of the body can undergo degenerative changes. It may happen that the lumen (space) inside the vessel narrows gradually owing to progressive thickening and hardening of the arteries. As a consequence of this, the volume of blood supplied to the heart muscle is reduced and the action of the heart is weakened. Degenerative changes of the artery wall may cause the inside surface to become roughened as well. This roughened artery wall is highly conducive to the formation of a *thrombus*, or blood clot. The thrombus may cause sudden closure of the vessel with complete obstruction of the blood flow. This life-threatening condition is known as *coronary thrombosis*. The area that has been cut off from its blood supply is called an *infarct*. The outcome of a myocardial infarction depends upon the extent of the damage and whether or not other branches of the artery can supply enough blood to maintain the heart's action. Death may occur swiftly if a large area of heart muscle is suddenly deprived of blood supply. If a smaller area is involved, the heart may continue to function. However, complete and prolonged lack of blood supply to any part of the myocardium results in death of tissue and weakening of the heart wall. In some cases, the weakened area may rupture, but in other cases there is a scar formed in the area of the infarct.

The person who suffers an acute coronary occlusion must be put on complete bed rest for a variable period of time, depending upon the severity of the attack and upon the time required for the damaged heart muscle to be replaced by scar tissue. During this period the most meticulous medical and nursing care is required.

Although myocardial infarction is one of the leading causes of death in the United States, prompt and effective treatment enables many individuals to survive a “heart attack,” or “coronary.” Despite the fact that the heart is damaged, it may be possible for the person to lead a fairly normal life so long as he moderates his activities, gets sufficient rest, follows a prescribed diet, and tries to minimize stressful situations.

When the blood flow to the heart muscle is inadequate, there results a characteristic agonizing pain, felt in the region of the heart and in the left arm and the shoulder, called *angina pectoris*. A feeling of suffocation and a general sensation of forthcoming doom may accompany angina pectoris. Heart disease is a common cause of angina pectoris, although there are other causes as well.

Atrial and ventricular fibrillations

These are rapid ineffective muscle contractions with symptoms of heart failure. Fibrillations of the heart muscle begin as small local contractions of a few cells followed by convulsive movements of groups of cells within the muscle wall. They may affect the atria by themselves or they may involve the ventricles, a very serious cardiac disorder. First-aid procedures include cardiopulmonary resuscitation (CPR) and then transfer to a hospital.

Degenerative heart disease

During a person’s lifetime, many toxins, infection and other kinds of injuries may cause weakening of the heart muscle. High blood pressure, known as *hypertension*, over a period of years may cause an enlargement of the heart, and finally heart failure. Malnutrition, chronic infections, and severe anemias may cause degeneration of heart muscle. Hyperthyroidism with its tendency to cause over-activity of all parts of the body, including the heart, is another cause of heart failure. Although heredity may be responsible for an undue susceptibility to degenerative heart disease, it may also be a result of other diseases that cause damage to the heart.

230. Blood vessel and circulatory disorders

This lesson provides information on some of the more common disorders of blood vessels and circulation. The topics covered here include abnormal blood pressure, aneurysms, arterial degeneration, hemorrhage, shock, varicose veins, phlebitis, stasis dermatitis and ulcers, and arterial obstruction.

Abnormal blood pressure

Hypotension

Lower than normal blood pressure is called hypotension. However, there are individual variations in normal pressure levels, and what would be a low pressure for one person might be a normal or even a high pressure for someone else. For this reason, hypotension is best evaluated in terms of how well the body tissues are being supplied with blood. For example, a person whose systolic pressure is consistently below his or her normal range may experience episodes of fainting because of inadequate blood flow to the brain. The sudden lowering of blood pressure below a person’s normal level is one symptom of shock. It may occur also in certain chronic diseases as well as in heart block.

Hypertension

Hypertension, which is high blood pressure, has received a great deal of attention. Often it occurs temporarily as a result of excitement or exertion. It may be persistent in a number of conditions including:

1. Kidney disease and uremia or other toxic conditions.

2. Endocrine disorders such as hyperthyroidism and acromegaly.
3. Artery disease including the hardening of the artery walls.
4. Tumors of the central portion of the adrenal (suprarenal) gland.

Hypertension that has no apparent medical cause is called *essential hypertension*. This condition is fairly common and is seen as a cause of strokes, heart failure, or kidney damage. Treatment is begun with young patients when the diastolic pressure is over 90 mm Hg. An excess of a hormone produced in the kidney, called renin, seems to play a role in the severity of this kind of hypertension. Drugs may be given to block excessive renin production and to prevent fluid retention. General health measures such as weight control and avoidance of excessive alcohol and cigarette consumption plus adequate exercise are all beneficial.

Although stress has been placed on the systolic blood pressure, in many cases the diastolic pressure is even more important. The condition of small arteries may have more effect on the diastolic pressure. At any rate, the determination of what really constitutes hypertension depends on each person's normal range. As previously noted, a pressure that is normal for one individual may be abnormal for another.

Aneurysm

An *aneurysm* is a bulging sac in the wall of an artery or a vein, owing to a localized weakness in that part of the vessel. The aorta is the vessel most commonly involved. The damage to the wall may be congenital, due to infections, or due to degenerative changes referred to as hardening of the arteries. Whatever the cause, the aneurysm continues to grow in size. Sometimes, as it swells, it may cause some derangement of other structures, in which case definite symptoms are manifested. Eventually, however, the walls of the weakened area yield to the pressure, and the aneurysm bursts like a balloon, usually causing immediate death. Some lives may be saved by surgical replacement of the damaged segment with a synthetic graft.

Arterial degeneration

Changes in the walls of arteries frequently lead to loss of elasticity. This loss of elasticity is accompanied by irregular thickening of the artery wall at the expense of the lumen (space inside the vessel). Areas of yellow, fat-like material may replace the muscle and elastic connective tissue, leading to a disorder called *atherosclerosis*. Sometimes the lining of the artery is damaged, and a blood clot (*thrombus*) may form at this point. Such a thrombus may more or less completely obstruct the vessel, as it sometimes does in coronary thrombosis. In other cases, calcium salts and scar tissue (fibrous connective tissue) may cause hardening of the arteries, known as *arteriosclerosis*.

Artery damage may be present for years without causing any noticeable symptoms. As the thickening of the wall continues and the diameter of the passage for blood flow is decreased, a variety of symptoms will appear. The nature of these disturbances will vary with the parts of the body affected and with the extent of the changes in the artery walls. Here are some examples:

1. Muscle cramps and sudden lameness while walking may be due to insufficient blood supply to the lower extremities as a result of artery wall damage.
2. Headaches, dizziness, and mental disorders may be the result of cerebral artery sclerosis.
3. Hypertension may be due to the decrease in size of the lumens within many arteries all over the body. Although hypertension may be present in many younger persons with no apparent artery damage, and arteriosclerosis may be present without causing hypertension, the two are more often found together in older people.
4. Palpitation, dyspnea, paleness, weakness, and other symptoms may be the result of arteriosclerosis of the coronary arteries. The severe pain of angina pectoris may follow the lack of oxygen and myocardial damage associated with sclerosis of the vessels that supply the heart. There is an increase in the amount of urine with the appearance of *albumin*. Albumin is

a normal body protein usually found in the urine only if there is kidney damage. Other symptoms referable to the kidneys may be due to damage to the renal arteries.

The gradual narrowing of the interior of the arteries, with a consequent reduction of the volume of blood that passes through them, gives rise to a general condition known as *ischemia*, which means literally “a suppression of blood.” Those parts that are supplied by the damaged artery therefore will suffer from an inadequate blood supply, and the result is that certain vital cells of these organs will gradually die. The death of cells, for whatever cause, is called *necrosis*.

Once these vital cells die, the organ loses its effectiveness. One example of necrosis due to ischemia is the death of certain cells of the brain, with mental disorders as a possible result. Another example of this is the chain of complications resulting from the gradual closure of the arteries of the leg or (rarely) of the arm. The circulation of blood in the toes or the fingers, never too brisk even at the best of times, may cease altogether. Necrosis occurs; bacteria invade the dead tissue, and putrefaction sets in. This condition is called *gangrene*. Gangrene can result from a number of disorders that may injure the arteries, such as diabetes. Diabetic gangrene is a fairly common occurrence in elderly diabetic patients.

Hemorrhage

A profuse escape of blood from the vessels is known as *hemorrhage* a word that means, “a bursting forth of blood.” Such bleeding may be external or internal, may be from vessels of any size, and may involve any part of the body. Capillary oozing usually is stopped by the normal process of clot formation. Flow from larger vessels can be stopped by appropriate first-aid measures carried out at the scene. In most cases, pressure with a clean bandage directly on the wound will stop the bleeding effectively.

The loss of blood from a cut artery may be rapid and unpleasantly spectacular. Often it is rapidly fatal, and yet immediate appropriate action can be lifesaving. The Red Cross and other organizations give instructions in first aid and agree that excessive loss of blood can and should be prevented in all circumstances. Since hemorrhage is the number one problem in case of an accident, everyone should know that certain arteries could be pressed against a bone to stop hemorrhage. The most important of these “pressure points” are outlined in the following table:

Artery	Pressure Point
Brachial	The brachial artery may be pressed against the humerus (arm bone) if one pushes inward along the natural groove between the two large muscles of the arm. This stops hand, wrist, and forearm hemorrhage.
Common carotid	The common carotid artery, in the neck, may be pressed back against the spinal column for bleeding in the neck and the head. Avoid prolonged compression, which can result in lack of oxygen in the brain.
Facial	This artery may be pressed against the lower jaw as the vessel extends along the side of the face for hemorrhage around the nose, the mouth, and the cheek.
Femoral	The femoral artery (in the groin) may be pressed in order to avoid serious hemorrhage of the lower extremity.
Subclavian	The subclavian artery may be pressed against the first rib by a downward push with the thumb to stop bleeding from the shoulder or arm.
Temporal	The temporal artery may be pressed against the side of the skull just in front of the ear to stop hemorrhage on the side of the face and around the ear.

Shock

The word “shock” has a number of meanings. However, in terms of the circulating blood it refers to a life-threatening condition in which there is inadequate blood flow to the tissues of the body. The factor common to all cases of shock is an inadequate output by the heart. A wide range of conditions that reduce the effective circulation can instigate shock. The exact cause of shock is often not known; however, a widely used classification is based on causative factors. The most important of these are:

Shock	Description
Anaphylactic	Is a severe allergic reaction to foreign substances to which the person has been sensitized. In many cases, the cause of shock is not known and so it is classified according to its severity.
Cardiogenic	Is sometimes called pump failure. It is often a complication of heart muscle damage as is found in myocardial infarction. It is the leading cause of shock death.
Hypovolemic	Is due to a decrease in the volume of circulating blood, and may follow severe hemorrhage or burns.
Septic	Is second only to cardiogenic shock as a cause of shock death. It is usually due to an overwhelming bacterial infection.

Mild shock

In mild shock, regulatory mechanisms act to relieve the circulatory deficit. Symptoms are often subtle changes in heart rate and blood pressure. Constriction of small blood vessels and the detouring of blood away from certain organs increase the effective circulation. Mild shock may develop into a severe, life-threatening circulatory failure.

Severe shock

Severe shock is characterized by poor circulation that causes further damage and deepening of the shock. Symptoms of late shock include clammy skin, anxiety, very low blood pressure, rapid pulse, and rapid, shallow breathing. Contractions of the heart are weakened owing to the decrease in blood supply to the heart muscle. The muscles in the blood vessel walls are also weakened so that they dilate. The capillaries become more permeable and lose fluid owing to the accumulation of metabolic wastes.

Treatment of the victim of shock includes first-aid measures, such as placing him/her in a horizontal position and covering him/her with a blanket. Bleeding should be stopped if it is present. The head should be kept turned to the side to prevent aspiration (breathing in) of vomitus, an important cause of death in shock cases. Further treatment of shock depends largely on treating the causative factors. For example, shock due to fluid loss such as hemorrhage or burns is treated with blood products or plasma expanders. Shock due to heart failure is treated with drugs that will improve the contractions of the heart muscle. In any case, all measures are aimed at supporting the circulation and improving the output of the heart. Oxygen is frequently administered to improve the delivery of oxygen to the tissues.

Varicose veins

Varicose veins is a condition in which superficial veins have become swollen and ineffective. It may be a problem in the esophagus or in the rectum, but the veins most commonly involved are the saphenous veins of the lower extremities. This condition is found frequently in people who spend a great deal of time standing (e.g., salespeople). Also, pregnancy, with the accompanying pressure on the veins in the pelvis, may be a predisposing cause. Varicose veins in the rectum are called *hemorrhoids*, or *piles*. The general term for varicose veins is *varices*, the singular form being *varix*.

Phlebitis

Inflammation of a vein is called *phlebitis*. There is marked pain, often considerable swelling, and involvement of the entire vein wall. A blood clot may form, causing the dangerous condition called *thrombophlebitis*, with the possibility of a piece of the clot becoming loosened and floating in the blood as an *embolus*. If this embolus reaches the lungs, sudden death from *pulmonary embolism* may be the result. Prevention of infection, early activity to ensure circulation following an injury or an operation, and the use of anticoagulant drugs when appropriate has greatly reduced the incidence of this complication.

Arterial obstruction

When the lumen of an artery is completely blocked by arteriosclerosis, the condition is known as *arteriosclerosis obliterans*. The complete obstruction to blood flow causes intense pain. If the disease is allowed to progress and is not treated, the affected part or parts may become ulcerated or gangrenous. In such cases, it is often possible to treat the disease surgically.

In some cases, the obstruction is removed by making an incision into the artery after clamps are placed above and below the plug. Then the plug is removed by a special instrument.

In other instances, the circulation can be restored by the use of vascular grafts. This is done by cutting out the diseased segment and suturing (sewing) a graft in its place. More often, however, grafts are implanted to bypass the obstructed segment. A vein from the patient's own body, usually the saphenous vein, may be used; or a synthetic vessel made of Dacron® or Teflon® may be chosen. Sometimes, a patch graft is used to increase the lumen of small, narrowed areas of arteries. To accomplish this, the artery is clamped above and below the narrowed area and then incised in the long axis of the vessel. A patch of Teflon® is sewn to the edges of the incision, thereby increasing its diameter.

Self-Test Questions

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

228. Blood disorders

1. What are the three groups of blood disorders?
2. Which group of blood disorders is characterized by an abnormal tendency of the body to bleed, which is caused by a breakdown in the body's clotting mechanism?
3. What type of anemia occurs as a result of nutritional deficiency?
4. What is the most common nutritional anemia?
5. What type of anemia is characterized by a deficiency of vitamin B₁₂?
6. List chemical substances that injure the bone marrow?

7. What condition results from a mass reproduction of white cells stemming from a tumor of the bone marrow?
8. What term is used to describe a group of inherited disorders characterized by a deficiency in certain clotting factors?

229. Heart disorders

1. What is endocarditis?
2. What term is used to describe inflammation of the heart muscle?
3. What term refers to disease of the serous membrane on the heart surface, as well as that lining the pericardial sac?
4. What term is used to describe heart disease due to deterioration of the heart tissues, frequently the result of disorders of long duration such as high blood pressure?
5. What are the most common congenital heart defects?
6. What type of infections causes rheumatic fever and rheumatic heart disease?
7. Describe a coronary occlusion.
8. What is angina pectoris?

230. Blood vessel and circulatory disorders

1. What term is used to describe blood pressure that is lower than normal?
2. What term is used to describe high blood pressure that has no apparent medical cause?

3. What is an aneurysm?
4. What blood vessel is most commonly involved in an aneurysm?
5. What is the condition called, when hardening of the arteries is caused by calcium salts and scar tissue?
6. What is ischemia?
7. Define necrosis.
8. What pressure point should be used to stop hemorrhage on the side of the face and around the ear?
9. In terms of the circulating blood, what is shock?
10. What type of shock is the leading cause of shock death?
11. What are the symptoms of severe shock?
12. What term is used to describe a condition in which superficial veins have become swollen and ineffective?
13. What is arteriosclerosis obliterans?

4-3. Drugs Used to Treat Conditions Associated with the Circulatory System

This section wraps up the discussion of blood disorders; heart disorders; and disorders of the blood vessels and circulation. It covers the drugs used to treat these conditions associated with the circulatory system.

231. Drugs affecting the blood

Anticoagulants

Blood coagulation resulting in the formation of a stable fibrin clot involves a chain of reactions involving the interaction of clotting factors, platelets, and tissue materials. Clotting factors exist in the blood in inactive form and must be converted to an enzymatic or activated form before the next step in the clotting mechanism can be stimulated. Each factor is stimulated in turn until an insoluble fibrin clot is formed.

Two separate pathways, intrinsic and extrinsic, lead to the formation of a fibrin clot. Both pathways must function for hemostasis.

Pathway	Description
Extrinsic	Coagulation is activated by release of tissue thromboplastin, a factor not found in circulating blood. Clotting occurs in seconds because factor III bypasses the early reactions.
Intrinsic	All the protein factors necessary for coagulation are present in circulating blood. Clot formation may take several minutes and is initiated by activation of factor XII.

Anticoagulants used therapeutically include heparin and warfarin. We'll discuss these two together and look at a newer type of heparin—low molecular weight heparin—separately.

The methods of action in heparin and warfarin are similar. Heparin, derived from cow's lungs or pig's intestinal mucosa, limits the activation of factor X in both the intrinsic and extrinsic pathways. This inhibits the conversion of prothrombin to thrombin and fibrinogen to fibrin. Without these steps, platelets will not form a clot. Warfarin interferes with the use of vitamin K. Without vitamin K, clotting factors II, VII, IX, and X are depleted, and again the clotting chain is broken.

Neither one of these drugs will break up a clot that is already formed. If used quickly enough though, heparin may keep the clot from enlarging. Heparin treatment is normally started first and patients are switched to warfarin for long-term therapy. Injectable warfarin is normally only used for those patients who can't take oral medications.

Heparin is available only as an injection. Warfarin is available as an injection and tablet. Dosing on these medications is individualized. Patients bleeding times must be monitored to ensure that the proper dose is being used.

Indications and dosage

Both heparin and warfarin are indicated in the prophylaxis and treatment of venous thrombosis, atrial fibrillation with embolism, and pulmonary embolism (a clot).

Heparin is given subcutaneously or IV and is measured in units. An initial dose of 10,000 units SC may be followed with up to 20,000 daily. Remember that dosing is individualized. Bleeding times must be monitored and dosage adjusted accordingly.

Warfarin is loaded orally at 5–10 mg for 2–3 days and then individualized anywhere from 1 mg to 5 mg, depending on the patient. Injectable warfarin is dosed in the same way as oral.

Contraindications

Warfarin has many more contraindications than heparin does. However, both are contraindicated in thrombocytopenia (abnormally low platelet count) and uncontrolled bleeding. Warfarin is also contraindicated in pregnancy.

Warnings

The most serious risks associated with anticoagulant therapy are hemorrhages in any tissue or organ and, less frequently, necrosis or gangrene of skin and other tissues. This has resulted in death or permanent disability. The risk of hemorrhage is related to the intensity and duration of therapy. Necrosis appears to be associated with local thrombosis and usually appears within a few days of the start of therapy. In severe cases, debridement or amputation of the affected tissue or limb has been reported.

Although heparin has not been tested in pregnancy and therefore gets a category C, it shouldn't be considered safe. Injected heparin does not cross the placenta; however, its use during pregnancy has been associated with 13–22% unfavorable outcomes, including stillbirth and prematurity. Compare this to warfarin, which is category X and has a 31% unfavorable outcome percentage. Oral anticoagulants do cross the placenta and have a direct affect on the fetus. Neither of these drugs have an affect on lactation, even though warfarin is excreted into breast milk.

Drug interactions

The oral anticoagulants have a great potential for clinically significant drug interactions. Warn all patients about potential hazards and instruct against taking any drug, including nonprescription products, without the advice of a physician or pharmacist. In addition, advise against sudden change in life habits (eg, drastic change in diet or alcohol consumption).

The following medications may increase bleeding when used with oral warfarin:

Acetaminophen	Hydantoins	Quinidine
Aminoglycosides	Isoniazid	Quinine
Amiodarone	Gemfibrozil	Quinolones
Beta Blockers	Glucagon	Propoxyphene
Cephalosporins	Ketoconazole	Salicylates
Chloral hydrate	Loop diuretics	SMZ-TMP
Chloramphenicol	Lovastatin	Streptokinase
Chlorpropamide	Metronidazole	Sulfonamides
Cimetidine	Miconazole	Tamoxifen
Corticosteroids	Mineral oil	Tetracyclines
Diffunisal	NSAIDs	Thyroid hormones
Fluconazole	Omeprazole	Vitamin E
	Penicillins	

These drugs may decrease the effectiveness of oral warfarin:

Ascorbic acid	Contraceptives, oral	Griseofulvin	Sucralfate
Barbiturates	Dicloxacillin	Nafcillin	Thiazide diuretics
Carbamaze	Estrogens	Rifampin	Trazodone
Cholestyramine	Ethanol	Spirolactone	Vitamin K

These drugs may increase the effectiveness when injected anticoagulants are used:

Antihistamines	Digitalis	Nicotine	Tetracyclines
Aspirin	Dipyridamole	NSAIDs	Ticlopidine
Cephalosporins	Hydroxychloroquine	Penicillins	

Patient information

1. Since heparin is injectable only and normally used in the in-patient setting only, no patient information is given.
2. Warfarin dosing is highly individualized and may have to be adjusted several times based on lab test results. Strict adherence to prescribed dosage schedule is necessary.
3. Do not take or discontinue any other medication, except on advice of physician or pharmacist. Avoid alcohol, salicylates and drastic changes in dietary habits.
4. Notify physician if unusual bleeding or bruising, red or dark brown urine (blood), red or tar black stools or diarrhea occurs. Also report bleeding from the gums or nose, patches of discoloration or bruises on the arms, legs or toes, or excessive bleeding following minor cuts (e.g., while shaving).
5. Do not change brands without consulting a physician or pharmacist.
6. Discuss with physician any plan to become pregnant or report any pregnancy promptly.
7. Consult physician before undergoing dental work or elective surgery.

Low molecular weight heparin

Ok, I know that I promised you, so here it is. Until recently, patients who had to be heparinized needed to be admitted so that bleeding times could be closely monitored. If anticoagulation therapy was continued to an outpatient setting, a conversion to warfarin took place over a 3–4 day period, entailing closer monitoring and dose adjustments. Enter low molecular weight heparin (LMWH). There are currently 3 LMWHs available: enoxaparin, dalteparin, and ardeparin. These three have some distinct advantages over heparin:

1. A standardized dose, opposed to individualized.
2. No need to check bleeding times.
3. Prepackaged, can be used on an outpatient basis.

Indications

All three of the LMWHs are indicated for prophylaxis of deep-vein thrombosis (DVT).

Contraindications

The LMWHs are contraindicated in patients who have active, major, bleeding; thrombocytopenia; or are allergic to pork products.

Warnings

These are for subcutaneous use only. Enoxaparin and dalteparin are pregnancy category B and ardeparin is category C. Use these drugs only if clearly needed. It isn't known if any of the LMWHs are excreted into breast milk.

Drug interactions

Use LMWHs with care in patients receiving oral anticoagulants or platelet inhibitors (e.g., aspirin, salicylates, NSAIDs, dipyridamole, sulfipyrazone, ticlopidine), because there is an increased risk of bleeding.

Patient information

1. Contact the physician if you experience bleeding, bruising, dizziness, lightheadedness, itching, rash, fever, swelling, or difficulty breathing.
2. Injections are given around the navel, upper thigh, or buttocks. Change the injection site daily.
3. Use proper technique; inject deep under the skin, not into muscle.
4. If excessive bruising occurs at the injection site, it may be lessened with an ice cube massage of the site prior to injection.

Antiplatelet agents

Blood clots differ in veins, as opposed to arteries. Venous clots consist mainly of fibrin and red blood cells. Arterial clots are mainly made up of platelets. Theoretically, anticoagulant drugs should be effective for reducing risks involved with venous clot formation; antiplatelet drugs should be more effective for reducing risks of arterial clot formation. This part of the lesson will cover two antiplatelets, dipyridamole and ticlopidine. These two drugs are different enough that they will be covered separately.

Dipyridamole***Indications and dosage***

It is believed that platelets react to prosthetic heart valve surfaces. This reaction shortens platelet life and is a significant factor in thromboembolic complications following prosthetic heart valve replacement. Dipyridamole lengthens the abnormally shortened survival time by inhibiting the red blood cell uptake of adenosine, a platelet activity inhibitor. Therefore, dipyridamole is indicated as an adjunct to anticoagulant therapy in the prevention of postoperative thromboembolic complications of cardiac valve replacement.

The recommended dose of dipyridamole after cardiac valve replacement is 75–100 mg four times daily as an adjunct to the usual warfarin therapy.

Contraindications

There are no listed contraindications for dipyridamole.

Warnings

Dipyridamole is pregnancy category B. Dipyridamole is excreted into breast milk.

Drug interactions

There are no listed interactions for dipyridamole.

Patient information

There is no listed patient information for dipyridamole.

Ticlopidine

Ticlopidine is a platelet aggregation inhibitor. Ticlopidine inhibits the platelet-fibrinogen binding ability. The effect on the platelet is irreversible for the life of the platelet.

Indications and dosage

Ticlopidine is indicated to reduce the risk of thrombotic stroke in patients who have experienced stroke indications, and in patients who have already had a thrombotic stroke. The usual dose is 250 mg twice daily, with food.

Contraindications:

Thrombocytopenia, bleeding ulcer, or severe liver impairment.

Warnings

1. Ticlopidine may cause thrombocytopenia and cholesterol elevation.
2. Ticlopidine is in pregnancy category B. Ticlopidine is also excreted in breast milk with potential for serious adverse reactions.

Drug interactions

The following drugs affect Ticlopidine:

1. Antacids lower the effects of ticlopidine.
2. Cimetidine increases the effects of ticlopidine.

Ticlopidine affects these drugs:

1. Aspirin – ticlopidine potentiates the anti-coagulant effects of aspirin.
2. Digoxin – levels are increased.
3. Phenytoin – levels are increased.
4. Theophylline – elimination of half-life is increased (acts longer).

Patient information

1. A decrease in the number of white blood cells (neutropenia) or platelets (thrombocytopenia) can occur, especially during the first 3 months of treatment. If neutropenia is severe, it could result in an increased risk of infection. It is critically important to obtain the scheduled blood tests to detect neutropenia or thrombocytopenia. Have patients contact their physician if they experience any indication of infection such as fever, chills, or sore throat, all of which may be consequences of neutropenia. Thrombocytopenia may be part of a syndrome called TTP. Immediately report symptoms and signs of TTP, such as fever, weakness, difficulty speaking, seizures, yellowing of skin or eyes, dark or bloody urine, pallor, or petechiae (pinpoint hemorrhagic spots on the skin).
2. It may take longer than usual to stop bleeding when taking ticlopidine. Have patients report any unusual bleeding to their physician. Have patients tell physicians and dentists that they are taking ticlopidine before any surgery is scheduled and before any new drug is prescribed.
3. Promptly report side effects such as severe or persistent diarrhea, skin rashes or SC bleeding, or any signs of cholestasis (e.g., yellow skin or sclera, dark urine, or light colored stools).
4. Take ticlopidine with food or just after eating in order to minimize GI discomfort.

Vitamin K

Unlike all of the previous blood modifying drugs, vitamin K is an antihemorrhagic factor. It helps blood to clot. Some of the other agents we've discussed inhibit or break the coagulation chain.

Vitamin K promotes the synthesis of factors II, VII, IX, and X.

Indications and dosage

Vitamin K is indicated in coagulation disorders due to faulty formation of factors II, VII, IX, and X caused by vitamin K deficiency. It is also indicated in anticoagulant-induced prothrombin deficiency, hypoprothrombinemia induced by salicylates or antibiotics.

Normally, vitamin K is given IM or SC. Clinical disorders prevent proper oral absorption. Doses of 2.5 to 10 mgs are given and then bleeding times are monitored for 6–8 hours after parenteral administration. The dose may be repeated after that time as necessary. A 1 mg dose may be given to newborns whose mothers were on anticoagulant therapy during pregnancy.

Contraindications

Hypersensitivity to any component of the product

Warnings

1. Vitamin K will not contract heparin. Immediate coagulation will not occur; vitamin K must be processed through the liver.
2. Vitamin K is pregnancy category C. It is also excreted into breast milk.

Drug interactions

1. Vitamin K is a warfarin antagonist; temporary resistance to anticoagulants may occur.
2. Mineral oil may decrease absorption of oral vitamin K.

Patient information

There is no specific patient information listed for vitamin K.

232. Drugs affecting the heart**Antiarrhythmic drugs**

Remember, in the anatomy and physiology portion of this lesson, that electrical impulses stimulate the heart muscle to contract and pump our blood? When the muscle gets “out of sync” and an arrhythmia occurs, this group of drugs can help to get the rhythm back to normal. We’ll look at three drugs in this class: quinidine, procainamide, and lidocaine.

The antiarrhythmic class works by suppressing the electrical conduction or making the heart muscle less reactive to the impulses. We’re resetting the switch so that the muscles can get back into sync with each other.

Indications and dosage

The basic indication for all of these is the treatment of ventricular arrhythmia. Lidocaine is only indicated for acute treatment, quinidine and procainamide are used both for acute and maintenance therapy.

Drug	Dosage form	Dose
Lidocaine	10,20,40,100, 200 mg/ml injection	(a) IM 300 mg (a) IV 50–100 mg then 1–4 mg/min
Procainamide	250, 375,500, 1000 mg tablets 100,500 mg/ml injection	(m) 50 mg/kg/day in divided doses (oral and IM) (a) 1000 mg infused over 3 hours
Quinidine (Gluconate)	324 mg tablet 80mg/ml injection	(a) Symptom dependent, 200 – 600 mg orally every 3–4 hours (m) 200–300 mg 3–4 times daily (a) 600 mg IM followed by 400 mg up to every 2 hours
Quinidine (Sulfate)	200, 300 mg tablet 300 mg SR tablet	(a) Symptom dependent, 200 – 600 mg orally every 3–4 hours (m) 200–300 mg 3–4 times daily

(m) maintenance dose

(a) acute dose

Contraindications

These drugs are contraindicated for people who have complete heart blockage or are sensitive to any component of these medications. Lidocaine is also contraindicated in people who are sensitive to local anesthetics or have artificial pacemakers.

Warnings

Each of these has some pretty distinct warnings, so we'll look at them separately.

Quinidine

1. Quinidine may cause an atrial flutter or fibrillation before it restores a regular rhythm.
2. Quinidine is pregnancy category C. It crosses the placenta and achieves fetal serum levels similar to maternal levels. There are also reports of oxytocic properties reported with quinidine. Quinidine is excreted into breast milk. However, the American Academy of Pediatrics considers quinidine compatible with breast-feeding.

Procainamide

Procainamide is pregnancy category C, it does cross the placenta. Procainamide is also excreted into breast milk with potential serious adverse reactions in nursing infants.

Lidocaine

Lidocaine is in category B, it readily crosses the placenta. Lidocaine is excreted into breast milk at about 40% serum levels. An infant would ingest about 1.5 mg.

Drug interactions

The following drugs increase the action of Quinidine:

1. Amiodarone.
2. Antacids.
3. Cimetidine.
4. Urinary alkalinizers.
5. Verapamil.

These drugs decrease the action of Quinidine:

1. Barbiturates.
2. Cholinergic drugs.
3. Hydantoins.
4. Nifedipine.
5. Rifampin.
6. Sulcralfate.

Quinidine increases the effects of the following drugs:

1. Anticholinergics.
2. Anticoagulants.
3. Beta Blockers.
4. Cardiac Glycosides.
5. Procainamide.
6. Succinylcholine.
7. Tricyclic Antidepressants.

The following drugs increase the actions of Lidocaine:

1. Beta Blockers.
2. Cimetidine.
3. Procainamide.

The following drugs increase the actions of Procainamide:

1. Beta Blockers.
2. Cimetidine.
3. Ranitidine.
4. Quinidine.
5. Trimethoprim.

Patient information

1. Close cooperation in adhering to the prescribed dosage schedule is of great importance in safely controlling the cardiac arrhythmia. More medication is not necessarily better and may be dangerous. Skipping doses or increasing intervals between doses to suit personal convenience may lead to loss of control of the heart problem, and “making up” missed doses by doubling up later may be hazardous.
2. The patient should disclose any history of drug sensitivity, especially to procaine, and other local anesthetic agents or aspirin. The patient should also report any history of kidney disease, congestive heart failure, myasthenia gravis, liver disease or lupus erythematosus.
3. The patient should promptly report any symptoms of arthralgia, myalgia, fever, chills, skin rash, easy bruising, sore throat or sore mouth, infections, dark urine or icterus, wheezing, muscular weakness, chest or abdominal pain, palpitations, nausea, vomiting, anorexia, diarrhea, hallucinations, dizziness or depression.
4. Do not discontinue therapy unless instructed by physician.
5. May cause GI upset, so take with food.
6. Notify physician if ringing in the ears, visual disturbances, dizziness, headache, nausea, skin rash or breathing difficulty occurs.
7. Do not crush or chew sustained release tablets.

Anti-anginals

Angina is the sharp pain in the chest that occurs when cardiac tissue is starved for oxygen. The class of drugs in this category that we will discuss is *nitrates*. Nitrates relax vascular smooth muscle. They mainly work on venous muscle. Nitrates redistribute coronary blood flow along collateral channels increasing the passage of blood to the myocardium. Nitroglycerin works just a little differently from the rest. It works on both venous and arterial muscles giving a faster response.

Nitrates	Dosage form	Onset (minutes)	Duration
Isosorbide dinitrate	Sublingual	2–5	1–3 hours
	Oral	20–40	4–6 hours
	Oral, sustained rel	up to 4 hrs	6–8 hours
Isosorbide mononitrate	Oral	30–60	no data
Nitroglycerin	IV	1–2	3–5 min
	Sublingual	1–3	30–60 min
	Translingual spray	2	30–60 min
	Transmucosal tablet	1–2	3–5 hours
	Oral, sustained rel	20–45	3–8 hours
	Topical ointment	30–60	2–12 hours
	Transdermal	30–60	up to 24 hours

Indications and dosage

Nitrates	Dosage form	Indication	Dose
Isosorbide dinitrate	Sublingual	Angina pectoris	2.5 - 5 mg acutely, 2.5 – 5 mg every 2–3 hours prophylactically
	Oral	Angina pectoris (non abortive)	Initially 5–20 mg followed by 10–40 mg every 6 hours for maintenance
	Oral, sustained rel	Angina pectoris (non abortive)	40 – 80 mg every 12 hours
Isosorbide mononitrate	Oral	Angina pectoris (non abortive)	20 mg twice daily
Nitroglycerin	IV	Perioperative hypertension CHF Angina pectoris	Start at 5 mcgm/min and increase every 3–5 mins until suitable response is noted
	Sublingual	Angina pectoris	1 tablet under the tongue or in buccal pouch, repeat every 5 mins, up to 3 times
	Translingual spray	Angina pectoris	1–2 sprays under tongue
	Transmucosal tablet	Angina pectoris	1 mg every 3–5 hours while awake. Used buccally
	Oral, sustained rel	Angina pectoris	2.5 mg 3–4 times daily increase as needed up to 26 mg 4 times daily
	Topical ointment	Angina pectoris	1–2 inches every 8 hours, up to 4–5 inches every 4 hours
	Transdermal	Angina pectoris	0.2 – 0.4 mg/hr patch

Contraindications

All of these are contraindicated in patients with severe anemia, closed-angle glaucoma, postural hypotension, head trauma or cerebral hemorrhage.

Warnings

All nitrates discussed are in pregnancy category C. It is not known whether they are excreted into breast milk.

Drug interactions

1. Alcohol and aspirin increase the actions of nitrates. Calcium channel blockers decrease nitrate effects.
2. Nitroglycerin decreases the effects of heparin.

Patient information

1. Avoid alcohol.

2. Brand interchange: Do not change from one brand of this drug to another without consulting your pharmacist or physician. Products manufactured by different companies may not be equally effective.
3. May cause headache, dizziness or flushing. Notify physician if blurred vision, dry mouth or persistent headache occurs. In patients who get headaches, the headaches may be a marker of the drug's activity. Patients should not try to avoid headaches by altering the treatment schedule, since loss of headache may be associated with simultaneous loss of efficacy. Aspirin or acetaminophen may be used for relief.
4. Take oral nitrates on an empty stomach with a glass of water.
5. Carefully follow the prescribed schedule of dosing.
6. Keep tablets and capsules in original container. Keep container closed tightly.
7. The following table lists dosage instructions:OK?]

Doage Form	Directions
Inhalant	Use when lying down only. Highly flammable, so do not use where it might be ignited. Use in a well-ventilated room.
Sublingual tablet	Dissolve tablet under tongue; do not swallow. A lack of burning or stinging sensation does not indicate a loss of potency. Use when seated. Take at the first sign of an anginal attack before severe pain develops. If angina is not relieved in 5 minutes, dissolve a second tablet under the tongue. If pain is not relieved within another 5 minutes, dissolve a third tablet. If pain continues or intensifies, notify physician immediately or report to the nearest hospital emergency room. Unused tablets should be discarded 6 months after the original bottle is opened.
Sustained release nitroglycerin	Swallow whole; do not chew. Not for sublingual use.
Topical ointment	Patient instructions are available with products. Spread a thin layer on skin using applicator or dose-measuring papers, do not use fingers, and do not rub or massage. Keep tube tightly closed.
Transdermal nitroglycerin	Patient instructions are available with products. Advise patients that there is enough residual nitroglycerin in discarded patches that they are a potential hazard to children and pets. Use caution when discarding.
Translingual spray	Spray onto or under tongue. Do not inhale spray.
Transmucosal tablet	Place under the upper lip or in a buccal pouch (between cheek and gum). Permit to dissolve slowly over a 3 to 5 hour period. Do not chew or swallow tablets. Release of nitroglycerin begins immediately upon contact with the mucosa and will continue until the tablet dissolves. Time to dissolution increases as patients familiarize themselves with the tablet's presence. Touching the tablet with the tongue or drinking hot liquids may increase rate of dissolution.

Cardiac Glycosides

The cardiac glycosides have direct action on cardiac muscle and its conduction system. They also have indirect actions on the cardiovascular system through the autonomic nervous system. The direct effects include increasing the force and velocity of myocardial systolic contractions and slowing the rate of contractions. The only cardiac glycoside that we will discuss is digoxin.

Indications and dosage

Digoxin is indicated in all degrees of congestive heart failure (CHF) for “low output failure” and atrial fibrillation and flutter for slowing and regulating rate.

Digoxin must accumulate and build plasma levels; this can take time at maintenance doses.

Therefore, an initial loading dose is used to rapidly establish effective levels. Maintenance doses are individualized to maintain therapeutic effects.

Loading dose

Rapid – 0.6 mg initially, followed by 0.4 mg, then 0.2 mg at intervals of 4 – 6 hours.

Slow – 0.2 mg twice daily for 4 days followed by a maintenance dose.

Maintenance

The maintenance dose range is 0.05 to 0.3-mg daily, the most common dose being 0.15 mg daily.

Contraindications

Ventricular fibrillation and ventricular tachycardia.

Warnings

Digoxin is pregnancy category C. 50 to 80% of maternal levels pass rapidly into the fetus. Fetal harm from digoxin is unknown. Digoxin does pass into breast milk at 0.6% of maternal levels. No adverse reactions have been reported.

Drug interactions

Drugs that may increase digitalis serum levels, possibly increasing therapeutic and toxic effects:

Alprazolam	Cyclosporine	Flecainide	Omeprazole
Aminoglycosides, oral	Diltiazem	Hydroxychloroquine	Quinidine
Amiodarone	Diphenoxylate	Ibuprofen	Quinine
Anticholinergics	Erythromycin	Indomethacin	Tetracycline
Benzodiazepines	Esmolol	Itraconazole	Verapamil
Captopril	Felodipine	Nifedipine	

The following agents may decrease digitalis serum levels, possibly decreasing therapeutic effects:

Aminoglycosides, oral	Cholestyramine	Kaolin/pectin	Rifampin
Antacids	Colestipol	Metoclopramide	Sulfasalazine
Antihistamines	Hydantoins	Neomycin	Sucralfate
Barbiturates	Hypoglycemic agents (oral)	Penicillamine	

Patient information

1. Do not discontinue medication without first checking with a physician.
2. Avoid OTC antacids, cough, cold, allergy and diet drugs, except on professional advice.
3. Notify physician if loss of appetite, lower stomach pain, nausea, vomiting, diarrhea, unusual tiredness or weakness, drowsiness, headache, blurred or yellow vision, skin rash or hives, or mental depression occurs.

233. Drugs affecting the blood vessels

This is probably the largest and most diverse section of the entire course. There are a multitude of drugs that affect the blood vessels, too many for us to discuss in one place. All of the drugs discussed in this section have the primary purpose of improving the flow of blood, mainly to reduce blood pressure or increase circulation. This section will cover vasodilators, alpha-adrenergic blocking agents, beta-adrenergic blocking agents, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, calcium channel blockers, diuretics, and finally antihyperlipidemic agents. Get ready, here we go with the longest section. Let's start with vasodilators.

Vasodilators

The only drug that we'll look at here is hydralazine. Hydralazine produces its vasodilation through direct relaxation of vascular smooth muscle. Hydralazine changes the muscle's ability to metabolize calcium, which interferes with initiating and maintaining contractions. Hydralazine works on arteries, lowering diastolic blood pressure and decreasing vascular resistance.

Indications and dosage

Hydralazine is indicated in essential hypertension. The dosage is individualized, starting at 10 mg 4 times daily orally, for a few days, then increased to 25 mg for the remainder of the first week of therapy. Later, the dose may be increased to 50 mg 4 times daily. Parenterally, the usual dose is 20 to 40 mg, repeated as needed.

Contraindications

Hydralazine hypersensitivity, coronary artery disease, or mitral valve rheumatic heart disease.

Warnings

Hydralazine is pregnancy category C. Cleft palate and facial and cranial bone malformations have occurred. Hydralazine is excreted into breast; however, the American Academy of Pediatrics has labeled hydralazine compatible with breast-feeding.

Drug Interactions

1. Hydralazine interacts with beta-blockers. Concurrent use may increase the effectiveness of either or both drugs.
2. Indomethacin decreases the effects of hydralazine.

Patient information

1. Take with meals.
2. Notify physician of any unexplained prolonged general tiredness or fever, muscle or joint aching or chest pain.

Alpha-adrenergic blocking agents

Alpha-adrenergic blockers selectively block alpha-1 receptors in arteriols and veins. This causes blood pressure to fall. The selectivity of these drugs allows for this action without an increase in heart rate. As an extra, added benefit for the males, these alpha-blockers can also help relieve the symptoms of benign prostate hyperplasia (BPH). The drugs that we will discuss here include terazosin, doxazosin, and prazosin.

Indications and dosage

All three of our alpha-blockers are indicated for hypertension. Terazosin and doxazosin are also indicated for the urinary obstruction and obstructive and irritative symptoms associated with BPH.

Drug	Dosage form	Dosing
Doxazosin	1,2,4,8 mg tabs	HTN: 1–16 mg once daily, BPH: 1–8 mg once daily
Prazosin	1,2,5 mg capsules	HTN: 1 mg 2–3 times daily, may increase to 6–15 mg
Terazosin	1,2,5,10 mg tablets and capsules	HTN: 1 – 5 mg at bedtime (individualized) BPH: 1–10 mg at bedtime

Contraindications

The only contraindication is a hypersensitivity to the class.

Warnings

“First-dose” effect: All alpha-blockers can cause marked hypotension and syncope (fainting) with the first few doses, if dosing is increased rapidly, or if another antihypertensive is added.

Drug interactions

1. Verapamil and Beta-blockers increase the effects of alpha-blockers when used concurrently.
2. Indomethacin may decrease the actions of alpha-blockers.

Patient information

1. Inform patients of the possibility of syncopal and orthostatic symptoms, especially at the initiation of therapy. Avoid driving or hazardous tasks for 12 to 24 hours after the first dose, after a dosage increase and after interruption of therapy when treatment is resumed. Use caution when rising from a sitting or lying position. If dizziness or palpitations are bothersome, report to the physician so that dose adjustment can be considered.
2. Drowsiness or somnolence can occur. Use caution when driving or operating heavy machinery.

Beta-adrenergic blocking agents

Beta-adrenergic receptor blocking agents compete with beta-adrenergic agonists for available beta-receptor sites. Propranolol and nadolol inhibit both the β_1 receptors (located chiefly in cardiac muscle) and β_2 receptors (located chiefly in the bronchial and vascular muscles), inhibiting the chronotropic, inotropic and vasodilator responses to β -adrenergic stimulation. Metoprolol and atenolol are cardioselective and preferentially inhibit β_1 receptors.

Indications and dosage

Drug	Dosage form	Indication	Dose
Atenolol	25,50,100 mg tablets 5mg/10 ml injection	Hypertension (oral)	50 –100 mg once daily
		Angina (Oral)	50–200 mg daily
		Myocardial Infarction (Inj)	10 mg (divided) then 50–100 mg twice daily

Drug	Dosage form	Indication	Dose
Metoprolol	50,100 mg tablets 50,100,200 ER tablets 1 mg/ml injection	Hypertension (oral) Angina (Oral) Myocardial Infarction (Inj)	100 mg/day, may increase 100–400 mg/day, divided 5mg X3, then 50mg every 6 hours
Nadolol	20,40,80,120,160 mg tablets	Angina Hypertension	40–320 mg daily (individualized)
Propranolol	10,20,40,60,80,90 mg tablets 60,80,120,160 mg ER capsules 80 mg/ml oral solution 1mg/ml injection	Cardiac arrhythmia Myocardial infarction Hypertension Migraine prophylaxis Angina	10–30mg three times daily 180–240 mg/day 3–4 doses 40–320 mg once daily ER 160–240 mg/day divided ER 80–320 mg divided or ER

Contraindications

All of the beta-blockers are contraindicated in patients with bradycardia, congestive heart failure, overt cardiac failure, or hypersensitivity to beta-blocking agents.

Propranolol and nadolol are contraindicated in patients with bronchial asthma or bronchospasm, including chronic obstructive pulmonary disease.

Warnings

All of the beta-blockers discussed here are in pregnancy category C. They all are also excreted into breast milk with atenolol being the only drug discussed that created ill effects on breastfeeding infants.

Drug interactions

The following drugs may decrease the effects of β -blockers:

Barbiturates	Rifampin
Cholestyramine	Salicylates
Colestipol	Penicillins
NSAIDs	Thyroid hormones

The following drugs may increase the effects of β -blockers:

Calcium-channel blockers	H ₂ antagonists	Quinidine
Haloperido	Loop diuretics	Quinolones
Hydralazine	Oral contraceptives	

β-blockers may increase the effects of the following drugs:

Acetaminophen	Epinephrine
Anticoagulants	Lidocaine
Benzodiazepines	Prazosin
Clonidine	

β-blockers may decrease the effects of Sulfonylureas

Patient information

1. Do not discontinue medication abruptly, except on advice of physician. Sudden cessation of therapy may precipitate or exacerbate angina.
2. Consult pharmacist or physician before using other products which may contain a-adrenergic stimulants (e.g., nasal decongestants, etc cold preparations).
3. Notify physician if symptoms of coronary heart failure (CHF) occur (e.g., difficult breathing, especially on exertion or when lying down; night cough; swelling of the extremities).
4. Notify physician if any of these occur: Slow pulse rate, dizziness, lightheadedness, confusion or depression, skin rash, fever, sore throat, or unusual bleeding or bruising.
5. May produce drowsiness, dizziness, lightheadedness, blurred vision; patient should observe caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity.
6. Diabetics: These agents may mask signs of hypoglycemia or alter blood glucose levels.
7. Propranolol and metoprolol: Food may enhance bioavailability; take at the same time each day.
8. Nadolol and atenolol may be taken without regard to meals.

Angiotensin-converting enzyme (ACE) inhibitors

The use of ACE inhibitors has increased greatly over the past few years. These drugs are becoming more and more popular. These drugs block the action of the renin-angiotensin system. Renin is released into circulation by the kidneys. It produces angiotensin I, which is then converted to angiotensin II by the angiotensin-converting enzyme. Angiotensin II is a potent vasoconstrictor that also stimulates aldosterone secretion from the adrenal cortex, contributing to sodium and fluid retention. ACE inhibitors (ACEI) prevent the conversion of angiotensin I to angiotensin II by inhibiting ACE. We will be discussing four of the ACE I inhibitors here, captopril, lisinopril, benazepril, and enalapril. There are specific ACE II receptor antagonists that will be discussed later.

Indications and dosage

ACEI	Dosage form	Indication	Dosage
Benazepril	5,10,20,40 mg tablet	Hypertension	20–40 mg daily
Captopril	12.5, 25,50,100 mg tablets	<ul style="list-style-type: none"> • Hypertension • Left ventricular dysfunction 	<ul style="list-style-type: none"> • 25–50 mg 2–3 times daily • 50 mg 3 times daily
Enalapril	2.5,5,11,20 mg tablets 1.25mg/ml injection	<ul style="list-style-type: none"> • Hypertension • Heart failure 	<ul style="list-style-type: none"> • 2.5–40 mg daily (oral) • 1.25mg every 6 hours (inj) • 5–20 mg daily divided

ACEI	Dosage form	Indication	Dosage
Lisinopril	2.5,5,10,20,40 mg tablets	<ul style="list-style-type: none"> Hypertension Congestive heart failure Myocardial infarction 	<ul style="list-style-type: none"> 20–40 mg daily single dose 5–20 mg daily single dose 5 mg, then 5 mg, then 10 mg, then 10 mg daily

Contraindications

Any patients with a history of hypersensitivity to these products.

Warnings

1. Captopril may cause a low white blood count (neutropenia).
2. ACEIs may cause a large fall in blood pressure following the first dose.
3. ACEIs are pregnancy category C during the first trimester and category D in the second and third trimesters. When pregnancy is detected, discontinue ACEIs as soon as possible. ACEIs have been detected in breast milk. There is a potential for serious side effects to the child.

Interactions

The following drugs decrease the effectiveness of ACEIs:

1. Antacids.
2. Indomethacin.
3. Rifampin.

The following drugs increase the effects of ACEIs:

1. Capsaicin.
2. Phenothiazines.
3. Probenecid.

ACE Inhibitors increase the actions of the following:

1. Allopurinol.
2. Digoxin.
3. Lithium.
4. Potassium products.
5. Potassium-sparing diuretics.

ACE Inhibitors decrease the effectiveness of tetracycline.

Patient information

1. Take captopril 1 hour before meals.
2. Notify physician if any of the following occur: sore throat, fever, swelling of hands or feet, irregular heartbeat, chest pains, signs of angioedema (swelling of face, eyes, lips, tongue, difficulty swallowing or breathing, hoarseness). Excessive perspiration, dehydration, vomiting and diarrhea may lead to a fall in blood pressure.
3. May cause dizziness, fainting or lightheadedness, especially during the first days of therapy; avoid sudden changes in posture. If actual syncope occurs, discontinue drug until physician has been contacted. Heart failure patients should avoid rapid increases in physical activity.
4. May cause skin rash or impaired taste perception. Notify physician if these persist.

5. Do not use potassium supplements or salt substitutes containing potassium without consulting a physician.
6. A persistent dry cough may occur and usually does not subside unless the medication is stopped. If this effect becomes bothersome, consult a physician.

Angiotensin II receptor antagonists (AIIRAs)

We discussed earlier how angiotensin I is converted to angiotensin II and the effects that angiotensin II had on the body. Where ACE inhibitors stopped the conversion to angiotensin II, these receptor antagonists work farther down the line of action. After the conversion from angiotensin I to II takes place, these receptor antagonists compete for receptor sites with the angiotensin II at vascular smooth muscles and the adrenal gland. The two AIIRAs that we will discuss are losartan and valsartan.

Indications and dosage

ACIIRA	Dosage form	Indication	Dose
Losartan	25,50 mg tablets	Hypertension	Once or twice daily, total of 25 – 100 mg
Valsartan	80, 160 mg tablets	Hypertension	80 – 320 mg once daily

Contraindications

Hypersensitivity to any component of these products.

Warnings

1. Patients who have been treated with diuretics may be volume or salt depleted, symptomatic hypotension may occur in these people.
2. As with ACEIs, these drugs are pregnancy category C in the first trimester and category D in the second and third. It isn't known if these drugs are excreted in breast milk.

Drug interactions

No drugs interact with the AIIRAs discussed.

Patient information

Tell patients of childbearing age about the consequences of second- and third-trimester exposure to drugs that act on the renin-angiotensin system, and tell them that these consequences do not appear to have resulted from intrauterine drug exposure that has been limited to the first trimester. Ask these patients to report pregnancies to their physicians as soon as possible.

Calcium channel blockers

In specialized automatic and conducting cells in the heart, calcium is involved in many actions. In contracting cells of the myocardium, it links excitation to contraction and controls energy storage and use. Movement of calcium across cell membranes of vascular smooth muscle influences systemic and coronary arteries. Contractile processes of cardiac and vascular smooth muscle depend upon movement of extracellular calcium ions into cells through specific channels.

The calcium channel blockers have the ability to inhibit movement of calcium ions across the cell membrane. The effects on the cardiovascular system include depression of mechanical contraction of myocardial and smooth muscle, and depression of impulse formation and conduction velocity. We will be discussing amlodipine, diltiazem, felodipine, nifedipine, and verapamil in this category.

Indications and dosage

Drug	Dosage form	Indication	Dose
amlodipine	2.5, 5, and 10 mg tablets	<ul style="list-style-type: none"> Hypertension Angina 	5 – 10 mg once daily
ditiazem	30,60,90,120 mg tablets 120,180,240 mg ER tablets 60,90,120,180,240,300 mg Sustained release capsules 5mg/ml injection	Hypertension <ul style="list-style-type: none"> Angina Atrial fibrillation or flutter 	<ul style="list-style-type: none"> 120 – 360 mg daily in four doses (reg tabs) 240–360 mg daily in two doses (SR) 20 mg over 2 min, then 25 mg over 2 min 10
felodipine	2.5, 5, and 10 mg ER tablets	Hypertension	2.5 - 10 mg once daily
nifedipine	10 and 20 mg capsules 30,60, and 90 mg SR tablets	Angina/ Hypertension	Caps: 10 - 30 mg 3–4 times daily SR Tabs: 30 - 90 mg once daily
verapamil	40,80, and 120 mg tablets 120, 180, and 240 mg SR tablets 120,180,240, and 360 mg SR capsules 5mg/2ml vials, ampules and disposable syringes	<ul style="list-style-type: none"> Angina Arrhythmia Hypertension Supraventricular tachyarrhythmia 	<ul style="list-style-type: none"> 80 - 120 mg three times daily 240 - 480 mg daily divided into 3–4 doses 240 mg daily (80 mg TID or 240 SR QAM) 10 mg IV over 2 minutes (may repeat in 30 minutes if needed)

Contraindications

Hypersensitivity to any of the drugs, sick sinus syndrome, severe Arterial-Ventricular block except with a functioning pacemaker, hypotension with systolic pressure less than 90mm.

Warnings

- Hypotension, usually modest and well tolerated, may occasionally occur during initial therapy or with dosage increases, and may be more likely in patients taking concomitant beta-blockers. Hypotensive episodes may be caused by excess vasodilation induced by nifedipine

or by direct cardiopressor effects of verapamil and diltiazem. Nifedipine has the greatest effect on vascular smooth muscle; therefore, incidence of adverse reactions resulting from vasodilation (i.e., headache, flushing) is greater. Since amlodipine-induced hypotension is gradual in onset, acute hypotension has rarely occurred.

2. Congestive Heart Failure (CHF) has developed in rare cases when patients have received beta-blockers after beginning nifedipine. Calcium channel blockers should be used with caution in CHF patients.
3. Calcium channel blockers have been noted to cause the inhibition of platelet function. Patients may easily bruise and bleed.
4. Abrupt withdrawal from calcium channel blockers may cause an increase in frequency and duration of chest pains. This is called "rebound angina" and is probably the result of sudden increased flow of calcium into cells causing the coronary arteries to spasm.
5. Calcium channel blockers are in pregnancy category C. Severe effects have been demonstrated in test animals. There are no studies involving humans. Calcium Channel Blockers should only be used when clearly needed and when potential benefits outweigh potential hazards to the fetus.
6. Most of the calcium channel blockers are excreted into breast milk. A choice must be made to discontinue the medication or breast-feeding, taking into account the importance of the drug to the mother.

Drug interactions

The following drugs lower the effects of calcium channel blockers			
Barbiturates	Carbamazepine	Rifampin	Vitamin D
Calcium salts	Hydantoins	Sulfipyrazone	

These drugs increase the effects of calcium channel blockers	
Dantrolene	H ₂ Antagonists
Erythromycin	Quinidine

Calcium Channel Blockers increase the effects of these drugs		
Anticoagulants	Cyclosporine	Muscle relaxants
Beta-blockers	Digitalis glycosides	Prazosin

Patient information:

1. Notify physician if any of the following occur: irregular heart beat, shortness of breath, swelling of the hands and feet, pronounced dizziness, constipation, nausea, or hypotension.
2. Any of the sustained or extended release products must be taken whole. Do not crush, chew, or open the tablet/capsule.

Diuretics

The term diuretic is given to a drug that increases the discharge of urine. We use this increase in urinary flow to reduce the amount of fluid in the tissues. This reduces pressure on the veins and

arteries, decreasing blood pressure. Our discussion of diuretics will include thiazide, loop, and potassium sparing diuretics.

Thiazide diuretics

Thiazide diuretics increase the urinary excretion of sodium and chloride in equal amounts. They inhibit the reabsorption of sodium and chloride in the loop of Henle and distal tubules. Sodium depletion is the primary action of thiazide diuretics. A downside to the use of thiazide diuretics is the potassium depletion, which is normally directly proportional to the sodium depletion. The antihypertensive action of thiazide diuretics requires several days to produce effects. It normally takes up to 2–4 weeks for full effects to be seen. This time period implies that a relationship between plasma levels and diuretic effect is evident. However, this is not the case. The thiazide diuretics we'll look at are chlorothiazide, hydrochlorothiazide, indapamide, and chlorthalidone.

Indications and dosage

Thiazide diuretics are indicated in treating edema that is associated with CHF, hepatic cirrhosis, and corticosteroid and estrogen therapy. They are also indicated in the treatment of hypertension. Thiazide diuretics are used alone in mild hypertension and used to enhance other antihypertensive drugs in more severe forms of hypertension. The duration of antihypertensive effects of thiazide diuretics is long enough that a single daily dose of these medications will control blood pressure.

Diuretic	Dosage form	Indication	Dose (mg)
Chlorothiazide	500mg vial 250, 500 mg tablet 250mg/5ml suspension	Edema Hypertension	500 mg - 1 gm/day in single or divided doses. IV for edema only
Chlorthalidone	15,25,50,100 mg tablets	Edema Hypertension	50 - 100 mg QAM 15 - 50 mg daily
Hydrochlorothiazide	25, 50, 100 mg tablets 12.5 mg capsules 50mg/5ml oral solution	Edema Hypertension	25 - 100 mg daily 50 mg daily
Indapamide	1.25, 2.5 mg tablets	Edema Hypertension	2.5 - 5.0 mg daily

Contraindications

Thiazide diuretics are contraindicated in patients who show hypersensitivity to thiazides or sulfonamide-derived drugs, or suffer from anuria (no urine output from kidneys).

Warnings

1. As mentioned earlier, potassium loss is a problem in using thiazide diuretics. A potassium supplement should be considered to prevent hypokalemia.
2. The IV form of chlorothiazide should only be used in an emergency. Also, chlorothiazide use should be avoided when a patient is receiving whole blood products.
3. All of the thiazide diuretics that we have discussed are in pregnancy category B; however, routine use of diuretics during normal pregnancy is inappropriate.

Drug interactions

1. Amphotericin B, Corticosteroids, and Anticholinergics increase the actions of thiazides.
2. Bile acid sequestrants, methenamines, and NSAIDs decrease the effectiveness of thiazides.
3. Thiazide diuretics decrease the actions of anticoagulants and antigout agents.
4. Thiazide diuretics increase the actions of the following medications:

Allopurinol	Antineoplastics	Diazoxide	Lithium
Anesthetics	Calcium salts	Digitalis glycosides	

Patient information

1. May cause GI upset; may be taken with food or milk.
2. Drug will initially increase urination, which should subside after a few weeks. Take early during the day or as directed.
3. Notify physician if muscle pain, weakness or cramps, nausea, vomiting, restlessness, excessive thirst, tiredness, drowsiness, increased heart rate or pulse, diarrhea or dizziness occurs.
4. May cause photosensitivity (sensitivity to sunlight). Avoid prolonged exposure to the sun and other ultraviolet light. Use sunscreens and wear protective clothing until tolerance is determined.
5. May increase blood sugar levels in diabetics.
6. Do not drink alcohol or take other medications without physician's approval; this includes nonprescription medicines for appetite control, asthma, colds, cough, hay fever or sinus.
7. Do not interrupt, discontinue, or adjust the dose even if feeling well. Follow physician's instructions regarding missed dose.
8. May cause gout attacks. Contact physician if significant sudden joint pain occurs.

Loop diuretics

Loop diuretics get their name because of where they work. All of the action of this class takes place in the kidney's loop of Henle. Loop diuretics are very potent. Great care must be taken when using furosemide, bumetanide, ethacrynic acid, or torsemide because excess amounts can lead to a profound diuresis with water and electrolyte depletion. The dosage for all of these medications is highly individualized. For brevity though, furosemide will be the only loop diuretic that we discuss in-depth.

Indications and dosage

Furosemide is indicated for edema associated with CHF, hepatic cirrhosis, and renal disease. It is particularly useful when greater diuretic potential is desired. Furosemide is also indicated for hypertension, alone or in combination with other antihypertensive drugs.

The dosage of furosemide for edema is 20–80 mg/day as a single dose. Normally, diuresis follows quickly. Depending on the response of the patient, a second dose can be given 6–8 hours later. If dosage increases must be made, make them in increments of 20 mg. In extreme cases, doses up to 600 mg/day have been given.

The dosing for hypertension is a little different. Standard dosing is 40 mg twice daily, according to response. If the patient does not respond, add other antihypertensive agents.

Furosemide is available in 20, 40, and 80 mg tablets, 10 mg/ml and 40 mg/5 ml oral solution as well as 10 mg/ml injection.

Contraindications

Just as with the thiazide diuretics, furosemide is contraindicated in anuria or in anyone sensitive to the drug or sulfonylureas.

Warnings

Dehydration is a main concern due to the potency of furosemide. Ototoxicity with tinnitus and reversible as well as irreversible hearing impairment may occur. Diarrhea may occur, especially when the liquid form of furosemide is used. This is due to the high amount of sorbitol in the solution vehicle.

Furosemide is in pregnancy category C. It has caused unexplained maternal deaths and abortions in rabbits. Data indicates that fetal lethality can precede maternal death. Furosemide appears in breast milk. Because of the potential for adverse effects in nursing infants, a choice must be made to discontinue nursing or the use of furosemide.

Drug interactions

1. The following drugs lower the effectiveness of all loop diuretics:

Charcoal	Hydantoins	NSAIDs	Probenecid	Salicylates
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2. Thiazide diuretics have a synergistic effect with loop diuretics, serious diuresis and electrolyte loss can occur.

3. Loop diuretics increase the effects of the following drugs:

Aminoglycosides	Beta blockers	Digitalis glycosides
Anticoagulants	Cloral hydrate	

4. Lithium Loop diuretics decrease the effects of sulfonylureas.
5. This hasn't been discussed before, but due to significance, it needs to be mentioned that the bioavailability and diuretic effect of furosemide is decreased when taken with food.

Patient information

1. May cause GI upset. If this happens take with food or milk (see Drug Interactions).
2. Drug will increase urination; take early in the day.
3. Notify physician if muscle weakness, cramps, nausea, or dizziness occurs.
4. Orthostatic hypotension may occur; get up slowly.
5. May increase blood glucose levels, affecting urine glucose tests in diabetes mellitus patients.
6. Photosensitivity may occur in some patients. Caution patients to take protective measures (i.e., sunscreens, protective clothing) against exposure to ultraviolet light or sunlight.
7. Hypertensive patients should avoid medications that may increase blood pressure, including OTC products for appetite suppression and cold symptoms.

Potassium-sparing diuretics

In the kidney, potassium is absorbed parallel to sodium, resulting in a direct correlation in the amount of potassium/sodium loss. As we said earlier, diuretics work by increasing the amount of sodium excreted, reducing fluid. The potassium-sparing diuretics interfere with sodium reabsorption at the distal tubule of the loop of Henle through the inhibition of aldosterone. Aldosterone causes the formation of proteins important in sodium transport. So, decreasing aldosterone decreases the protein, which decreases sodium excretion thus decreasing potassium secretion. They have only a weak diuretic and anti-hypertensive effect when used alone. Their major use is to enhance the action of and counteract the kaliuretic effects of thiazide and loop diuretics. Our discussion of potassium-sparing diuretics will include spironolactone, and triamterene. Once again, these two drugs in the same class are different enough that they warrant individual discussion.

Spironolactone

Spironolactone is indicated in hyperaldosteronism and edematous conditions when other therapies are inadequate (i.e., CHF, managing edema and sodium retention, or cirrhosis of the liver accompanied by edema). It is also indicated in essential hypertension, usually in combination with other drugs and hypokalemia occurring from digitalis use.

The dosage for treating edema ranges from 25–200 mg given in a single daily dose or divided as needed. When treating essential hypertension, start with 50 - 100 mg/day for two weeks, then

individualize. Spironolactone has also been useful in treating hypokalemia. The dosage for this is 25 - 100 mg/day. Spironolactone is available in 25, 50, and 100 mg tablets.

Additional information about Spironolactone follows:

1. **Contraindications** - Spironolactone is contraindicated in patients with anuria or those suffering from hyperkalemia.
2. **Warnings** - No pregnancy category has been assigned to spironolactone; however, spironolactone, or its metabolites may cross the placental barrier. As for lactation, canrenone, a metabolite of spironolactone appears in breast milk. Labeling suggests an alternate method of infant feeding; however, the American Academy of Pediatrics considers this drug to be compatible with breast feeding.
3. **Drug interactions** - ACE inhibitors increase the effects of spironolactone, while Salicylates decrease spironolactone's effects. Spironolactone decreases the effects of anticoagulants and, logically, increases the effects of potassium preparations.
4. **Patient information** – Spironolactone may produce drowsiness, lack of coordination, and mental confusion; observe caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity. It may cause GI cramping, diarrhea, lethargy, thirst, headache, skin rash; menstrual abnormalities and deepening of the voice can occur in women; breast enlargement might occur in men. Notify physician if these effects are apparent.

Triamterene

Triamterene is indicated for edema associated with CHF, hepatic cirrhosis, steroid-induced edema, and edema secondary to hyperaldosteronism. It may be used alone or with other diuretics for additive diuretic effects or antikaliuretic effect.

When used alone, the usual starting dose of Triamterene is 100 mg twice/daily after meals. When combined with other diuretics or antihypertensives, decrease the total daily dosage of each agent initially, and then adjust to the patient's needs. Do not exceed 300 mg/day. Triamterene is available in 50 and 100mg capsules.

Additional information about Triamterene:

1. **Contraindications** - Triamterene is contraindicated in patients taking Spironolactone, or those with kidney problems or elevated potassium levels.
2. **Warnings** - The main warning with Triamterene is hyperkalemia. Triamterene is pregnancy category B. It also appears in breast milk. If the use of Triamterene is essential, discontinue breast feeding.
3. **Drug interactions** - Triamterene increases the effects of Amantadine and any other potassium preparations. ACE inhibitors, cimetidine, and indomethacin increase the actions and side effects of Triamterene.
4. **Patient information** – Triamterene may cause GI upset; take after meals. It may also cause weakness, headache, nausea, vomiting, and dry mouth; notify physician if these become severe or persistent. Notify physician if fever, sore throat, mouth sores, or unusual bleeding or bruising occurs. Avoid prolonged exposure to sunlight; photosensitivity may occur. If single daily dose is prescribed, take in morning to minimize effect of increased frequency of urination on nighttime sleep. If dose is missed, do not take more than prescribed dose at next dosing interval.

Antihyperlipidemic agents

The emphasis on cholesterol levels has risen drastically over the past few years. Studies show that lowering cholesterol levels, especially low-density lipoproteins (LDL) levels, can significantly decrease the chances for heart attack and atherosclerosis. Drug therapy in this state is combined with diet modification and alcohol moderation. Even if cholesterol levels are lowered by only 10%, the patient realizes a 20–30% reduction in the incidence of coronary heart disease and heart attack. In this last section of our unit we'll cover bile acid sequestrants, HMG-CoA reductase inhibitors, and two miscellaneous lipemic agents. Let's get this last section started with bile acid sequestrants.

Bile acid sequestrants

Cholesterol is the major precursor of bile acids. During normal digestion, bile acids are secreted from the liver and gallbladder into the intestines to emulsify the fat and lipid materials in food and facilitate absorption. A major portion of the bile acids secreted are reabsorbed from the intestines and returned through the portal circulation to the liver, completing the enterohepatic cycle.

Bile acid sequestering resins bind bile acids in the intestine to form an insoluble complex that is excreted in the feces. This results in a reduced reabsorption of bile acids. Without the recycling of the bile acids, more cholesterol is used to produce enough bile to facilitate digestion. If the cholesterol is used up making bile, then there isn't as much floating around to clog arteries. The two bile acid sequestrants that we'll discuss are cholestyramine and colestipol.

Indications

The indication for the bile acid sequestrants (BAS) is hyperlipoproteinemia (high cholesterol), especially high LDL. Cholestyramine also has a secondary indication for the relief of pruritis associated with partial biliary obstruction.

Drug	Dosage Form	Doseage
Colestipol	1 gm tablet 5gm/7.5 gm powder	Start with 2 gm daily, may increase to 2–16 gms daily in single or divided doses
Cholestyramine	4gm resin/9 gm powder	4 gm 1–2 times daily (individualized)

Contraindications

Sensitivity to components or complete biliary obstruction.

Warnings

Avoid accidental inhalation; do not take dry. These agents are not absorbed systemically and will not cause fetal harm in recommended doses. However, they do interfere with the absorption of fat-soluble vitamins. The possible lack of proper vitamin absorption may have an effect on nursing infants.

Interactions

BASs decrease the absorption and effectiveness of the following medications:

Anticoagulants	Gemfibrozil	Penicillin	Thyroid hormones
Aspirin	Glipizide	Phenytoin	Vitamins A, D, E, and K
Clindamycin	Hydrocortisone	Propranolol	
Digitalis glycosides	Imipramine	Tetracyclines	
Furosemide	Niacin	Thiazide diuretics	

Patient information

1. Medication is usually taken before meals.

2. Do not take the powder in dry form; mix with beverages, highly fluid soups, cereals or pulpy fruits.
3. Swallow colestipol tablets whole; do not cut, crush or chew.
4. Medication may interfere with absorption of concomitant drugs. Take other drugs 1 hour before or 4 to 6 hours after cholestyramine or colestipol . (See Drug Interactions.)
5. Constipation, flatulence, nausea, and heartburn may occur and may disappear with continued therapy. Notify physician if these effects become bothersome or if unusual bleeding (e.g., from the gums or rectum) occurs.

HMG-CoA reductase inhibitors

Wow! That's quite a mouthful. We'll talk about how these drugs got their name and then I'll give you a new name to remember them by for the rest of this lesson. HMG-CoA reductase is an enzyme which forms mevalonate. Mevalonate is a required step in the synthesis of cholesterol. So, we inhibit the HMG-CoA reductase enzyme and mevalonate is not made. Without mevalonate, cholesterol is not produced. Sounds simple, huh? Now, here's what I promised you. The name of this drug class is better known as the "statins." That name should sound more familiar to you. We'll talk about four of the statins here: Atorvastatin, Cerivastatin, Pravastatin, and Simvastatin

Indications

The statins are indicated as an adjunct to diet to reduce elevated total and LDL cholesterol levels in primary hypercholesterolemia and dyslipidemia. The statins can also be indicated to slow the progression of coronary atherosclerosis—in patients with congenital heart disease—to lower cholesterol, reducing the risk of acute coronary events.

Drug	Dosage form	Dosage
Atorvastatin	10, 20, and 40 mg tablets	10 to 80 mg per day, single dose
Cerivastatin	0.2 and 0.3 mg tablets	0.3 mg once daily in the evening
Pravastatin	10, 20, and 40 mg tablets	10 to 40 mg once daily at bedtime
Simvastatin	5, 10, 20, and 40 mg tablets	5 to 40 mg once daily in the evening

Contraindications

Hypersensitivity to any component or active liver disease. Pregnancy and lactation are also contraindications for the use of statins.

Warnings

1. Since the statins have an effect on the liver they must be used with caution in patients who consume large quantities of alcohol.
2. The statins are in pregnancy category X. In fact, pregnancy and lactation are both contraindications for the use of statins. Skeletal malformations have occurred in animal tests. Statins are excreted into breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking these drugs should not nurse infants.

Drug interactions

The following drugs increase the effects (and side effects) of the statins:

1. Erythromycin.
2. Gemfibrozil.
3. Itraconazole.
4. Nicotinic acid.

Statins increase the levels and actions of Digoxin and Warfarin.

Patient information

1. May cause photosensitivity (sensitivity to sunlight). Avoid prolonged exposure to the sun and other ultraviolet light. Use sunscreens and wear protective clothing until tolerance is determined.
2. Promptly report unexplained muscle pain, tenderness, or weakness, especially if accompanied by fever or malaise.
3. Follow dietary recommendations.

Miscellaneous lipemics

Well, this is it, the last group of drugs in this volume. There are two drugs used to help treat high cholesterol that don't fall in to either of the classes already discussed. This section will cover the use of Gemfibrozil and Niacin.

Gemfibrozil

Gemfibrozil decreases triglycerides and very low-density lipoprotein cholesterol, and increases high density lipoprotein cholesterol. It does this by inhibiting lipolysis (the chemical decomposition of fat) and keeps the liver from extracting some fatty acids. Gemfibrozil also inhibits the synthesis of a protein that is required for our bodies to make very low density lipoproteins (VLDL).

Additional information about Gemfibrozil follows:

1. Indication - Gemfibrozil is indicated in hypertriglyceridemia and is used to reduce the risks in patients with coronary heart disease. Gemfibrozil is contraindicated in patients with hepatic or severe renal dysfunction, or preexisting gallbladder disease.
2. Dosing - 1200 mg/daily in two divided doses, 30 minutes before the morning and evening meals. Gemfibrozil is manufactured only in 600 mg tablets.
3. Warnings - Gemfibrozil may increase cholesterol excretion into the bile. This may cause gallstones. Gemfibrozil is pregnancy category C. There are no adequate studies in women. Women taking gemfibrozil should not nurse their infants because Gemfibrozil is excreted into breast milk and has caused tumors in lab tests.
4. Drug interactions - Gemfibrozil interacts with the statins and oral anticoagulants. It increases the effects of both of these medications.
5. Patient information - May cause dizziness or blurred vision; patients should observe caution while driving or performing other tasks requiring alertness, coordination, or physical dexterity. Medication may cause abdominal or epigastric pain, diarrhea, nausea, or vomiting. Notify physician if these become pronounced.

Niacin

Niacin is vitamin B₃, also called nicotinic acid. Its pharmacologic action in reducing lipids involves its ability to decrease the production of VLDL in the liver, the breakdown of fatty acids in fat tissue in the body, and inhibit the formation of triglycerides in the liver. Niacin is indicated in significant hyperlipidemia. It is contraindicated in patients with hepatic dysfunction, active peptic ulcer, severe hypotension, and arterial bleeding.

Niacin is dosed at 1 – 2 grams three times daily, with or following meals. The usual maximum dose is 8 grams per day. Niacin is available in many different strength tablets, both normal and extended release. The extended release form is preferred when using niacin to treat hyperlipidemia.

Additional information about Niacin:

1. Warning - Niacin is in pregnancy category C if used in doses above the RDA. Use doses in excess of nutritional requirements during pregnancy or lactation only when clearly needed and when potential benefits outweigh potential hazards to the fetus or nursing infant.
2. Drug interactions - There are no significant reports of drug interactions reported with Niacin.

3. Patient information - Cutaneous flushing and a sensation of warmth, especially of the face and upper body, may occur. Itching or tingling and headache may also occur. These effects are transient and usually subside with continued therapy. May cause GI upset; take with meals. If dizziness occurs, avoid sudden changes in posture.

Self-Test Questions

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

231. Drugs affecting the blood

1. Describe the two pathways that lead to coagulation.
2. What monitoring method is used to ensure proper anticoagulation dosing?

232. Drugs affecting the heart

1. How do antiarrhythmic drugs work?
2. In what pregnancy category are the anti-anginals discussed?

233. Drugs affecting the blood vessels

1. On what type of blood vessel does hydralazine work.
2. What are the indications for the alpha-adrenergic blocking agents?
3. What drugs decrease the effectiveness of beta-adrenergic blocking agents?
4. Describe the renin-angiotensin system.
5. How do Angiotensin II receptor antagonists differ from Angiotensin converting enzyme inhibitors?
6. What are the effects of calcium channel blockers on the cardiovascular system?

7. What is the primary method of action of thiazide diuretics?
8. Where do loop diuretics get their name?
9. What is the major use of potassium sparing diuretics?
10. What purpose do bile acids serve?
11. What is the common name of HMG-CoA reductase inhibitors?
12. What is the vitamin name of nicotinic acid?

Answers to Self-Test Questions

225

1. Blood's color varies depending on how much oxygen it is carrying.
2. Plasma.
3. Albumin.
4. Glucose.
5. Formation of bone, production of hormones by certain glands (iodine for the production of thyroid hormone), transportation the gases oxygen and carbon dioxide (iron), maintenance of acid-base balance (sodium and potassium carbonates and phosphates).
6. The mature form of erythrocytes found in the circulating blood does not have a nucleus.
7. Substances that promote clotting.
8. A, B, AB, and O.
9. The volume percentage of red blood cells in whole blood.
10. A patient's white blood count is in excess of 10,000 per cubic millimeter of blood.

226

1. Slightly bigger than a fist and is located between the lungs in the center and a bit to the left of the midline of the body.
2. Myocardium.
3. The right atrium.
4. The right and left coronary arteries.
5. A relatively slow heart rate.
6. A heart rate over 100 beats per minute.
7. Sinus arrhythmia.

227

1. Arteries, veins, and capillaries.
2. Arteries.
3. Aorta.
4. Those veins that drain blood from capillaries in the spleen, stomach, pancreas, and intestine.
5. To transport blood from the digestive organs and spleen to the liver sinusoids so the liver cells can carry out their functions.
6. Pulse.
7. Systolic pressure and diastolic pressure.

228

1. Anemias, neoplastic diseases, and hemorrhagic disorders.
2. Hemorrhagic disorders.
3. Nutritional anemia.
4. Iron deficiency anemia.
5. Pernicious anemia.
6. Benzene, arsenic, nitrogen mustard, gold compounds, and chloramphenicol (in some persons).
7. Myelogenous leukemia.
8. Hemophilia.

229

1. Inflammation of the lining of the heart cavities.
2. Myocarditis.
3. Pericarditis.
4. Degenerative heart disease.
5. Holes in the septum or partition between the left and right sides of the heart.
6. Streptococcal infections.
7. A closure of one or more branches of the coronary arteries.
8. It is a condition where the blood flow to the heart muscle is inadequate, resulting in a characteristic agonizing pain, felt in the region of the heart and in the left arm and the shoulder.

230

1. Hypotension.
2. Essential hypertension.
3. A bulging sac in the wall of an artery or a vein, owing to a localized weakness in that part of the vessel.
4. Aorta.
5. Arteriosclerosis.
6. The gradual narrowing of the interior of the arteries, with a consequent reduction of the volume of blood that passes through them.
7. The death of cells.
8. The pressure point at the temporal artery.
9. A life-threatening condition in which there is inadequate blood flow to the tissues of the body.
10. Cardiogenic shock.
11. Clammy skin, anxiety, very low blood pressure, rapid pulse, and rapid, shallow breathing.
12. Varicose veins.
13. It is when the lumen of an artery is completely blocked by arteriosclerosis.

231

1. Intrinsic—all protein factors for coagulation are present in the blood and are activated by factor XII, and extrinsic, coagulation is activated by the release of thromboplastin.
2. Bleeding times are monitored.

232

1. By suppressing the electrical conduction.
2. Pregnancy category C.

233

1. Arteries by direct relaxation of vascular smooth muscle.
2. All three are indicated for hypertension; terazosin and doxazosin are also indicated for urinary obstruction and symptoms associated with BPH.
3. Barbiturates, Penicillins, Cholestyramine, Rifampin, Colestipol, Salicylates, NSAIDs, and thyroid hormones.
4. Renin is released into circulation by the kidneys. It produces angiotensin I, which is then converted to angiotensin II by the angiotensin-converting enzyme. Angiotensin II is a potent vasoconstrictor that also stimulates aldosterone secretion from the adrenal cortex, contributing to sodium and fluid retention.
5. AIRAs work further down the line from ACE inhibitors. After angiotensin I is converted to angiotensin II, the AIRAs block the receptors from receiving the angiotensin II.
6. They include depression of mechanical contraction of myocardial and smooth muscle, and depression of impulse formation and conduction velocity.
7. Sodium depletion.
8. Because of where they work. All of their action takes place at the loop of Henle in the kidney.
9. To enhance the action of, and counteract the kaliuretic effects of loop and thiazide diuretics.
10. Bile acids are released into the intestines to emulsify fats and lipids in food to help with absorption.
11. Statins.
12. Vitamin B₃.

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.

57. (225) The name for the liquid element of blood is
- a. erythrocytes.
 - b. leukocytes.
 - c. platelets.
 - d. plasma.
58. (225) What element of blood is responsible for carrying oxygen from the lungs to tissues?
- a. Erythrocytes.
 - b. Leukocytes.
 - c. Platelets.
 - d. Plasma.
59. (225) Which element of blood destroys pathogens through phagocytosis?
- a. Erythrocytes.
 - b. Leukocytes.
 - c. Platelets.
 - d. Plasma.
60. (225) Which element of blood is essential for coagulation?
- a. Erythrocytes.
 - b. Leukocytes.
 - c. Platelets.
 - d. Plasma.
61. (226) The thickest layer of the heart is the
- a. pericardium.
 - b. myocardium.
 - c. endocardium.
 - d. pericardial sac.
62. (226) Which chamber of the heart sends venous blood to the lungs for oxygenation?
- a. Right atrium.
 - b. Right ventricle.
 - c. Left atrium.
 - d. Left ventricle.
63. (226) Heart “murmurs” are usually caused by
- a. ventricular relaxation.
 - b. normal closing of a valve orifice.
 - c. abnormal narrowing of a valve orifice.
 - d. blood leaking from a valve not closing tightly.
64. (227) What type of blood vessels allow for exchanges between the blood and body cells?
- a. Veins.
 - b. Arteries.
 - c. Arterioles.
 - d. Capillaries.

65. (227) In which section of the circulatory system does the “first pass” effect occur?
- a. Pulmonary circulation.
 - b. Venous sinuses.
 - c. Thoracic.
 - d. Portal.
66. (228) Which blood disorder is characterized by a reduction in hemoglobin with impaired delivery of oxygen?
- a. Anemia.
 - b. Myelogenous leukemia.
 - c. Lymphocytic leukemia.
 - d. Bone marrow suppression.
67. (229) Which type of heart disease is caused by a childhood disease?
- a. Coronary.
 - b. Rheumatic.
 - c. Congenital.
 - d. Degenerative.
68. (230) The term given to hypertension that has no apparent medical cause is
- a. arterial.
 - b. diastolic.
 - c. essential.
 - d. secondary.
69. (230) What circulatory disorder includes areas of yellow, fat-like material replacing muscle and connective tissue?
- a. Aneurysm.
 - b. Thrombosis.
 - c. Atherosclerosis.
 - d. Atherosclerosis.
70. (230) Which pressure point should be pressed to stop bleeding from the shoulder or arm?
- a. Femoral.
 - b. Brachial.
 - c. Temporal.
 - d. Subclavian.
71. (230) Which type of shock is due to a decrease in the volume of circulating blood?
- a. Septic.
 - b. Cardiogenic.
 - c. Hypovolemic.
 - d. Anaphylactic.
72. (231) The effectiveness of warfarin is decreased by
- a. vitamin K.
 - b. streptokinase.
 - c. corticosteroids.
 - d. acetaminophen.

-
-
73. (231) The medication indicated for postoperative cardiac valve replacement patients due to blood platelets reaction to prosthetic heart valve surfaces is
- dipyridamole.
 - ticlopidine.
 - vitamin K.
 - digoxin.
74. (232) Which antiarrhythmic drug may cause arterial flutter or fibrillation before restoring regular rhythm?
- Lidocaine.
 - Quinidine.
 - Procainamide.
 - Nitroglycerin.
75. (232) The name for the class of heart medications that redistribute coronary blood flow to increase the passage of blood to the myocardium is
- nitrates.
 - antiarrhythmic.
 - cardiac glycosides.
 - calcium channel blockers.
76. (233) The actions of alpha-adrenergic blockers are decreased by the NSAID called
- naproxen.
 - piroxicam.
 - ibuprophen.
 - indomethacin.
77. (233) Which beta-adrenergic blocker is cardioselective?
- Nadolol.
 - Atenolol.
 - Propranolol.
 - Haloperidol.
78. (233) Which anti-hypertensive agents may cause a persistent dry, hacky cough?
- Thiazide diuretics.
 - Calcium channel blockers.
 - Angiotensin II receptor antagonists.
 - Angiotensin-converting enzyme inhibitors.
79. (233) A medication that works in the kidney at the loop of Henle is
- indapamide.
 - triamterene.
 - furosemide.
 - spironolactone.
80. (233) Which of the following drugs act by binding bile acids in the intestine?
- Cholestyramine.
 - Atorvastatin.
 - Gemfibrozil.
 - Niacin.

Student Notes

Student Notes

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