Section One: Cellular Physiology
Introduction

Appreciating the correlation of pathophysiology with disease process

– Can better understand and anticipate patient needs

– Can better direct and provide appropriate care to patients

· Correlation of disease process with care provided to patients

– Once knowledge of physical laws and principles have been gained, the paramedic can apply these to the mechanisms and complications of disease

– Cells of the immune system and inflammatory responses are found with every type of trauma or disease process

Terms to know: (3 questions on exam)

Homeostasis - relative constancy in the internal body environment.

Ions - molecules with either a positive or negative charge.

Cation - positively charged ion.

Anion - negatively charged ion.

Section One: Cellular Physiology

I. BASIC CELLULAR REVIEW

A. The cell

1. Fundamental unit found in higher life forms

2. All cells require various key components and structures

a. Cell membrane

1) Holds the cell together

2) Separates internal (cellular) environment from external environment

b. Enzymes to bring about biochemical processes

c. Internal membranes to encapsulate chemicals

d. Genetic material for producing components for their own replication

3. Cells form the four basic tissue types that include:

a. Epithelial

b. Connective (including hematologic tissue)

c. Muscle

d. Nervous

II. THE CELLULAR ENVIRONMENT

A. Overview

Text Reference

Review Cell Functions from A&P Lecture

1. Cells of the body live in a fluid environment of which water is the main component

2. Importance of body water is highlighted by two facts

a. It is the medium in which all metabolic reactions occur

b. Precise regulation of the volume and composition of body fluid is essential to health

3. Human body contains two fluid compartments: intracellular and extracellular fluid

B. Intracellular and extracellular fluid

1. Intracellular fluid (ICF)

a. Fluid found in all body cells

b. Accounts for 40% of total body weight

2. Extracellular fluid (ECF) (1 question on exam)

a. Water found outside the cells

1) Includes intravascular and interstitial compartments

b. Accounts for about 20% of total body weight

Talk about which fluids can move from space to space.

1) Intravascular component (blood plasma) comprises about one third of this

c. Interstitial fluid

1) Extracellular fluid between the cells and outside the vascular bed (i.e., connective tissue, cartilage, and bone)

2) Also includes special fluids such as:

a) Cerebrospinal fluid (CSF)

b) Intraocular fluid

3) Accounts for about 15% to 16% of total body weight

C. Aging and the distribution of body fluids

1. Water is main component of body mass

a. Accounts for 50% to 60% of total body weight in adults

b. Distribution and amount of total body water (TBW) change with age

1) TBW in newborn infants accounts for about 80% of their body weight

2) During childhood, TBW decreases to 60% to 65% or body weight and further declines with age

The normal reduction in TBW in the older adult is clinically important in the presence of fever or dehydration. Loss of body fluids with illness or injury can be severe or life-threatening.

D. Water movement between ICF and ECF

1. Body fluids constantly move from one compartment to another

a. In healthy individuals, the volume of fluid in each compartment remains about the same

b. To keep the volume stable, the body uses osmosis, diffusion, and mediated transport mechanisms

2. Osmosis

a. Movement of molecules within a cell or across cell membranes is essential for normal body functioning

b. Fluid compartments are separated by membranes

1) Most allow water to pass freely but regulate or restrict the flow of solutes (substances dissolved in solution) based on their size, shape, electrical charge, or other chemical properties

2) These membranes are called semipermeable membranes

3) Channels in membranes permit passage of solutes

a) They can be open at all times to specific solutes or closed at times, depending on the physiology of the cell

c. Osmosis is the flow of fluid across a semipermeable membrane from a lower solute concentration to a higher solute concentration

The ability of the cell membrane to selectively regulate solute transition enables the cell to maintain a relative constancy in the internal environment of the body (homeostasis).

d. Gases

In any mixture of gases, the combination of the pressures exerted by all the gases is called the total pressure, and the pressure exerted by a single gas is called the partial pressure. The partial pressure of a gas in a mixture is denoted by a "P" preceding the gas (e.g., PO2 and PCO2).

1) Driving force of osmosis is produced by the partial pressure of the dissolved gases (osmotic pressure)

2) Include oxygen, nitrogen, carbon dioxide, and water

e. Nongaseous particles (e.g., electrolytes)

Electrolytes are salt substances whose molecules dissociate into charged components when in water, producing positively and negatively charged ions. An ion with a positive charge is called a cation, and an ion with a negative charge is called an anion. Sodium is the most abundant ECF cation and is responsible for the osmotic balance of the ECF space. Potassium is the most abundant ICF cation and maintains the osmotic balance of the ICF space. The body also contains nonelectrolytes (substances with no electrical charge), such as glucose and urea.

1) Osmotic pressure depends on:

a) Number and molecular weights of particles on each side of the membrane

b) Permeability of the membrane to these particles

f. Hypertonic solution (1 question on exam)

1) When a living cell is placed in a solution that has a higher solute concentration (and thus a lower water concentration) than that inside the cell, the solution is called hypertonic with respect to the cell

2) Osmotic pressure exerted on the cell produces a net movement of water molecules out of the cell; this net movement causes the cell to dehydrate, shrink (crenate), and if severe enough will lead to cellular death

50% dextrose is a hypertonic solution.

g. Hypotonic solution

1) When a living cell is placed in a solution that has a lower solute concentration (and thus a higher water concentration) than that inside the cell, the solution is called hypotonic with respect to the cell

2) Osmotic pressure draws water molecules from the surrounding solution into the cell causing the cell to swell and perhaps burst, or lyse

0.45% normal saline is a hypotonic solution.

h. Isotonic solution (1 question on exam)

Intravenous therapy is based on hypertonic, hypotonic, and isotonic properties. Lactated Ringer's and normal saline are isotonic solutions.

1) When a living cell is placed in a solution in which the solute concentration (and water concentration) is the same as the solution inside the cell, the solution is called isotonic.

2) There is no net movement of water molecules in isotonic solutions.

3. Diffusion

A fun example of diffusion is to open a container of something that smells bad. As the molecules diffuse through the air, everyone will know it.

a. Results from the constant, random motion of all the atoms, molecules, or ions in a solution

b. This passive process moves molecules or ions form an area of higher concentration to an area of lower concentration

c. Because there are more solute particles in an area of high concentration and because the particles move randomly, more solute particles move from the higher to the lower concentration than in the opposite direction.

1) In contrast, at equilibrium the net movement of solute stops

a) Random molecular motion continues, but the movement of solutes in one direction is balanced by equal movement in the opposite direction

d. If a solute concentration is greater at one point than at another point in the solvent, a concentration gradient exists

Place a few drops of food coloring in a clear glass of water. After diffusion occurs, the color will be evenly distributed in the water.

1) Solutes diffuse down their concentration gradients from high to low concentration until equilibrium is achieved

e. Some nutrients enter and some waste products leave the cell by diffusion

1) The maintenance of appropriate intracellular concentrations of certain substances depends on this process

4. Mediated transport mechanisms

a. Necessary to move large water-soluble molecules or electrically charged molecules across the cell membranes

1) Many essential molecules (e.g., glucose) cannot enter most cells by diffusion

2) Many products (e.g., some proteins) cannot exit most cells by diffusion

b. Carrier molecules

1) Proteins, acting as transport mechanisms, that combine with solutes on one side of a membrane and transport the solute to the other side

2) Two kinds of mediated transport:

a) Active transport

b) Facilitated diffusion

c. Active transport (1 question on exam)

1) Carrier-mediated process that can move substances against a concentration gradient from areas of lower concentration to areas of higher concentration

2) Energy is expended by the cell to work against this concentration gradient

Ask the students to recall the form of energy being referenced here. (ATP)

3) Occurs at a faster rate than diffusion

d. Facilitated diffusion (1 question on exam)

Example: The sodium-potassium pump in the action potential depends on active transport to move potassium back into the cell during repolarization.
Exapmle: Insuline is a carrier molecule that is necessary to transport glucose into the cell.

1) Carrier-mediated process that moves substances into and out of cells from a high to a low concentration

2) Direction of movement is with the concentration gradient

3) Movement is faster than ordinary diffusion

4) Distinguished from active transport in that it does not require an expenditure of energy

Discuss the connection between necessary cellular processes (e.g., production of ATP) and good patient care (e.g., ensuring adequate ventilation and oxygenation).

5) Its moving force is a downhill concentration gradient

E. Water movement between plasma and interstitial fluid

1. Transfer of fluid between the circulating blood and the interstitial fluid

a. Occurs because of pressure changes at the arterial and venous ends of the capillary

2. Anatomy of the capillary network

There are about 10 billion capillaries in the human body, and few functional cells of the body are more than 5/1000 of an inch (20 to 30 microns) away from one.

a. The typical capillary is a thin-walled tube of endothelial cells without elastic tissue, connective tissue, or smooth muscle that would impede the transfer of water and solutes

b. Blood enters the capillary network from the arterioles

1) Flows through the capillary network into the venules

2) Ends of the capillaries closest to the arterioles are called arteriolar capillaries

3) Ends closest to the venules are called venous capillaries

c. Arterioles give rise directly to capillaries or, in some tissues, to metarterioles, which then lead to capillaries

The exchange of nutrients and metabolic end products takes place at the capillary level.

d. Most tissues appear to have two distinct types of capillaries

1) True capillaries

2) Thoroughfare channels

a) From a metarteriole, blood can flow into a thoroughfare channel that connects arterioles and venules directly, bypassing the true capillaries

b) Blood flow through thoroughfare channels is relatively constant

c) From these thoroughfare channels, fluid commonly exits and reenters the network of true capillaries where exchange of nutrients and metabolic cell products takes place

e. Capillary sphincters

1) Small cuffs of smooth muscle found in some tissues that encircle their proximal and distal portions

a) Sphincter at the arterial end is known as the precapillary sphincter

b) Sphincter at the venous end is known as the postcapillary sphincter

2) Control capillary blood flow by opening and closing the entrance and exit to the capillary

Discuss the capillary refill test in children and the implications of various findings.

3) Blood flow in true capillaries is not uniform

a) Depends on contractile state of the arterioles and the precapillary and postcapillary sphincters (if present)

f. Nutritional flow

1) Blood flow through the capillaries that provides the exchange of gases and solutes

2) Blood that bypasses the capillaries in traveling from the arterial to the venous side of the circulation is known as nonnutritional or shunt flow

3) Arteriovenous asastomoses (AV shunts)

a) True AV shunts occur naturally in the sole of the foot, the palm of the hand, the terminal phalanges, and nail beds

(1) Important in regulating body temperature

b) Some evidence also suggests the presence of AV shunts upstream from the capillary sphincters

g. Sympathetic innervation

1) Sympathetic fibers innervate all blood vessels of the body except:

a) Capillaries

b) Capillary sphincters

c) Most metarterioles

2) Sympathetic innervation of blood vessels includes both vasoconstrictor and vasodilator (vasomotor) fibers

a) Sympathetic vasoconstrictor fibers are the most important in regulating blood flow

3) During normal circulation in the healthy body when arterial blood pressure is adequate:

a) Arterioles are open (with some vasomotor tone)

b) AV shunts are closed

c) About 20% of the capillaries are open at any given time

h. Diffusion across the capillary wall

1) Tissue cells do not exchange material directly with blood

a) Interstitial fluid always acts as a middleman

Consider using a coffee filter analogy here.

b) Nutrients must diffuse across the capillary wall into the interstitial fluid to enter cells

c) Metabolic end products must first move across cell membranes into interstitial fluid to diffuse into the plasma

2) Capillary flow

a) At the arteriole end of the capillary, the forces moving fluid out of the capillary are greater than the forces attracting fluid into it

b) At the venous end, these forces are reversed, so more fluid is attracted into the capillary

c) Hydrostatic and osmotic pressures are the two forces responsible for this movement of fluid

d) Oncotic pressure (1 question on exam)

(1) Osmotic pressure that results from the presence of plasma proteins (mostly albumin) that are too large to pass through the wall of the capillary

(a) Also called blood colloid osmotic pressure

e) At the venous end of the capillary, the hydrostatic pressure is lower

(1) The concentration of proteins in the capillary increases slightly because of the movement of fluid out of the arteriolar end

(a) Results in a greater plasma protein concentration and a greater colloid osmotic pressure

Teaching Tip

Have the students think of plasma proteins as little sponges.

(b) Nearly all of the fluid that leaves the capillary at its arteriolar end reenters the capillary at its venous end

(c) Remaining fluid enters the lymphatic capillaries and eventually is returned to the general circulation

i. Cyclic dilation and constriction of the capillary sphincter

The movement of fluid back and forth across the capillary wall is called net filtration and is best described by Starling's hypothesis: Net filtration = forces favoring filtration –forces opposing filtration. The forces favoring filtration include capillary hydrostatic pressure and the interstitial oncotic pressure. The forces opposing filtration are the plasma oncotic pressure and the interstitial hydrostatic pressure.

1) When the capillary sphincter dilates, the pressure rises in the capillary, forcing fluid to move into the interstitial spaces

2) When the capillary sphincter constricts, the pressure in the capillary drops, and fluid moves into the capillary

3. Capillary and membrane permeability

a. Integrity of the capillary membrane is an important factor in the movement of fluid back and forth across the capillary wall

1) Changes in membrane permeability may permit the escape of plasma proteins into the interstitial space

2) Resultant increase in interstitial oncotic pressure alters the relationship defined by Starling's law and leads to osmotic movement of water into the interstitial space, causing tissue edema

F. Alterations in water movement

1. Edema is the accumulation of fluid within the interstitial spaces

    a. Results from any condition that leads to a net movement of fluid out of capillaries and into the interstitial tissues

    b. A problem of fluid distribution and does not necessarily indicate fluid excess

2. Pathophysiology of edema

    a. The normal flow of fluid through the interstitial space depends on four factors:

Compare the process in the lymphatic system to the drainage tile and sump pump system in a basement.

1) Capillary hydrostatic pressure that filters fluid from the blood through the capillary wall

2) Oncotic pressure exerted by the proteins in the blood plasma that attracts fluid from the interstitial space back into the vascular compartment

3) Permeability of the capillaries that determines the ease with which fluid can pass through the capillary wall

4) Presence of open lymphatic channels that collect some fluid forced out of the capillaries by the hydrostatic pressure of the blood and return the fluid to the circulation

b. When normal flow is disturbed, alterations in water movement can develop

c. Common mechanisms responsible for edema

Classroom Activity

Show pictures of edema of the hands, ankles, and sacral area. Discuss the pathophysiology of these conditions.

1) Increased capillary hydrostatic pressure

a) Increase can result from:

Classroom Activity

If practical, take the class outside. Connect a piece of hose that has small puncture holes in it to a water faucet. Turn the water on at a very low pressure and note the amount of the leak. Increase the flow and observe the leak. Compare this to an increase in hydrostatic pressure. Turn the flow to low again, and then crimp the end of the hose. Have the class describe the effects of the obstruction on fluid leak.

(1) Venous obstruction

(a) Can cause the hydrostatic pressure of fluid within the capillaries to become great enough to cause fluid to escape into the interstitial spaces

(b) Conditions that can lead to venous obstruction and edema:

i. Thrombophlebitis

ii. Hepatic obstruction

iii. Tight clothing around an extremity

iv. Prolonged standing

(2) Sodium and water retention

(a) Can cause a volume overload and edema

(b) Conditions associated with sodium and water retention:

i. Congestive heart failure (CHF)

ii. Renal failure

2) Decreased plasma oncotic pressure

a) Decreases in plasma albumin will lead to a decrease in plasma oncotic pressure and cause fluid to move into the interstitial space

b) Most commonly results from liver disease or protein malnutrition

3) Increased capillary permeability

Discuss how burns alter capillary permeability.

a) Increases in capillary permeability cause the filtration of fluid into the interstitial space to be greater than normal

b) Is usually associated with inflammation and the immune response that result from:

(1) Trauma

(a) Burns

(b) Crushing injuries

(2) Allergic reactions

c) Proteins escape from the vascular bed and produce edema through a loss of capillary oncotic pressure and a gain in interstitial fluid oncotic pressure

4) Lymphatic vessel obstruction

a) When lymphatic channels become blocked from infection or are surgically removed, proteins and fluid accumulate in the interstitial space

(1) The obstruction blocks the normal pathway by which fluid is returned from the interstitial space into the circulation

(a) Leads to edema in the region that is normally drained by the lymphatic channels

(b) Conditions that can cause obstruction in the lymphatic channels:

i. Certain malignancies

ii. Parasitic infections

iii. Surgical removal of lymphatics, as often performed following a radical mastectomy (axillary lymph node dissection)

Discuss why, in patients who have undergone mastectomies, blood pressure measurements should not be taken on the side on which the mastectomy was performed.

3. Clinical manifestations of edema

   a. Edema may be localized or generalized

   b. Localized edema usually limited to:

      1) Injury site (e.g., a sprained ankle)

      2) Organ system (e.g., cerebral edema, pulmonary edema)

   c. Generalized edema

Edema of specific organs such as the brain, lungs, or larynx can be life-threatening.

1) More widespread

2) Most conspicuous in dependent parts of the body

3) Usually noted first in gravity-dependent areas of the body:

   a) Legs and ankles when standing or sitting

   b) Sacrum and buttocks when lying down

4) Usually associated with:

   a) Weight gain

   b) Swelling

   c) Puffiness

5) Often associated with other symptoms from the underlying illness

6) Common diseases that cause generalized edema

   a) Industrialized countries

      (1) Heart disease

      (2) Kidney disease

(3) Liver disease

b) Developing countries

(1) Malnutrition

(2) Parasitic disease

G. Water balance, sodium, and chloride

When edematous tissue is compressed with a finger, the fluid is pushed aside, leaving a pit or indentation that gradually refills with fluid. This condition is called pitting edema.

Fluid that accumulates in the peritoneal cavity is called ascites. (1 question on exam)

1. Osmotic gradient
    a. Water follows the osmotic gradient established by changes in sodium concentration
    b. Sodium and water balance are closely related
2. Water balance (1 question on exam)
    a. Primarily regulated by antidiuretic hormone (ADH)

1) Secretion of ADH and the perception of thirst help regulate water balance

2) Release of ADH is initiated by:

a) Increase in plasma osmolality (the osmotic pressure of a solution)

b) Decrease in circulating blood volume and a lowered venous and arterial pressure

3) Increased plasma osmolality:

a) Stimulates hypothalamic neurons (osmoreceptors)

(1) Cause the perception of thirst

(2) Increase the release of ADH from the posterior pituitary gland

4) Responses to ADH release

a) Reabsorption of water into the plasma from the renal tubules and collecting ducts of the kidneys

b) Decrease in the amount of water lost in the urine

c) Decrease in plasma osmolality (returning it to normal) as the water is reabsorbed

5) Volume-sensitive receptors and baroreceptors (found in the heart and great vessels)

a) Stimulate the release of ADH when body fluids are depleted from conditions such as vomiting, diarrhea, or excessive sweating

3. Sodium and chloride balance (1 question on exam)

Volume-sensitive receptors and baroreceptors are nerve endings that are sensitive to changes in volume or pressure. Volume-sensitive receptors are found in the right and left atrium and thoracic vessels. Baroreceptors are found in the aorta, pulmonary arteries, and carotid sinus. (1 question on exam)

a. Sodium (Na+)

1) Major ECF cation

2) Balance is regulated by the aldosterone, a hormone secreted from the adrenal cortex

3) Regulates osmotic forces, along with chloride and bicarbonate, and therefore regulates water balance

b. Chloride (Cl-)

1) Major ECF anion

2) Provides electroneutrality in relation to sodium

3) Increases or decreases in chloride are proportional to changes in sodium

c. Secretion of aldosterone

1) Initiated when sodium levels are decreased or potassium levels are increased

2) Increases the reabsorption of sodium and secretion of potassium by the distal tubules of the kidneys

d. Renin-angiotensin system: mechanism for regulating sodium and water

1) Renin

a) Renin is an enzyme secreted by the kidneys when circulating blood volume or water balance is reduced

b) Renin stimulates the formation of angiotensin I that is then converted to angiotensin II

2) Angiotensin II (1 question on exam)

a) A potent vasoconstrictor that acts to stimulate the secretion of ADH

b) Results in:

(1) Reabsorption of sodium and water

(2) Elevation in systemic blood pressure

e. Natriuretic hormone

1) Helps regulate sodium balance by promoting urinary secretion of sodium

a) Result is a decrease in tubular reabsorption of sodium and a subsequent loss of sodium and water

4. Alterations in sodium, chloride, and water balance

Atrial natriuretic factor, a substance released from the atrial cells of the heart, also helps control the balance of sodium and water by promoting renal elimination of sodium.

a. In the healthy body, homeostatic mechanisms maintain a constant balance between intake and excretion of water

1) The water gained each day approximately equals the water lost

b. The body gains water primarily by:

1) Drinking fluids

2) Ingesting food containing moisture

3) Forming water through the oxidation of hydrogen in food during the metabolic process

c. The body loses water through:

1) Kidneys as urine

2) Bowel as feces

3) Skin as perspiration

4) Exhaled air as vapor

5) Excretion of tears and saliva

d. Two abnormal states of body-fluid balance can occur

1) If the water lost exceeds the water gained, there is a water deficit or dehydration

2) If the water gained exceeds the water lost, there is a water excess or overhydration

5. Dehydration

Discuss how dehydration might present in patients of various ages, from infants to adults.

a. Classifications of dehydration

1) Isotonic: excessive loss of sodium and water in equal amounts

2) Hypernatremic: loss of water in excess of sodium

3) Hyponatremic: loss of sodium in excess of water

b. Isotonic dehydration

1) Causes:

a) Usually, severe or long-term vomiting or diarrhea

b) Systemic infection

c) Intestinal obstruction

2) Signs and symptoms:

Discuss why mucous membranes become dry in patients who are dehydrated.

a) Dry skin and mucous membranes

b) Poor skin turgor

c) Longitudinal wrinkles or furrows of the tongue

d) Oliguria (decreased urinary output)

e) Anuria (essentially no urinary output—100 ml or less in 24 hours)

f) Acute weight loss

g) Depressed or sunken fontanelles in infants

3) Treatment: (1 question on exam)

a) IV infusion of an isotonic solution that has a solute concentration equal to that of blood (typically 0.9% sodium chloride or normal saline)

c. Hypernatremic dehydration

1) Possible causes:

a) Excessive use or misuse of diuretics

b) Continued intake of sodium without water consumption

c) Excessive loss of water with little loss of sodium

d) Profuse, watery diarrhea

2) Signs and symptoms

Teaching Tip

Inhalation or ingestion of saltwater (e.g., near-drowning) may cause hypernatremia without dehydration.

a) Dry, sticky mucous membranes

b) Flushed, doughy skin

c) Intense thirst

d) Oliguria or anuria

e) Increased body temperature

f) Altered mental status

3) Treatment: volume replacement

a) Usually begun with isotonic fluids because the patient is often both salt- and water-depleted (but more water-depleted)

b) Isotonic fluids are relatively hypotonic in these patients

d. Hyponatremic dehydration

1) Possible causes:

a) Use of diuretics

b) Excessive perspiration (heat-related illness)

c) Salt-losing renal disorders

d) Increased water intake (e.g., excessive use of water enemas)

2) Signs and symptoms may include:

Teaching Tip

Inhalation or ingestion of fresh water (e.g., near-drowning) and compulsive water drinking may cause hyponatremia without dehydration.

a) Abdominal or muscle cramps

b) Seizures

c) Rapid, thready pulse

d) Diaphoresis

e) Cyanosis

3) Treatment:

a) IV fluid replacement with normal saline or lactated Ringer’s solution

b) Occasionally, hypertonic saline (e.g., in seizures caused by hyponatremia)

6. Overhydration

    a. An increase in body water with a resultant decrease in solute concentration

        1) The total body amount of solute actually can be increased, but because body water is increased more, the solute concentration is decreased

    b. Causes

Ask the class how they can predict what types of patients will be at risk for overhydration.

        1) Parenteral administration of excessive fluids

        2) Impaired cardiac function

        3) Impaired renal function

        4) Some endocrine dysfunctions

    c. Signs and symptoms

        1) Shortness of breath

        2) Puffy eyelids

        3) Edema

        4) Polyuria (voiding a large volume of urine in a given time)

        5) Moist crackles (on pulmonary examination)

Discuss crackles as a sign of fluid excess.

        6) Acute weight gain

    d. Treatment

        1) Depends on the cause

        2) Excessive water administration and certain endocrine problems are treated with water restriction

        3) Cardiac or renal impairment can be treated with diuretics

        4) Profound hyponatremia associated with overhydration (associated seizures or altered consciousness) may require administration of saline

7. Electrolyte imbalances

    a. Potassium (K+)

        1) Major cation in ICF

2) Narrow range of normal values needed for normal nerve, cardiac, and skeletal muscle function

3) Obligate (those that cannot be avoided) potassium losses are usually minimal

   a) Replenished through dietary intake

4) Excessive potassium is usually excreted readily by the kidneys

5) Plays a major role in:

   a) Muscle contraction

   b) Enzyme action

   c) Nerve impulses

   d) Cell membrane function

6) Potassium imbalances

Discuss sources of potassium and why some patients take potassium supplements.

   a) Interfere with neuromuscular function

   b) May cause cardiac rhythm disturbances (dysrhythmias), including sudden cardiac death

7) Hypokalemia (potassium deficit)

   a) Causes

      (1) Reduced dietary intake (rare)

      (2) Poor potassium absorption by the body

      (3) Increased gastrointestinal (GI) losses from vomiting or diarrhea

      (4) Renal disease

      (5) Infusion of solutions poor in potassium

      (6) Medications

         (a) Diuretics most common

         (b) Steroids

         (c) Theophylline

         (d) Others

      (7) Diuretic use

b) Signs and symptoms

(1) Malaise

(2) Skeletal muscle weakness

(3) Cardiac dysrhythmias

(4) Decreased reflexes

Teaching Tip

U waves may be observed on the patient's ECG.

(5) Weak pulse

(6) Faint or distant heart sounds

(7) Shallow respirations

(8) Low blood pressure

(9) GI problems

(a) Anorexia

(b) Vomiting

(c) Gaseous distention

(10) Excessive thirst (rare)

c) Treatment

(1) In-hospital treatment is IV or oral potassium replacement

8) Hyperkalemia (potassium excess)

a) Causes

(1) Acute or chronic renal failure

(2) Burns

(3) Crush injuries

(4) Severe infections or other conditions in which large amounts of potassium are released

(5) Excessive use of potassium salts

(6) Shift of potassium from the cells into the extracellular fluid (such as occurs in acidosis)

b) Signs and symptoms

(1) Cardiac conduction disturbances

(2) Irritability

Teaching Tip

Tall, peaked T waves may be observed on the patient's ECG.

(3) Abdominal distention

(4) Nausea

(5) Diarrhea

(6) Oliguria

(7) Weakness (an early sign) and paralysis (a late sign of severe hyperkalemia)

c) Treatment

(1) In-hospital treatment involves restricting potassium and administering a cation exchange resin (orally or by NG tube)

(2) Hyperkalemic emergencies may require:

(a) IV administration of glucose and insulin to lower serum potassium levels by forcing potassium intracellularly along with glucose

(b) Sodium bicarbonate to shift potassium intracellularly

(c) IV calcium as an antagonist to cardiac effects of high potassium levels

Discuss why calcium works to counteract high potassium levels.

b. Calcium (Ca++) (1 question on exam)

1) A bivalent ion (an ion with two positive charges) essential for body functions including:

a) Neuromuscular transmission

b) Cell membrane permeability

c) Hormone secretion

d) Growth and ossification of bones

e) Muscle contraction both voluntary and involuntary.

Describe the effects of calcium on cardiac function.

(1) Smooth, cardiac, and skeletal muscle

2) Calcium intake in a balanced diet is sufficient for normal body needs

3) Calcium is excreted through urine, feces, and perspiration

4) Hypocalcemia (calcium deficit)

a) Causes

(1) Endocrine dysfunction (mostly parathyroid)

(2) Renal insufficiency

(3) Decreased intake or malabsorption of calcium

(4) Deficiency, malabsorption, or inability to activate vitamin D

b) Signs and symptoms

Ask students what other conditions might cause these signs and symptoms.

(1) Paresthesia

(2) Tetany

(3) Abdominal cramps

(4) Muscle cramps

(5) Neural excitability

(a) Personality changes

(b) Abnormal behavior

(c) Convulsions

c) In-hospital treatment

(1) IV administration of calcium ions

(2) Calcium salt and vitamin D may be given orally for maintenance

5) Hypercalcemia (calcium excess)

a) Causes

(1) Various neoplasms (tumors)

(2) Parathyroid dysfunction

(3) Diuretic therapy

(4) Excessive administration of vitamin D (as in treatment of osteoporosis)

b) Calcium can be deposited into various body tissues, including many organ systems

Teaching Tip

The detection of hypocalcemia and hypercalcemia is unlikely in the prehospital setting. Laboratory analysis is needed to confirm these imbalances.

(1) GI systems

(2) Central nervous system (CNS)

(3) Neuromuscular system

(4) Cardiovascular system

c) Signs and symptoms

(1) Hypotonicity of the muscles (decreased muscle tone or tension)

(2) Renal stones (calculi)

Discuss the signs and symptoms of renal stones.

(3) Altered mental status

(4) Deep bone pain

d) In-hospital treatment

(1) Aimed at controlling underlying disease, hydration, and drug therapy to lower calcium

(2) May include:

Discuss how Lasix works to decrease fluids in the body.

(a) Forced diuresis with normal saline and furosemide

(b) Administration of thyrocalcitonin, steroids, and plicamycin (a cytotoxic drug that inhibits bone reabsorption of calcium)

c. Magnesium (Mg++)

Alterations in serum phosphate levels also can occur, resulting in hypophosphatemia and hyperphosphatemia. Low serum phosphate levels may be caused by intestinal malabsorption and increased renal excretion of phosphate. Elevated serum phosphate levels are associated with acute or chronic renal failure or low activity of the parathyroid gland.

1) A bivalent cation that activates many enzymes

2) Approximately 50% of the body's magnesium exists in an insoluble state in bone

a) 45% as an intracellular cation

b) 5% in extracellular solution

3) Excreted by the kidneys

4) Has physiological effects on the nervous system similar to those seen with calcium

5) Hypomagnesemia (magnesium deficit)

Discuss why low levels of magnesium may cause confusion or seizure.

a) Causes

(1) Alcoholism

(2) Malabsorption

(3) Starvation

(4) Diarrhea

(5) Diuresis

(6) Diseases causing hypocalcemia and hypokalemia

b) Characterized by increased irritability of the nervous system

c) Signs and symptoms

(1) Tremors

(2) Nausea and vomiting

(3) Diarrhea

(4) Hyperactive deep reflexes

(5) Confusion (including hallucinations)

(6) Seizures or myoclonus (muscle spasms)

(7) Cardiac dysrhythmias

d) In-hospital treatment

(1) IV fluid administration of a solution that contains magnesium

(a) Most commonly, magnesium sulfate

6) Hypermagnesemia (magnesium excess)

a) Causes

(1) Chronic renal insufficiency (most common)

(2) Ingesting large amounts of magnesium-containing compounds such as cathartics or antacids

(a) Magnesium citrate

(b) Magnesium sulfate

(c) Magnesium hydroxide

(3) Possible consequences of hypermagnesemia

(a) CNS depression

(b) Profound muscular weakness

(c) Areflexia (absence of reflexes)

(d) Cardiac rhythm disturbances (including sudden death)

b) Signs and symptoms

(1) Sedation

(2) Confusion

(3) Muscle weakness

(4) Respiratory paralysis

c) In-hospital treatment may include:

(1) Hemodialysis (most effective treatment) can return blood levels to normal within 4 hours

(2) Calcium salts act as an antagonist to magnesium

(3) IV glucose and insulin to drive magnesium back into cells can be used in an emergency when respiratory depression or cardiac conduction defects are present

H. Acid-base balance (1 question on exam)

1. Acids are produced by the body through normal metabolism

   a. Respiratory acids—culminating in CO_2

   b. Nonrespiratory acids—metabolic acids

2. Bases are used in metabolic disturbances to return plasma to normal

3. A balance between acids and bases must be maintained in a narrow range 7.35 to 7.45

4. The body’s principle regulators are:
    a. Lungs—secrete respiratory acids
    b. Kidneys—secrete metabolic acids
5. pH (1 question on exam)
    a. Acids: substances that release or donate hydrogen ions (protons with a positive charge)
    b. Bases: alkaline substances that receive, or absorb, hydrogen ions
6. Hydrogen ion concentration
    a. Expressed by pH (an abbreviation for the “potential for hydrogen”)
    b. pH is the negative logarithm (base 10) of the hydrogen ion concentration measured as activity in moles per liter

Teaching Tip

107 moles/L = pH 7.0.

    c. A mole (in chemistry) is 6.023 x 1023 molecules (Avogadro’s number)
        1) Grasping the meaning of a number this large is not necessary, however the significance of a small change in pH should be understood
        2) The strength of an acid or base changes by 10 times with each unit change of pH
7. A solution increases in: (1 question on exam)

Suggest that the students “visualize” the following relationship:

PH ~ 1/[H+] (Note: The brackets denote concentration.)

This will help them remember that when the hydrogen ion concentration increases, the pH decreases, representing an increase in the acidity of the solution.

    a. Acidity as the hydrogen ion concentration increases
    b. Alkalinity (basicity) when the hydrogen ion concentration falls
8. Buffer systems (1 question on exam)
    a. The healthy body is sensitive to changes in the concentration of hydrogen ions and tries to maintain the pH of extracellular fluid at 7.4
    b. This is accomplished through three interrelated compensatory mechanisms:
        1) Carbonic acid-bicarbonate buffering
        2) Protein buffering

3) Renal (kidney) buffering

c. These compensatory mechanisms are stimulated by changes in pH and require normal organ function to be effective in maintaining acid-base balance

The bicarbonate-carbonic acid buffer system in the plasma activates within seconds, the lungs activate within minutes, and the kidneys take hours to activate.

d. Carbonic acid-bicarbonate buffering

1) Bicarbonate, carbon dioxide, and carbonic acid are always present in a dynamic balance in the blood

2) Bicarbonate (HCO_3^{-}) arises form the transport of carbon dioxide in the blood

a) Under the influence of the enzyme carbonic anhydrase, carbon dioxide dissolves in the water of blood and reacts with water in red blood cells to form carbonic acid (H_2CO_3)

b) Carbonic acid breaks down into hydrogen and bicarbonate ions

3) At a physiological pH of 7.4, the normal ratio of carbonic acid to bicarbonate is 1:20, respectively

a) Summarized by the chemical equation: $CO_2 + H_2O$ D H_2CO_3 D $H^+ + HCO_3^{-}$

4) Bicarbonate (HCO_3^{-}) may link with a cation to form base bicarbonate (e.g., $NaHCO_3$)

5) It is the ratio of carbonic acid to base bicarbonate that determines the concentration of hydrogen ions

a) If there is 1 mEq of carbonic acid for each 20 mEq of base bicarbonate in the extracellular fluid, the hydrogen ion concentration stays within normal limits

Define mEq. What drugs are administered in mEq?

6) This compensatory mechanism occurs immediately in response to changes in pH with the respiratory rate in maintaining this balance

e. Protein buffering

1) Both intracellular and extracellular proteins have negative charges and can serve as buffers for alterations in hydrogen ion concentration

a) Because most proteins are inside cells, this is primarily an intracellular buffer system

2) Hemoglobin (Hb) is an excellent intracellular buffer because of its ability to bind with hydrogen ions (forming a weak acid) and carbon dioxide

Describe ways to assess Hb saturation.

a) After oxygen is released in the peripheral tissues, hemoglobin binds with carbon dioxide and hydrogen ions

b) As the blood reaches the lungs, these actions reverse themselves

c) Hemoglobin binds with oxygen, releasing carbon dioxide and hydrogen

d) The hydrogen ions released combine with bicarbonate ions, forming carbonic acid

e) The carbonic acid breaks down into carbon dioxide and water, and the lungs expire the carbon dioxide

f) Therefore in normal circumstances, respirations help maintain pH

3) Increasing alveolar ventilation to lower carbon dioxide concentrations occurs within minutes in response to decreases in pH

Because the respiratory centers are more responsive to pH changes than oxygen, it is the amount of carbon dioxide (and therefore the pH) in the blood, rather than the need for oxygen in the tissues, that controls the rate of breathing in normal healthy individuals.

f. Renal buffering (1 question on exam)

1) Kidneys help maintain acid-base balance through three mechanisms

a) Recovery of bicarbonate, which is filtered into the tubules

b) Excretion of hydrogen ions against a gradient to acidify the urine

c) Excretion of ammonium ions (NH4), each of which carries a hydrogen ion with it

2) The renal system compensates for acid-base imbalances slowly in comparison with the protein and bicarbonate buffer systems

a) The kidneys can take from several hours to days to restore the pH to within the normal physiological range

9. Acid-base imbalance

The concentration of carbonic acid (dissolved carbon dioxide) is controlled by the lungs. The concentration of bicarbonate is controlled by the kidneys.

a. Basically two components: respiratory and metabolic

b. Any condition that increases the carbonic acid or decreases the base bicarbonate causes acidosis

1) Makes the pH more acidic than normal

c. Any condition that increases base bicarbonate or decreases carbonic acid causes alkalosis

1) Makes the pH less acidic than normal

d. A patient may have both disorders at the same time

When this occurs, one usually dominates and the other attempts to compensate.

e. Respiratory acidosis

1) Caused by retention of carbon dioxide, leading to an increase in PCO_2

2) Usually caused by an imbalance in the production of carbon dioxide and its elimination through alveolar ventilation

3) $\downarrow$Respiration = $\uparrow CO_2 + H_2O \rightarrow \uparrow H_2CO_3 \rightarrow \uparrow H^+ + HCO_3^-$

4) Reductions in alveolar ventilation may occur because of the following:

Discuss how sedatives can cause a reduction in alveolar ventilation.

a) Respiratory depression

b) Respiratory arrest

c) Cardiac arrest

d) Neuromuscular impairment

e) Medications (sedatives, hypnotics)

f) Chest wall injury

(1) Flail chest

(2) Pneumothorax

g) Pulmonary processes

h) Obstructed airway

i) Chronic obstructive pulmonary disease

j) Pulmonary edema

5) When the respiratory system cannot serve as a compensatory mechanism to correct the acidosis:

Teaching Tip

In respiratory acidosis, the primary abnormality is failure of the lungs to excrete carbon dioxide efficiently.

a) The body's renal system must conserve bicarbonate and excrete more hydrogen ions to help bring the pH back to normal limits—a slower compensatory mechanism

6) Treatment

a) Improve ventilation to quickly eliminate carbon dioxide

b) Assist ventilations to decrease PCO_2

Describe ventilation methods to reduce CO2.

c) Provide supplemental oxygen to correct any accompanying hypoxemia

(1) Hypoxemia can lead to acidosis

f. Metabolic acidosis

1) Results from an accumulation of acid or a loss of base

2) When excessive acid is produced by the body, the acid spills into the extracellular fluid, consuming some bicarbonate buffers

a) Results in an increase in acid and a decrease in available base

b) $\uparrow H^+ + HCO_3^- \rightarrow \uparrow H_2CO_3 \rightarrow H_2O + \uparrow CO_2$

3) The healthy respiratory system immediately attempts to compensate for the acidosis by increasing the rate and depth of ventilation to reduce carbon dioxide

Metabolic acidosis occurs when the amount of acid generated exceeds the body's buffering capacity.

a) As the carbon dioxide level falls, so does the concentration of carbonic acid, returning pH toward normal

b) The kidneys also excrete more hydrogen ions to equilibrate the excess acid in the extracellular fluid

4) Four common forms of metabolic acidosis:

a) Lactic acidosis

b) Diabetic ketoacidosis

c) Acidosis resulting from renal failure

d) Acidosis from ingestion of toxins

Discuss how toxic ingestion can produce acidosis.

5) Lactic acidosis

a) Produced when large cells are inadequately perfused

(1) Resulting in a shift from aerobic (with oxygen) to anaerobic (without oxygen) metabolism

(2) The end product of anaerobic metabolism is lactic acid, which releases hydrogen ions, creating systemic acidosis

(3) Under normal conditions, lactate is converted by the liver back to glucose or is oxidized to carbon dioxide and water

(4) When the rate of lactic acid production exceeds the rate of its metabolism, lactic acidosis occurs

Ask the students how they think the body will compensate for lactic acidosis.

b) Common causes of systemic lactic acidosis

(1) Extreme exertional states (e.g., seizures)

(2) Ischemia (reduced blood supply) to large muscles or organs (e.g., mesenteric ischemia)

Discuss how ischemia can produce acidosis.

(3) Circulatory failure

(4) Shock

c) Specific complications associated with lactic acidosis are thought to include:

Discuss why lactic acidosis would make the heart refractory to defibrillation.

(1) Decreased force of cardiac contraction

(2) Decreased peripheral response to catecholamines

(3) Hypotension and shock

(4) Cardiac muscle that is refractory to defibrillation

d) Treatment

(1) Reestablish tissue perfusion and cardiac output

(a) Permits the liver to regenerate bicarbonate by metabolizing lactate to carbon dioxide and water

(2) Medical direction may recommend

(a) Hyperventilation to induce respiratory alkalosis (controversial)

Discuss why hyperventilation to induce respiratory alkalosis is controversial.

(b) Vigorous rehydration to support circulation

(c) Possible IV of sodium bicarbonate for immediate compensation

(3) Correction of lactic acidosis frequently depends on identification and correction of the underlying cause

6) Diabetic ketoacidosis

a) A complication of diabetes mellitus

(1) Can be seen in alcoholics (alcoholic ketoacidosis)

Define alcoholic ketoacidosis.

Teaching Tip

An experienced paramedic may mistake the increased respiratory rate used to compensate in diabetic ketoacidosis for an anxiety-related problem. This could result in serious consequences.

b) May result when a patient fails to take adequate insulin or when the need for insulin increases (e.g., in cases of infection or trauma)

c) With impaired glucose use (insulin is required for many cells to absorb glucose), fatty acids are metabolized with the production of ketone bodies and release of hydrogen ions

d) Large quantities of ketone bodies exceed the ability of the body's buffering system to compensate

Prehospital care for patients with diabetic ketoacidosis is the administration of normal saline for volume repletion.

(1) Results in acidosis and a decrease in blood pH

7) Acidosis resulting from renal failure

a) The kidneys help maintain acid-base balance by reabsorbing or secreting either bicarbonate or hydrogen ions as needed to keep the pH constant

b) Renal failure affects the compensatory mechanisms of the kidneys to varying degrees

(1) Patients with moderate-to-severe renal failure frequently have mild-to-moderate acidosis

(2) Acidosis results because the failing kidneys are unable to excrete efficiently the acid waste products that are produced by normal metabolic processes

8) Acidosis resulting from ingestion of toxins

a) Ingested toxins that may cause metabolic acidosis include the following:

(1) Ethylene glycol

Discuss sources of ethylene glycol.

(2) Methanol

(3) Salicylates

(4) Others

Ask the class to list household products that contain these chemicals.

b) Ingestion of such toxins can lead to the production of toxic metabolites and may result in acid-base disorders characterized by metabolic acidosis and compensatory respiratory alkalosis

c) Treatment frequently includes:

(1) GI evacuation

(2) Hemodialysis

(3) Diuresis

(4) Hydration to promote excretion

(5) Specific antagonistic or antidotal therapy

g. Respiratory alkalosis

1) Usually caused by hyperventilation whereby PCO_2 is decreased

2) Common causes of hyperventilation include:

Teaching Tip

Respiratory alkalosis is due to hyperventilation, which lowers the alveolar PCO_2, and subsequently the level of PCO_2 in the blood.

Teaching Tip

An overly aggressive rescuer can inadvertently cause respiratory alkalosis by hyperventilating a patient's lungs.

a) Sepsis (early stages)

b) Peritonitis

c) Shock

d) Respiratory ailments

3) $\uparrow$Respiration = $\downarrow CO_2 + H_2O \rightarrow \downarrow H_2CO_3 \rightarrow \downarrow H^+ + HCO_3^-$

4) When carbonic acid is lacking because of excessive carbon dioxide elimination, the blood pH rises

a) The kidneys must excrete bicarbonate ions and retain hydrogen ions to return pH to normal

5) Treatment

a) Correct the underlying cause of the hyperventilation

b) Initial interventions include:

(1) Placing patient on low-concentration oxygen

(2) Providing calming measures to assist the patient with slow, controlled breathing

h. Metabolic alkalosis (rare)

Teaching Tip

IV fluid administration can rapidly lead to overhydration in patients with renal failure.

1) Most often results from:

a) Loss of hydrogen ions (primarily from the stomach)

b) Ingestion of large amounts of absorbable base sodium bicarbonate (baking soda) or calcium carbonate (Tums, other antacids)

c) Excessive IV administration of alkali (e.g., IV injection of sodium bicarbonate)

d) Diuretic use

2) $\downarrow H^+ + HCO_3 \rightarrow \downarrow H_2CO_3^- \rightarrow H_2O + \downarrow CO_2$

3) Loss of hydrogen ions is the initial cause of metabolic alkalosis

a) May result from:

(1) Vomiting (hydrochloric acid loss)

(2) Gastric suction

(3) Increased renal excretion of hydrogen ions in urine

4) When vomiting occurs, not only is gastric acid lost, but volume is depleted

5) Chronic diuretic use

a) Can result in volume depletion

b) Loss of sodium chloride and potassium causes a relative increase in bicarbonate

(1) The kidney defends against volume depletion by increasing its reabsorption of sodium, and thus, water

c) When sodium is reabsorbed, either potassium or hydrogen ions must be excreted to maintain electrical neutrality

d) Excretion of hydrogen ions can lead to a net increase in bicarbonate and subsequent metabolic alkalosis

6) Initially, the respiratory system tries to compensate by retaining carbon dioxide

a) This compensatory mechanism is limited by the development of hypoxemia

(1) The rise in PCO2 and decrease in PO2 because of hypoventilation will stimulate respiration

Discuss how hypoventilation can stimulate ventilation.

7) Treatment

a) Directed at correcting the underlying condition

b) Volume depletion, if present, should be corrected with isotonic solutions

c) Hypokalemia may require correction with potassium replacement

i. Mixed acid-base disturbances

1) Many conditions, including various forms of shock, may produce mixed abnormalities of acid-base regulation

Describe how shock can cause mixed abnormalities in acid-base balance.

a) Simultaneous respiratory and metabolic alterations commonly are seen because of pathology and physiological changes in both the respiratory and metabolic components of the acid-base system

2) Examples of mixed acid-base disturbances:

a) Combined respiratory and metabolic acidosis

b) Metabolic acidosis and respiratory alkalosis

c) Respiratory acidosis and metabolic alkalosis

d) Combined respiratory and metabolic alkalosis

Give a clinical example for each mixed acid-base disturbance.

Section Two: Cellular Injury and Disease

I. ALTERATIONS IN CELLS AND TISSUES

A. Cellular adaptation

1. Cells adapt to their environment to escape and protect themselves from injury

a. An adapted cell is neither normal nor injured

2. Cellular adaptations are common and a central part of the response to changes in physiological condition

a. Often, the adaptation enables cells to function more efficiently

b. It is difficult to determine a pathological response versus an extreme adaptation to changing conditions

3. The five most significant adaptive changes in cells include:

   a. Atrophy (a decrease in cell size)

   b. Hypertrophy (an increase in cell size)

   c. Hyperplasia (an excessive increase in cell number)

   d. Metaplasia (a change from one cell type to another that is better able to tolerate adverse conditions; a conversion into a form that is not normal for that cell)

   e. Dysplasia (abnormal cellular growth)

4. Atrophy

   a. A decrease or shrinkage in cellular size that adversely affects cell function

   b. Can affect any organ, but is most common in:

      1) Skeletal muscle

      2) Heart

      3) Secondary sex organs

      4) Brain

   c. Causes:

      1) Decreased use

      2) Chronic inflammation

      3) Inadequate nutrition or starvation

      4) Inadequate hormonal or nervous stimulation

      5) Reduced blood supply

   d. Atrophy may be reversed (in some conditions) when normal function is restored

An example of atrophy is a skeletal muscle reduced in size because of prolonged immobilization in a cast.

Have a student describe his or her muscle recovery after having a muscle immobilized in a cast.

5. Hypertrophy (1 question on exam)

   a. An increase in the size of cells (without an increase in numbers) with a subsequent increase in the size of the affected organ

b. Results when cells are required to do more work to accomplish a task

c. Examples:

1) “Normal” or physiological hypertrophy

a) Large muscles of a weight lifter

b) Increased growth of the uterus during pregnancy

c) Development of sexual organs in adolescence (initiated by sex hormones)

2) Pathological hypertrophy

a) Enlargement of the heart (myocardial hypertrophy)

b) Enlargement of the kidneys (which also can be physiological)

6. Hyperplasia

a. An excessive increase in the number of cells that results in an increase in the size of a tissue or organ

b. Occurs in response to increased demand

1) May be a normal adaptive mechanism that allows certain organs to regenerate (compensatory hyperplasia)

2) May be a pathological event

a) Compensatory hyperplasia

(1) Formation of a callus

(2) Increased red blood cell formation at high altitude

b) Pathological hyperplasia

(1) Endometrial hyperplasia (can cause excessive menstrual bleeding)

c. Hyperplasia and hypertrophy often occur together

7. Metaplasia

a. Conversion into a form that is not normal for that cell, or the reversible replacement of normal tissue cells by other cells that may be better able to tolerate adverse environmental conditions

b. Examples:

Discuss smoking prevention programs and the role paramedics can play in community education.

1) Changes that occur in the bronchial lining because of cigarette smoking where the normal ciliated epithelial cells are replaced by nonciliated squamous epithelial cells that are more resistant to irritation

a) Bronchial metaplasia can be revered when one quits smoking cigarettes

2) Chronic inflammation of the cervix

8. Dysplasia

a. Abnormal changes of mature cells

b. The individual cells vary in size, shape, and color, and their relationship to one another also is abnormal

c. Dysplastic changes:

1) Often considered precancerous

2) Most frequently seen in epithelial tissue

d. Changes often result from chronic irritation or inflammation and are frequently found next to cancerous cells

Dysplasia is not considered a true cellular adaptation, but rather an atypical hyperplasia.

B. Cellular injury

1. Many processes can cause cellular injury

2. Mechanisms involved in cellular injury are complex

3. The specific site of injury is often characteristic of a particular pathologic process

4. As a rule, cellular injury occurs if the cell is unable to maintain homeostasis because of:

a. Hypoxic injury

b. Chemical injury

c. Infectious injury (bacteria, viruses)

d. Immunological and inflammatory injury

e. Genetic factors

f. Nutritional imbalances

g. Physical agents

5. Hypoxic injury

a. Most common cause of cellular injury

1) May result from:

a) Decreased amounts of oxygen in the air

b) Loss of hemoglobin or altered hemoglobin function

c) Decreased number of red blood cells

d) Diseases of the respiratory or cardiovascular system

e) External compression (e.g., in trauma)

f) Poisoning and loss of cytochromes

g) Atherosclerosis (narrowing of arteries)

h) Thrombosis (complete blockages of anatomy by blood clots)

b. When ischemia is prolonged, it leads to infarction or death of cells

If cells do not have an adequate supply of oxygen, they cannot generate enough energy to maintain the mechanisms (ion pumps) required to move some substances across the cell membrane. This results in a loss of electrostatic potential and cellular swelling.

1) Atherosclerosis and thrombosis are the leading causes of myocardial infarction and stroke

6. Chemical injury

a. Many chemical agents can cause cellular injury

b. Examples of harmful chemicals include:

Discuss what effects are associated with lead poisoning and who is at risk for developing it.

1) Heavy metals (lead)

2) Carbon monoxide

3) Ethanol

4) Drugs

5) Complex toxins

c. Some chemicals injure cells directly (e.g., curare, cyanide)

1) Others are metabolized and yield a toxin that affects the cells (e.g., carbon tetrachloride [CCl4])

d. Injury begins with a biochemical interaction between a toxic substance and an integral part of the cellular structure

1) Some drugs and toxins (e.g., salicylate, some venoms) affect the cellular membrane

a) This interaction can damage the plasma membrane leading to:

(1) Increased permeability

(2) Cellular swelling

(3) Irreversible cellular injury

2) Others primarily affect the cytochrome system found in the mitochondria

a) Leads to a halt of oxidative metabolism

b) Example: carbon monoxide

3) Still others affect the genetic material (a primary target for chemotherapy medications)

7. Infectious injury

a. Virulence of microorganisms depends on their ability to survive and reproduce in the human body, where they injure cells and tissues

b. Disease-producing potential of microorganisms depends on their ability to:

1) Invade and destroy cells

2) Evade the defense of the organism

3) Produce toxins

4) Produce hypersensitivity reactions

c. Bacteria

1) Survival and growth of bacteria depend on:

a) Effectiveness of the body's defense mechanisms

b) Bacteria's ability to resist these mechanisms

2) Many bacteria that survive and proliferate in the body produce poisons or toxins (exotoxins and endotoxins) that can injure or destroy cells and tissues

3) Exotoxins

a) Toxins with highly specific effects

b) Produced by a microorganism and excreted into the medium surrounding it

c) Their effects are produced by their release as metabolic products during bacterial growth

d) Examples of exotoxins include those produced by:

(1) Several streptococci (causes sore throats and rheumatic fever)

(2) Clostridium botulinum (causes a particularly severe food poisoning

e) Toxoids are modified (harmless) toxins used as vaccines so that the body develops specific antibodies against them.

(1) The best-known toxoid is tetanus toxoid, made from tetanus toxin

4) Endotoxins

a) Contained in the cell walls of some bacteria

b) Are released when the walls disintegrate or during treatment with antibiotics

c) Do not stimulate strong antibodies

(1) Have been unable to develop vaccines

(2) Body uses the complement system to defend against endotoxins

d) Examples of bacteria that produce endotoxins:

(1) Gonococci (causes gonorrhea)

(2) Meningococci (causes meningitis)

e) Bacteria that produce endotoxins are also called pyrogenic bacteria because they not only activate the inflammatory process but also produce fever directly through the release of cell-membrane toxins

(1) Actions of the inflammatory process

(a) White blood cells are released from the bone marrow, causing increased white blood cell count

(b) Capillary permeability is increased, allowing substances that destroy bacteria to migrate from capillaries to the site of infection

(c) Fever is caused by the release of endogenous pyrogens (proteins that act on the thermoregulatory centers of the hypothalamus) from macrophages or circulating white blood cells attracted to the injury site

Discuss how antipyretics work to decrease fever.

(d) Life-threatening hypersensitivity reactions rarely occur

(e) If defense mechanisms fail and the microorganisms proliferate in the blood, bacteremia (septicemia) develops

d. Viruses

1) Responsible for many human diseases including:

a) Common cold

b) Influenza

c) Chickenpox (varicella)

d) Smallpox

e) Hepatitis

f) Herpes

g) Acquired immunodeficiency syndrome (AIDS)

h) Severe acute respiratory syndrome (SARS)

2) Are intracellular parasites that work very differently from bacteria

3) Lack much of the machinery that allows bacterial and other cells to grow rapidly and multiply

4) Can reproduce only by infecting the living cells of host tissue (often destroying the host cell)

5) Require nucleic acid, either DNA or RNA to replicate themselves

Viruses usually consist of a protein coat (capsid) that encloses a core of nucleic acid. They have no organelles and therefore have no metabolism. They do not produce endotoxins or exotoxins.

a) Unlike all other cellular forms of life, viruses never contain both DNA and RNA

6) Cells are thought to engulf the virus particles by surrounding them with part of the cell membrane

a) Once inside the cell, the virus loses it capsid and begins to replicate viral nucleic acids

7) Some viruses cause the cell to burst and others replicate without destroying the cell

a) The capsid allows the virus to resist phagocytosis, but often evokes a very strong immune response

8) Viruses can rapidly produce irreversible and lethal injury in susceptible hosts, immunosuppressed or not

Discuss why it is difficult to make drugs that effectively combat viruses.

a) Examples of viral illnesses that are highly infectious and associated with significant mortality and morbidity:

(1) Rabies

(2) Smallpox

(3) Influenza

9) Viral infections are easier to prevent than treat

10) Viral infections usually cause active illness, the signs and symptoms of which are based on the type and location of cells infected

a) Certain viruses tend to cause respiratory illness (such as influenza), whereas others cause gastroenteritis (enteroviruses), CNS disease (e.g., St. Louis B encephalitis, rabies), or liver disease (hepatitis)

11) Vaccines have been the best safeguards against viral disease

8. Immunological and inflammatory injury

a. Cellular membranes are injured by direct contact with cellular and chemical components of the immune and inflammatory responses

1) Phagocytic cells (e.g., monocytes, neutrophils, and macrophages)

2) Antibodies

3) Lymphokines

4) Complement

5) Proteases

b. If the cell membrane is injured or the transport mechanism (responsible for moving potassium into the cell and moving sodium out) begins to fail:

1) Intracellular water increases

a) Causes cellular swelling

b) If cellular swelling continues, the cell may eventually rupture

9. Injurious genetic factors

The term congenital refers to any abnormality that is present at birth, though it may not be detected until some time after birth.

a. Genetic disease results from:

1) Chromosomal abnormality

2) Defective gene

b. Genetic defects may:

1) Be inherited (as in sickle cell anemia)

2) Result from spontaneous mutations (e.g., Down syndrome)

c. Some genetic disorders can alter the cell's structure and function

1) Genetic disorders that cause alterations in the structural or metabolic component of the specific target cells:

a) Huntington's disease

b) Muscular dystrophy

10. Injurious nutritional imbalances

a. Cells require adequate amounts of essential nutrients to function normally

b. If required nutrients are not provided through diet and transported to cells (or if excessive amounts are consumed and transported to cells), pathophysiological cellular effects can occur

c. Examples:

1) Protein-calorie malnutrition

2) Obesity

3) Hyperglycemia

4) Scurvy

5) Rickets

11. Injurious physical agents

a. Many physical agents can injure cells and tissues

b. Examples of physical agents (including environmental agents) that can cause cellular or tissue injury:

1) Temperature extremes (hypothermic and hyperthermic injury)

2) Changes in atmospheric pressure (blast injury, decompression sickness)

3) Ionizing radiation (radiation injury)

4) Nonionizing radiation

5) Illumination (light injury, e.g., vision injury, skin cancer)

6) Mechanical stresses (e.g., noise-induced hearing loss, overuse syndromes)

C. Manifestations of cellular injury

1. An injured cell may exhibit various morphological (form and structure) abnormalities

2. Two most common changes:

a. Cell swelling

b. Fatty change

3. Cellular injury has both local and systemic manifestations

4. Cellular manifestations

a. Injured cells (and some healthy cells) experience cellular accumulations of substances such as:

1) Fluids and electrolytes

2) Triglycerides (lipids)

3) Glucose

4) Calcium

5) Uric acid

6) Protein

7) Melanin

8) Bilirubin

Define bilirubin.

b. These substances are normally present in certain cells of the body, but abnormal intracellular accumulations may lead to cellular damage

1) Injury may occur if injured cells are unable to rid themselves of excessive amounts of water, sodium, or calcium

2) If water, sodium, or calcium continues to accumulate, the cells will become irreversibly damaged

c. Some substances, such as lipids, also can accumulate in cells

d. Macrophages

1) Can ingest excessive extracellular lipids and cellular debris from injured cell

2) Some macrophages circulate throughout the body

3) Others remain fixed in tissues (such as the liver and spleen)

e. Phagocytes

1) Migrate to injured tissue and engulf dying cells and abnormal extracellular substances

2) As more phagocytes migrate to injured tissue to engulf the metabolites, the affected tissue begins to swell

3) It is phagocytosis by the fixed macrophages of the reticuloendothelial system that causes enlargement of the liver (hepatomegaly) or the spleen (splenomegaly) seen with many diseases associated with abnormal accumulation of various metabolic products (amyloidosis) or abnormal cells (hemolytic disease).

f. Cellular swelling

1) Swelling in injured cells results from membrane alterations associated with rapid leakage of potassium out of the cell and the influx of sodium and water

a) The increase in intracellular sodium:

(1) Increases osmotic pressure

(2) Draws more water into the cell

b) If the swelling affects all of the cells in an organ, the organ increases in weight and becomes distended

2) Cellular swelling is usually reversible

g. Fatty change

Inflammation, whether due to infection, trauma, or autoimmune reactions, is associated with cellular swelling, often accompanied by fever.

1) Occurs if the enzyme systems that metabolize fat are impaired or overwhelmed

a) Leads to intracellular lipid accumulations

2) Commonly seen in liver cells (fatty liver) because liver cells are actively involved in fat metabolism

3) Hepatic metabolism and secretion of lipids are crucial to proper body function

a) Deficiencies in these processes lead to major pathologic changes

4) Alcohol abuse is a common cause of fatty liver, which usually is a precursor to cirrhosis

5. Systemic manifestations

a. Systemic manifestations associated with cellular injury include:

1) Fever

2) Malaise

3) Loss of well-being

4) Altered appetite

5) Altered heart rate

6) Leukocytosis

7) Pain

b. Cellular enzymes may be present in extracellular fluid from injured cells or tissue

D. Cellular death/necrosis

1. Cell death caused by irreparable damage

a. Structural changes begin to occur within the nucleus and cytoplasm shortly after cell death

b. Membrane of the lyosome (a sac of digestive enzymes found in many cells) begins to break down; releases lysosomal enzymes that begin to digest the cell

c. Nucleus shrinks and dissolves or breaks into fragments

2. Necrosis

a. Death of cells or tissues resulting from injury, disease, or cellular self-destruction (autolysis)

b. Different types of necrosis tend to occur in different organs or tissues

1) Site of necrosis may indicate the cause of cellular injury

c. Necrotic changes take several hours to develop

1) Are easily recognized on histological examination by their structure and staining characteristics

II. GENETICS AND FAMILIAL DISEASES

A. Overview

1. People are born with a genetic predisposition to the development of certain diseases

a. Genetics of some diseases is well understood (e.g., hemophilia, sickle cell anemia)

2. Patients either have no genetic predisposition, are carriers of the disease, or have the disease

3. Other disease processes (e.g., arthritis, diabetes, and hypertension) are linked to genetics, but are also strongly associated with environmental factors

B. Factors causing disease

1. Factors that cause disease may be classified as genetic or environmental

a. Strong interaction between the two

1) Genes cannot exert their effects without an environment in which to operate

2) Environmental factors act differently on different people

3) Conversely, the environment may be the same, but people have unique genetic makeups

b. Interaction between genetics and environment is very complex

2. Genetic

a. Heredity is governed by the laws of chance and probability because each pair of chromosomes is sorted at random when packaged into eggs and sperm

b. Genetic diseases can arise from:

1) Individual genetic changes

2) Entire chromosomal abnormalities

c. Mistakes are sometimes made when chromosomes are packaged, resulting in chromosomes that are rearranged

1) Examples of diseases resulting from entire chromosomal abnormalities:

a) Down syndrome

b) Turner's syndrome

d. More commonly, a single gene on the chromosome is passed on, resulting in an abnormal protein

1) This type of genetic defect is responsible for sickle cell anemia and hemophilia

e. Some conditions are polygenic and multifactional, but with a strong inherited component

1) Coronary artery disease (CAD)

2) Hypertension

3) Cancer

3. Environmental

Genes are not entirely unchangeable units of inheritance. They can sometimes change or be changed by environmental influences.

a. Many common chronic diseases occur because of a mismatch between genetic and environmental factors

b. Important environmental factors include:

1) Microorganisms and immunological exposures

2) Personal habits and lifestyle

3) Chemical substances

4) Physical environment

5) Psychosocial environment

4. Age and gender

The goal in preventing disease is to identify the genetic and environmental influences that lead to major diseases. This knowledge will help people with specific susceptibilities to modify environmental factors, decreasing their risk of developing illness.

a. Play a major role in the occurrence of familial (hereditary) diseases

1) Particularly true for diseases that are not due to a single genetic defect

b. In the polygenic disorders, there are cumulative effects of genes and environment over time that lead to diseases associated with age-related changes in metabolism

1) May explain why heart disease, hypertension, and cancer are more common in people over age 40 than in those who are younger

c. Gender is associated with sex-specific diseases from hormonal and anatomical differences

1) Examples

a) Breast cancer in women

b) Testicular cancer in men

d. Lifestyle and environmental differences in gender-related activities may also be responsible for a predisposition to some diseases

1) One example is a higher rate of lung cancer and coronary artery disease in men who smoke cigarettes

C. Analyzing disease risk

Epidemiologists use disease rates and risk factor analysis. Rates help describe the occurrence of disease. Risk factors are indicators of a person's predisposition to developing a disease.

1. Disease rates

a. Three commonly used statistics to assess societal impact of disease:

An example of a study using disease rates to evaluate coronary artery disease in American men aged 50 to 64 years showed an incidence rate of 2.2%, a prevalence rate of 9.7%, and an annual mortality rate of 0.92% in this population.

1) Incidence rate: the number of new cases detected during a given period (usually 1 year) per number of people in a population surveyed

2) Prevalence rate: the number of people living with the disease per number of people in the population

3) Mortality rate: the number of people who have died of the disease during an interval (often 1 year) per number of people in the surveyed population

2. Risk factor analysis

a. The presence of particular risk factors in any group of individuals is associated with an increased disease rate in that group

b. Risk factors

1) Causal risk factors: risk factors that, when removed or eliminated, will result in the delay or prevention of the disease

2) Noncausal risk factors: helpful in predicting a person's chances of developing the disease but do not affect the underlying cause of the disease

D. Combined effects and interactions among risk factors

1. When one or more risk factors interact, the individual effects of risk factors may be greatly magnified

Risk factors cannot precisely predict whether a person will develop a disease, but they can provide clues about the probability of developing disease.

a. One risk factor alone may present almost no risk for disease, but in the presence of another factor, the risk increases substantially

2. Familial disease tendency

a. Family members (siblings, parents with offspring, spouse pairs, twins) are sometimes predisposed to develop certain diseases more often than individuals of the general population

1) Familial risk factors are often genetic or shared environmental factors

b. Examples include heart disease and pulmonary disease that result from choices in such things as smoking and consumption of dietary fat

3. Aging and age-related disorders

a. Increased age is a risk factor for many diseases (e.g., heart attack, stroke, cancer)

b. Probably represents the cumulative effects of genetics and environmental factors

c. Some age-related disorders occur throughout life

d. Some disorders are more common in specific age groups

1) Dental cavities and strep throat are more common in younger age groups

2) Degenerative disorders (e.g., arthritis) are more common in older age groups

E. Common familial diseases and associated risk factors

1. High-risk individuals can take steps to avoid many familial diseases

a. Examples

1) Coronary heart disease

2) Colorectal cancer

2. Table 7-7 lists some known familial diseases and environmental factors that might play a role in causing and eventually preventing the development of disease

III. HYPOPERFUSION

(1 question on exam) The term hypoperfusion is used to describe inadequate circulation of blood and nutrients to tissues. Hypoperfusion can result from many medical and traumatic conditions.

A. Pathogenesis

1. Hypoperfusion is often the result of decreased cardiac output

a. If prolonged, decreased cardiac output leads to:

1) Shock (a continued state of hypoperfusion)

2) Multiple organ dysfunction syndrome (MODS)

3) Other disease states associated with impaired cellular metabolism

2. Decreased cardiac output

a. Cardiac output

1) The total amount of blood pumped by the ventricles per minute

2) Determined by multiplying the heart rate by the volume of blood ejected by the ventricles during each beat (stroke volume)

For example, if the ventricle contracts 72 times per minute and ejects 42 mL of blood with each contraction, the cardiac output would be 72 beats per minute multiplied by 42 mL per beat, or 3.02 LPM.

a) Cardiac output = stroke volume Î heart rate (CO = SV Î HR)

b) Usually expressed in liters per minute (LPM)

3) A crucial determinant of organ perfusion

4) Depends on several factors:

a) Strength of contraction

b) Rate of contraction

c) Amount of venous return (preload)

5) Decreased cardiac output is usually associated with a decrease in:

Describe how blood pressure can affect cardiac output.

a) Blood pressure

b) Tissue perfusion

c) Impaired cellular metabolism

3. Compensatory mechanisms

a. Compensatory mechanisms used by the body to manage blood pressure and cardiac output include many negative feedback mechanisms (any mechanism that tends to balance a change in a system)

b. Negative feedback mechanisms important in maintaining cardiac output and tissue perfusion:

1) Baroreceptor reflexes

2) Chemoreceptor reflexes

3) Central nervous system ischemic response

4) Hormonal mechanisms

5) Reabsorption of tissue fluids

6) Splenic discharge of stored blood (seen in animals, but minimal in humans)

c. Baroreceptor reflexes (1 question on exam)

1) Baroreceptor reflexes help maintain blood pressure by two negative feedback mechanisms:

a) By lowering blood pressure in response to increased arterial pressure

b) By increasing blood pressure in response to decreased arterial pressure

2) Normal blood pressure partially stretches the arterial walls so that baroreceptors produce a constant, low-frequency stimulation

Describe "normal" blood pressure for various age groups.

a) Stimulation increases progressively from a lower pressure limit of 60 mm Hg, reaching a maximum at 180 to 200 mm Hg

3) When blood pressure increases, impulses from baroreceptors travel through the vagus and Herring's nerve to the glossopharyngeal nerve where they inhibit the vasoconstrictor center of the medulla and excite the vagal center

a) Results in vasodilation in the peripheral circulatory system and a decrease in heart rate and force of contraction

(1) Combined effect is a decrease in arterial pressure

4) Baroreceptors adapt in 1 to 3 days to the ambient pressure in the immediate locale; therefore, the baroreceptors are not responsible for modulating the average blood pressure on a long-term basis

5) Baroreceptors are not stimulated by pressures between 0 and 60 mm Hg

6) When baroreceptor stimulation ceases due to a fall in arterial pressure, several cardiovascular responses are evoked

a) Vagal (parasympathetic) stimulation reduces and sympathetic response increases

Teaching Tip

The vasoconstriction in these peripheral vascular beds results in the characteristic pale, cool skin of patients suffering from hypovolemic shock.

b) Increase in sympathetic impulses results in increased peripheral vascular resistance (PVR) and an increase in heart rate and stroke volume

Peripheral vascular resistance is the resistance to blood flow in the systemic circulation (small arteries, arterioles, venules, veins). Afterload (the systemic vascular resistance on the left side of the heart) is the pressure against which the ventricle has to contract to eject its contents.

(1) Sympathetic discharges also produce generalized arteriolar vasoconstriction, which decreases the size of the vascular compartment (container size)

c) Constricting capacitance vessels shift blood into the central circulation

(1) This, coupled with the constriction of blood vessels in skin, muscles, and viscera, helps maintain perfusion of the central organs

d. Chemoreceptor reflexes (2 question on exam)

1) Low arterial pressure (that leads to hypoxemia or acidosis) may also stimulate peripheral chemoreceptor cells that lie within the carotid and aortic bodies, which have an abundant blood supply

2) When oxygen or pH decreases, these chemoreceptor cells stimulate the vasomotor center of the medulla, and rate and depth of ventilation are also increased to help eliminate excess carbon dioxide and maintain acid-base balance

3) Chemoreceptors are more involved in regulation of respiration than in cardiovascular effects; however, during profound hypotension or acidosis, they can and do lead to vasoconstriction

4) Vasomotor stimulation results in enhanced peripheral vasoconstriction, which is initiated by the baroreceptors

e. Central nervous system ischemic response

1) When blood flow to the vasomotor center of the medulla is decreased enough to cause ischemia, the neurons in the vasomotor center become excited, raising arterial pressure

2) The degree of sympathetic vasoconstriction can be so intense that it elevates arterial pressure for as long as 10 minutes, sometimes to above 200 mm Hg

a) If the ischemia lasts longer than a few minutes, the vagal centers are activated, resulting in vasodilation in the periphery and bradycardia

3) Like the chemoreceptor reflex, the cerbral ischemia response functions only in emergencies

a) Does not become active until blood pressure falls below 50 mm Hg

f. Hormonal mechanisms

1) Adrenal medullary mechanism

a) When sympathetic stimulation of the heart and blood vessels increases, stimulation of the adrenal medulla also increases

b) The hormones secreted by the adrenal medulla (epinephrine and norepinephrine) affect the cardiovascular system in a way similar to the sympathetic nervous system

This response is sustained longer than the sympathetic response.

(1) Increase in heart rate, stroke volume, and vasoconstriction

2) Renin-angiotensin-aldosterone mechanism

a) Renin is an enzyme released by the kidneys into the circulatory system

b) Renin acts on a plasma protein called angiotensinogen by altering the structure to produce angiotensin I

c) Angiotensin I is in turn cleaved by angiotensin-converting enzyme (mostly in the lungs) to angiotensin II (active angiotensin)

(1 question on exam) Angiotensin-converting enzyme (ACE) inhibitors are medications that block the conversion of the precursor angiotensin I to the active molecule angiotensin II, thereby lowering blood pressure and putting less stress on the heart. Examples of ACE inhibitors include captopril (Capoten), enalapril (Vasotec), and lisinopril (Prinivil).

3) Angiotensin II causes vasocontriction in arterioles and to a lesser degree in veins, resulting in:

a) Increased peripheral resistance

b) Increased venous return to the heart

c) Resultant increase in blood pressure

4) Angiotension II also stimulates the release of aldosterone, which acts on the kidneys to conserve sodium and water

5) This mechanism is an important regulatory loop to increase blood pressure during circulatory shock

6) Requires approximately 20 minutes to become effective in hypovolemia caused by hypovolemic and hemorrhagic shock

a) Remains effective for approximately 1 hour

g. Vasopressin mechanism

1) When blood pressure drops or the concentration of solutes in the plasma increase (increased serum osmolality), neurons of the hypothalamus are stimulated

a) Causes the anterior pituitary to increase secretion of vasopressin or antidiuretic hormone (ADH)

b) ADH acts directly on blood vessels and causes vasoconstriction within minutes after a rapid fall in blood pressure

2) ADH also decreases the rate or urine production (by enhancing reabsorption of water), helping to maintain blood volume and blood pressure

3) Atrial natriuretic factor, a substance released by the atrial cells of the heart, also controls arterial pressure through negative feedback

a) Its release is initiated by elevated atrial pressure (usually a sign of volume overload)

b) Increases the rate of urine production

c) Water loss through urine decreases blood volume, thus decreasing atrial pressure

Explain why excessive urination has an effect on blood volume.

h. Reabsorption of tissue fluids

1) Arterial hypotension, arteriolar constriction, and reduced venous pressure during hypovolemia lower blood pressure in the capillaries (hydrostatic pressure)

2) The decrease promotes reabsorption of interstitial fluid into the vascular compartment

a) Considerable quantities of fluid may be drawn into the circulation during hemorrhage

(1) Approximately 0.25 mL/min/kg of body weight (1 L/hr in the adult male) can be autotransfused from the interstitial spaces after acute blood loss

i. Splenic discharge of blood

1) Some blood that circulates through the spleen continues through the microcirculation and is stored in the venous sinuses

a) Venous sinuses can store more than 300 mL of blood

2) Sudden reductions in blood pressure cause the sympathetic nervous system to stimulate constriction of these sinuses

a) Constriction can expel as much as 200 mL of this blood into the venous circulation, which helps restore circulatory blood volume or pressure

B. Types of shock (1 question on exam)

Increased preload or afterload or decreased stroke volume can lead to volume overload and pulmonary edema, which can also decrease tissue perfusion and impair cellular metabolism.

1. Shock, also referred to as hypoperfusion, can be classified based on the primary cause
   a. Although these classifications are separate and distinct, two or more types may be combined
   b. Whatever the classification, the underlying defect in shock is inadequate tissue perfusion
2. Hypovolemic shock: occurs because of a loss of circulating volume
   a. Most frequently due to hemorrhage
   b. May also be caused by severe dehydration
3. Cardiogenic shock results when cardiac action cannot deliver adequate circulation for tissue perfusion
4. Neurogenic shock results most often from spinal cord injury with resultant loss of sympathetic vasomotor tone
5. Anaphylactic shock occurs when the body is exposed to a substance that produces a severe allergic reaction
6. Septic shock most often results from a serious systemic bacterial infection

C. Multiple organ dysfunction syndrome (MODS)

1. MODS is a relatively new diagnosis first described in 1975
   a. It is the progressive failure of two or more organ systems after a very severe illness or injury
   b. Mortality rate is 60% to 90%, and it approaches 100% when three or more organs are involved, sepsis is present, and the patient is more than 65 years of age
2. Causes
   a. Common causes include sepsis and septic shock
   b. It may follow any period of prolonged shock, no matter the cause
3. Pathophysiology
   a. Any process that triggers the body's inflammatory response has the potential to initiate MODS including

Discuss the circumstances in which the paramedic is likely to care for a patient who has MODS.

1) Trauma
2) Sepsis
3) Burn injury

Describe how burn trauma initiates the inflammatory response.

b. The syndrome begins with vascular endothelial damage that results from endotoxins and inflammatory mediators released into the circulation

1) When this occurs, the vascular endothelium becomes permeable—allows fluid and cells to leak into the interstitial spaces

a) Contributes to hypotension and hypoperfusion

2) The release of mediators activates three major plasma enzyme cascades:

a) Complement

b) Coagulation

c) Kallikrein/kinin

3) The plasma protein cascade systems are responsible for mediating the inflammatory response

a) Each system consists of a series of inactive enzymes (proenzymes) converted to active enzymes, thereby initiating a cascade in which the substrate of the activated enzyme is the next component of the system

4) Complement

a) Activates phagocytes

b) Induces further inflammation and damage to the endothelium

5) Coagulation

a) Because of the endothelial damage, coagulation becomes uncontrolled

b) Results in microvascular thrombus formation and tissue ischemia

6) Kallikrein/kinin

a) Activation of the kallikrein/kinin system releases bradykinin (a potent vasodilator)

b) Contributes to low systemic vascular resistance

c. The overall effect of these three systems is a hyperinflammatory and hypercoagulable state that leads to:

1) Edema formation

2) Cardiovascular instability (hypotension)

3) Clotting abnormalities

d. These inflammatory processes cause maldistribution of systemic and organ blood flow

1) Results in a hyperdynamic circulation with increased venous return

2) A decrease in oxygen delivery to the tissues occurs because of:

a) Shunting of blood past selected regional capillary beds

b) Formation of interstitial edema from changes in permeability

3) Capillary obstruction occurs from:

a) Microvascular thrombi

b) Aggregation of inflammatory cells

4) Resultant ischemia contributes to MODS

4. Alterations in carbohydrate, fat, and lipid metabolism

a. The same hormonal responses that help conserve volume in shock also cause the body to enter a hypermetabolic (catabolic) state, altering carbohydrate, fat, and lipid metabolism to meet the increased demand for energy

1) Over time, sympathetic drive and hyperdynamic circulation place excessive demands on the heart

2) Net result is depletion of oxygen and fuel supplies

5. Imbalance in oxygen supply and demand

a. Occurs because of:

1) Decrease in oxygen delivery to the cells

2) Hypermetabolism—associated myocardial depression

6. Tissue hypoxia with cellular acidosis and impaired cellular function

a. Occurs soon after imbalance in oxygen supply and demand, and multiple organ failure results

7. Clinical presentation of MODS occurs 24 hours after initial resuscitation

a. Low-grade fever resulting from inflammatory response

b. Tachycardia

c. Dyspnea and adult respiratory distress syndrome (ARDS)

d. Altered mental status

e. Hyperdynamic state

f. Hypermetabolic states

g. Renal and liver failure (14-21 days)

h. Gastrointestinal and immune collapse (14-21 days)

i. Cardiovascular collapse and death (21-28 days)

8. Treatment

a. No specific therapy for MODS

b. Early detection is critical so that supportive measures can be initiated immediately

D. Cellular metabolism impairment

1. Nearly all cell activities require energy

2. The cell membrane requires most of the cell's energy production to maintain normal fluid and electrolyte composition within the cell

3. Adenosine triphosphate (ATP) and other high-energy phosphate molecules provide fuel for the cell

a. Most metabolism in healthy people is accomplished through aerobic metabolism

b. Anaerobic metabolism occurs in the absence of oxygen

1) Can provide only a small fraction of the energy produced by aerobic metabolism

2) Cannot meet the body's energy requirements alone

4. Glucose

Anaerobic metabolism is inefficient and produces lactic acid.

a. An important fuel for producing energy

b. Essentially the only fuel that can be used anaerobically under conditions of cellular hypoxia (as in shock)

c. During conditions of cellular hypoxia

1) Glucose is metabolized to lactate and pyruvate, producing a net sum of two ATP molecules

2) If oxygen is present (aerobic metabolism), pyruvate enters the Krebs cycle

a) A sequence of reactions that breaks down a molecule of pyruvic acid into molecules or carbon dioxide and water

b) Is 18 times more efficient in producing ATP than glycolysis (the breakdown of glucose to lactate)

c) Cannot occur without oxygen

d. Because anaerobic ATP production is so inefficient, the rate of glycolysis must be greatly increased to meet energy requirements

1) Leads to an increased production of lactic acid and metabolic acidosis

e. As metabolites continue to accumulate, they stimulate vasodilation

1) Vasodilation opposes the constriction of precapillary sphincters and helps continue tissue perfusion by maintaining the proper container size

2) Postcapillary sphincters are more resistant to the vasodilatory effects of tissue metabolites and stay constricted long after capillary sphincters dilate

f. Capillary hydrostatic pressure increases

1) Causes a fluid loss from the vascular space into the interstitial space

g. Anaerobic metabolism affects the cell's ability to maintain a normal sodium-potassium differential across the cell membrane

Increased hydrostatic pressure "pushes" fluid out of the vascular space.

1) Intracellular potassium leaks into the extracellular space}

Teaching Tip

Consider reviewing the topic of net filtration with the class.

2) Sodium leaks into the cell

3) Alterations are produced in the membrane potential

h. Finally, the cells are irreversibly damaged

IV. SELF-DEFENSE MECHANISMS

A. Lines of defense against illness and injury

1. First line—external barriers

The body's first line of defense against pathogens includes mechanical barriers such as intact skin and intact mucous membranes. Helping the skin and mucous membranes with their defense function are their secretions, which are chemical barriers.

a. Skin

1) Skin secretions make the surface of the epidermis acidic (pH 3 to 5), inhibiting the growth of bacteria

b. Mucous membranes of the respiratory, digestive, and genitourinary (GU) tract

1) Reflexes such as coughing and sneezing help remove pathogens from the respiratory tract. Nasal hairs, mucus, and cilia also work together to filter, trap, and propel pathogens from the respiratory tract.

2) Gastric juices contain hydrochloric acid and enzymes that destroy pathogens in the stomach. Vomiting and diarrhea also help rid the gastrointestinal (GI) tract of pathogens.

c. Surfaces form a continuous closed barrier between the internal organs and the environment

2. Second-line—inflammatory response

a. Involves the processes of phagocytosis, inflammation, fever, and protective proteins

3. Third-line—immune response

a. Mediated by lymphocytes

B. Inflammatory response

1. Inflammation is a local reaction to cellular injury

Teaching Tip

The inflammatory response begins within seconds of injury or invasion.

2. Can be initiated by physical, thermal, or chemical damage or by microbial infection

3. Is activated when invasion occurs to prevent further invasion of the pathogen by isolating, destroying, or neutralizing the microorganism

4. Is usually protective and beneficial

a. However, if the response is sustained or directed toward the host's own antigens, healthy tissue may be destroyed

5. Stages of the inflammatory response

An antigen is a substance that can be recognized as "foreign material" by the antibody system and bound by specific antibodies (protective protein substances developed by the body for this purpose). Specific antibodies bind to specific antigens when the two fit together. The attachment of antibodies facilitates antigen neutralization and removal from the body.

a. Cellular response to injury

1) Metabolic changes occur with any type of cellular injury

2) Most common primary effect of injury on the cell's aerobic respiration and ATP-generating process (oxidative phosphorylation) leads to decreasing energy reserves

3) When energy sources are depleted:

a) Sodium-potassium pump no longer functions effectively

b) Cell swells because of the accumulation of sodium ions

(1) Organelles within the cell also swell

c) This swelling, along with increasing acidosis, leads to:

(1) Further impairment of enzyme function

(2) Further deterioration in the integrity of membranes

4) Membranes of the cellular organelles begin to leak

5) Lysosomes release hydrolytic enzymes

a) Contributes to cellular destruction and autolysis

6) As the cellular contents are dissolved by enzymes, the inflammatory response is stimulated in surrounding tissues

b. Vascular response to injury

1) After cellular injury, localized hyperemia develops as the surrounding arterioles, venules, and capillaries dilate

2) The associated increase in filtration pressure and capillary permeability causes fluid to leak from the vessels into the interstitial space—produces edema

Teaching Tip

The vascular effects of inflammation are immediate, occurring in seconds.

3) Leukocytes (particularly neutrophils and monocytes):

a) Begin to collect along the vascular endothelium

Teaching Tip

During the inflammatory response, the bone marrow is stimulated to produce and release many neutrophils.

b) Eventually migrate to injured tissue because of release of chemotactic factors

c. Phagocytosis

Teaching Tip

Bacterial products interact with plasma factors and cells to produce agents that attract neutrophils to the invaded area. This process is called chemotaxis.

1) The process by which leukocytes engulf, digest, and destroy pathogens

Teaching Tip

As phagocytes work to engulf, digest, and destroy pathogens, they release pyrogens (fever-producing substances). Pyrogens stimulate the hypothalamus to reset the body's temperature, resulting in a fever. It is thought that a mild or moderate elevation in temperature is beneficial because it decreases the ability of some pathogens to multiply and speeds up the repair process by increasing the metabolic rate of tissue cells.

a) Circulating macrophages are also responsible for clearing the injured area of dead cells and other debris

2) Intracellular phagocytosis (ingestion of bacteria and dead cell fragments):

a) Occurs at the site of tissue invasion

b) May extend into the general circulation if the infection becomes systemic

c) Stimulates the release of chemicals that induce lysis of leukocytes

(1) These leukocytes combine with dead organisms and fluid to form an inflammatory exudate (pus)

Teaching Tip

Pus is a mixture of dead or dying leukocytes, broken-down tissue cells, living and dead pathogens, and tissue fluid. If the phagocytes are unable to remove debris from the area completely, the sac of pus may become walled off, forming an abscess.

6. Mast cells (1 question on exam)

a. Specialized cells that are widely distributed throughout connective tissues

b. The cytoplasm of mast cells is filled with granules containing:

1) Vasoactive amines (e.g., histamine, serotonin)

2) Chemotactic factors

c. When tissue is injured, mast cells discharge their granules (degranulation)

1) This process is stimulated by:

a) Physical injury (e.g., thermal or mechanical trauma)

b) Chemical agents (e.g., toxins, snake and bee venom)

c) Hypersensitivity reactions

d) As a direct result of complement components

7. Local and systemic response to acute inflammation

a. Acute inflammation may be characterized by both local and systemic effects

b. Local responses

1) Vascular changes (vasodilation and increased vascular permeability)

2) Formation of exudates

3) Characteristic signs of localized inflammation:

a) Heat

b) Redness

c) Swelling

d) Pain/tenderness

c. Systemic responses

Teaching Tip

The redness, swelling, and heat associated with localized inflammation care caused by local vasodilation, the leakage of fluid into the extravascular space, and blockage of lymphatic drainage. Pain occurs because of swelling and pressure and because of chemical irritation of pain receptors.

1) Fever

2) Leukocytosis

3) Increase in circulating plasma proteins

8. Chronic inflammation responses

a. Chronic inflammation

1) Inflammation lasting 2 weeks or longer

2) Can result from an unsuccessful acute inflammatory response resulting from:

a) Bacterial contamination by a foreign body (e.g., wood splinter, glass)

b) Persistent infection

c) Continued exposure to an antigen

b. If the inflammatory process is severe or prolonged, the body will attempt to repair or replace damaged tissue

1) This tissue repair occurs as cells produce connective tissue fibers and new blood vessels

2) If the area of tissue destruction is large, scar tissue will be formed

C. Immune response

Teaching Tip

The inflammatory response differs from the immune response. The inflammatory response is nonspecific and occurs about the same way each time after exposure to the same stimulus. The immune response has memory and is specific to individual pathogens (antigen-specific).

Teaching Tip

The immune response occurs much more slowly than the inflammatory response.

1. Types of immunity

   a. Natural (native)

      1) Present at birth

      2) Not produced by the immune response

   b. Acquired

      1) Gained after birth from exposure to a specific antigenic agent or pathogen

2. Acquired immunity

   a. Includes that resulting from inoculation (immunization) against certain infectious diseases (e.g., measles)

   b. Further classified as:

      1) Humoral immunity: associated with the production of antibodies that combine with and eliminate foreign material

      2) Cell-mediated immunity

Teaching Tip

Humoral immunity, also called antibody-mediated immunity, is provided by antibodies present in the body's "humors," or fluids.

a) Body's best defense against viruses, fungi, parasites, and some bacteria

b) Responsible for the body rejecting transplanted organs

c) Characterized by the formation of a population of lymphocytes that attack and destroy foreign material

3. Age and the immune response

Teaching Tip

Cell-mediated immunity is also called cellular immunity because the protective factor is living cells.

   a. Immune response is affected by age

   b. Most infants are born with enough natural immunity from disease to protect them until they have made their own antibodies

   c. Cells of the immune system become less efficient with age, and older people become more susceptible to diseases

d. The aging immune system also becomes less able to eliminated abnormal cells that may arise within the body

4. Induction of the immune response

a. An antigen is a substance (molecule or molecular complex) that reacts with preformed components of the immune system (e.g., lymphocytes and antibodies)

1) An immunogen is an antigen that can also induce the formation of antibodies

2) Therefore, some antigens are not able to induce the immune response

b. To be immunogenic, the antigen molecule must be:

1) Sufficiently foreign to the host

2) Sufficiently large

3) Sufficiently complex

4) Present in sufficient amounts

c. The immune response is triggered after foreign materials have been cleared from the area of inflammation

1) After phagocytes digest the pathogens, antigenic material appears on their surface

2) When the antigen is recognized by receptors on lymphocytes as foreign or "nonself," a chain of events begins to destroy or neutralize the antigen

a) This involves lymphocytes maturing into either:

(1) B lymphocytes that produce antibodies

Teaching Tip

B lymphocytes (B cells) originate in the bone marrow and mature into plasma cells. These plasma cells produce antibodies that destroy bacteria and viruses, preventing them from entering host cells. B cells are ultimately responsible for humoral immunity.

(2) T lymphocytes that are sensitized lymphocytes capable of interacting directly with the foreign antigen

Teaching Tip

T lymphocytes (T cells) attack the antigen directly. B cells produce antibodies that incapacitate the antigen. T cells are responsible for cell-mediated immunity.

Teaching Tip

Immune tolerance refers to the immune system's ability to allow self-antigens (versus nonself antigens) to exist by preventing their recognition by lymphocytes and antibodies.

5. Blood group antigens

a. When combined with foreign plasma, red blood cells either clump together (agglutinate) or do not

1) Two distinct agglutinins (substances on red blood cells acting as antigens) are responsible for this clumping

b. Based on possible combinations of these antigens, four types of human blood have been identified: A, B, AB, and O

c. Type A blood has anti-B antibodies in the plasma and will clump type B blood

d. Type B blood has anti-A antibodies and will clump type A blood

Teaching Tip

People with blood type A carry the A antigen on the red blood cells. People with blood type B carry the B antigen. Those with blood type AB carry both antigens and those with type O carry neither antigen.

e. Type AB blood has neither antibody and can receive any of the four types of blood (universal recipient)

f. Type O blood has both anti-A and anti-B antibodies, so it cannot receive any type of blood other than Type O

Ask the students what their blood types are—you may be surprised by how many don't know.

1) Type O blood has neither antigen, however, and can therefore be given to patients with any blood type

2) Type O blood is called the universal donor

g. Rh factor

1) Rh factor refers to the presence or absence of the Rh antigen on the surface of red blood cells

2) A person with the factor is Rh-positive; a person without it is Rh-negative

3) Antibodies to the Rh factor are acquired through exposure to Rh-positive blood

4) About 85% of Americans have Rh-positive blood

5) Percentages in the population of ABO and Rh blood groups:

O positive	38.4%
B positive	9.4%
O negative	7.7%

B negative	1.7%
A positive	32.3%
AB positive	3.2%
A negative	6.5%
AB negative	0.7%

V. VARIANCES IN IMMUNITY AND INFLAMMATION

A. Hypersensitivity: allergy, autoimmunity, and isoimmunity

1. Hypersensitivity

Ask the class to compare hypersensitivity to a “friendly fire” incident in wartime.

a. An altered immunologic reactivity to an antigen that results in a pathologic immune response after reexposure

b. These abnormal responses include:

1) Allergy: an exaggerated immune response to environmental allergens (1 question on exam)

a) Most common hypersensitivity reaction

b) Least life-threatening hypersensitivity reaction

2) Autoimmunity: an immune response against the host’s own cells (self-antigens)

3) Isoimmunity: an immune response directed against beneficial foreign tissues (e.g., blood transfusions and transplanted organs)

2. Mechanisms of hypersensitivity

a. Immediate hypersensitivity reactions

1) Associated with the presence of antibodies in the serum that with reexposure lead to an antigen-antibody reaction

2) Mild reactions associated with immediate hypersensitivity include itching and hives

3) Severe reactions may include life-threatening respiratory distress and anaphylaxis

b. Delayed hypersensitivity reactions

1) Products of cell-mediated immunity by which the body develops hypersensitivity after exposure to a foreign antigen from bacteria, parasites, or other microorganisms

2) Can take from several hours up to 1 to 2 days to appear

3) Are at maximum severity days after reexposure to the antigen

4) Examples

a) Response against grafted tissue

b) Poison ivy

c. IgE reactions

1) Antibodies, or immunoglobulins (Ig), are produced by plasma cells in response to antigenic stimulation

2) Five classes of immunoglobulins are produced in humans

a) IgG

(1) Accounts for 70% to 75% of antibodies in normal serum

(2) Most abundant in blood but is also found in lymph, cerebrospinal, synovial, and periotoneal fluid and breast milk

(3) Major antibody involved in secondary immune responses and the only antitoxin antibody developed

(4) IgG is also the only immunoglobulin that crosses the placenta, providing temporary immunity in neonates

b) IgM

(1) Accounts for approximately 5% to 10% of antibodies in normal serum and is the dominant antibody in ABO incompatibilities

(2) Triggers the increased production of IgG in acute infections and the complement fixation required for an effective antibody response

c) IgA

(1) Accounts for approximately 15% of antibodies in normal serum

(2) Found in blood, secretions such as tears and saliva, and the respiratory tract, stomach, and accessory organs

(3) Combines with a protein in the mucosa and defends body surfaces against invading microorganisms

d) IgD

(1) Accounts for less than 1% of antibodies in normal serum

(2) Its precise biological function is unknown

e) IgE

(1) Accounts for less than 1% of antibodies in normal serum

(2) Found in some tissues and on the surface membranes of basophils and mast cells

(3) Responsible for immediate (type I) hypersensitivity reactions

(a) When an antigen reacts with an IgE molecule bound to a mast cell or circulating basophil, these cells promptly release a host of chemical mediators into the extracellular space

(b) Target organs and the manifestations of the reaction vary from hives to hay fever to asthma to life-threatening anaphylaxis

B. Immunity and inflammation deficiencies

Hypersensitivity reactions are divided into four distinct types: type I (IgE-mediated allergic reactions), type II (tissue-specific reactions), type III (immune-complex-mediated reactions), and type IV (cell-mediated reactions).

1. Deficiencies in immunity and inflammation refer to the failure of these mechanisms of self-defense to function at their normal capacity

a. The source of the deficiency may be:

1) Congenital, which means it was caused by an anomaly present at birth

2) Acquired, which means it may have been caused by any of the following:

a) Infection (e.g., the human immunodeficiency virus [HIV])

b) Cancer (e.g., leukemia)

c) Immunosuppressive drugs

d) Aging

b. Whether congenital or acquired, the cause of the deficiency is usually the disruption of lymphocyte function, although neutrophil dysfunction has also been described

2. Acquired deficiencies

a. Acquired immune deficiencies are far more common than congenital forms

b. They can be classified in the following groups:

1) Nutritional deficiencies (e.g., severe deficits in calorie or protein intake)

2) Iatrogenic deficiencies (caused by some form of medical treatment)

3) Deficiencies caused by trauma (e.g., bacterial infection, burns)

4) Deficiencies caused by stress (depressed immune function)

5) Acquired immunodeficiency syndrome (AIDS)

VI. STRESS AND DISEASE

A. Neuroendocrine regulation of stress

1. The sympathetic nervous system is activated during the stress response

a. Causes the adrenal gland to release catecholamines (epinephrine, norepinephrine, and dopamine) into the bloodstream

b. Simultaneously, the hypothalamus stimulated the pituitary gland to release hormones:

1) ADH

2) Prolactin

3) Growth hormone

4) ACTH

c. ACTH stimulated the cortex of the adrenal gland to release cortisol

2. Catecholamines

a. Catecholamines act by stimulating two major classes of receptors:

1) α-Adrenergic receptors

2) β-Adrenergic receptors

b. These two classes are further divided into two subclasses:

1) Alpha1 and alpha2

a) Alpha1 receptors (1 question on exam)

(1) Postsynaptic

(2) Located on the effector organs

(3) Primary role is to stimulate contraction of smooth muscle

b) Alpha2 receptors

(1) Found on presynaptic nerve endings

(2) Stimulation of alpha2 receptors inhibits the further release of norepinephrine in a negative feedback mechanism

2) Beta1 and beta2

a) Beta1 receptors (1 question on exam)

(1) Located primarily in the heart

b) Beta2 receptors (1 question on exam)

(1) Located predominantly in bronchiolar and arterial smooth muscle

(2) Stimulate the heart

(3) Dilate bronchioles

(4) Dilate blood vessels in the skeletal muscle, brain, and heart

(5) Aid in glycogenolysis

c. Epinephrine activates both alpha and beta receptors

d. Norepinephrine primarily excites alpha receptors

3. Cortisol (hydrocortisone)

a. Circulates in the plasma

b. Mobilizes substances needed for cellular metabolism

c. Primary metabolic effect is the stimulation of gluconeogenesis

d. Enhances the elevation of blood glucose by decreasing glucose use

e. Acts as an immunosuppressant

1) Causes lymphocyte reproduction to decrease, particularly the T-lymphocye population; this leads to decreased cellular immunity

2) Decreases migration of macrophages into the inflamed area

Compare the immune system to a spy movie:

1. What weapons are there?

2. Are there secret codes?

3. What other resources does it rely on?

3) Decreases phagocytosis, in part by stabilizing lysosomal membranes

a) Decrease in immune cell activity may be beneficial because it prevents immune-mediated tissue damage

f. Effects are adaptive or destructive depending on the type of stress event and the duration of exposure to the stressor

B. Role of the immune system

1. Many immunological conditions and diseases may be triggered by stress, although the exact mechanisms linking stress to these conditions are not clearly defined

2. It is believed, however, that the immune, nervous, and endocrine systems communicate through complex pathways and are potentially affected by factors involved in the stress reaction

C. Stress, coping, and illness interrelationship

1. Ill effects of stress are affected by:
    a. Nature, intensity, and duration of the stressors and by the individual’s perception of these factors
    b. Coping skills of the individual

2. It is important to:
    a. Recognize signs and symptoms of stress
    b. Incorporate stress management techniques to reduce the effects of the stressful event
        1) Meditation
        2) Imagery

3. In healthy people, these interventions will help avoid harmful physiological and psychological illness associated with stress

End of this outline!!!!