Human Physiology (Biology 4)
Lecture Notes

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Chapter 1 **Homeostasis**

- Anatomy
  - the study of body structure

- Physiology
  - the study of body function
    1. mechanistic approach
       a. explain how events occur
       b. e.g., you shiver because a drop in body T leads to signals for muscle contraction
    2. teleological approach
       a. explain how a function fills a need, "why"
       b. e.g., you shiver because you need to keep warm
    3. both approaches can be useful in understanding concepts

- Levels of Organization
  - Chemical level
    1. atoms and molecules

  - Cells
    1. the basic unit of living things
    2. humans are multicellular
    3. several basic functions of all cells
       a. obtain nutrients and O_2
       b. make usable energy, Food + $O_2 \rightarrow CO_2 + H_2O$ + energy
       c. eliminate wastes
       d. synthesize needed molecules
       e. respond to environmental changes
       f. control exchange of materials with the environment
       g. transport molecules
       h. reproduce
    4. in multicellular organisms, cells specialize

  - Tissues
    1. group of cells with similar structure and function
       a. plus extracellular material

2. 4 major types
    a. muscle
        (1) specialized for contraction and force generation
        (2) skeletal - movement of body or body parts
        (3) cardiac - pump blood
        (4) smooth - movement of organs
    b. epithelial
        (1) specialized for exchange between cell and environment
        (2) 2 general types - sheets and secretory glands
        (3) sheets are tightly joined cells covering or lining parts of the body
        (4) glands secrete products (exocrine glands have ducts leading to a body surface, e.g. sweat glands; endocrine glands release products to interstitial fluid and it goes into blood, e.g. adrenal glands)
    c. nervous
        (1) specialized for initiating and transmitting electrical impulses
        (2) brain, spinal cord, nerves
    d. connective
        (1) specialized for connecting and supporting
        (2) found all over body

- Organs
    1. group of two or more tissues designed to perform specific functions

- Body System (organ system)
    1. group of organs designed to perform particular functions

- Whole Organism
    1. group of organ systems

• Homeostasis
- a dynamic equilibrium where body conditions are maintained within narrow limits
    1. necessary for each cell to survive
    2. each cell contributes
    3. all cells are in contact with the aqueous (watery) internal environment, connects all cells, exchanges made
        a. outside cells, inside body

b. extracellular fluid

(1) plasma (fluid in the blood)

(2) interstitial fluid (surrounding cells)

- Major factors maintained

1. concentration of nutrient molecules
    a. cells need energy and building blocks
2. concentration of O_2 and CO_2
    a. O_2 used to make usable energy (ATP)
    b. CO_2 made must be removed
3. concentration of waste products
    a. become toxic at high levels
4. pH
    a. acidity affects enzyme reactions and nerve cell impulses
5. concentration of water, salt and other electrolytes
    a. maintaining cell volume
    b. various functions of electrolytes
6. temperature
    a. too cold or too much heat harmful to cells
7. volume and pressure
    a. blood must be at appropriate volume and pressure to be transported around the body

- 11 Major Organ Systems

- Control Mechanisms
  - body controlled mainly by nervous and endocrine systems
  - parts of a control system (all interdependent)
    1. sensor
        a. monitors variable (factor being regulated)
        b. responds to changes (stimuli) by sending input to...
    2. integrator
        a. determines set point (appropriate level of variable)
        b. compares set point to input
        c. sends response to...
    3. effector
        a. responds to changes

- most control systems operate using negative feedback
    1. decreases or shuts off original stimulus
    2. resists change
- positive feedback
    1. enhances original stimulus
    2. uterine contractions during childbirth
    3. blood clotting

Chapter 2 **Cell Physiology**

- Cell basics
  - typical human cell 10-20 μm in diameter
    (μm = micrometer, 1/1000 mm, 1/1,000,000 m)

  - most cells have 3 major subdivisions
    1. plasma membrane (cell membrane)
       a. defines inside/outside
       b. intracellular fluid (ICF) - inside cell
       c. extracellular fluid (ECF) - outside cell
       d. selectively permeable - controls movement of molecules between ICF and ECF
    2. nucleus
       a. usually near cell center
       b. double layered membrane
       c. contains DNA, "genetic blueprint," directs protein synthesis, control center of cell
    3. cytoplasm
       a. area between nucleus and plasma membrane
       b. contains organelles
          (1) separation of chemical reactions
          (2) specialized for a particular function
       c. cytosol is semiliquid, site of chemical reactions

- Organelles (see table Summary of Cytoplasm Components)
  - endoplasmic reticulum (ER)
    1. interconnected fluid-filled membranous system
    2. two types
       a. smooth - interconnected tubules
       b. rough - interconnected flattened sacs
          (1) has ribosomes which help in protein synthesis (cell also has "free" ribosomes)
    3. rough ER
       a. synthesizes proteins and lipids, releases them to ER lumen
          (1) some will be secreted from the cell (hormones, enzymes), some will become new membrane for the cell or its organelles, or other protein parts of organelles
          (2) once in the lumen the protein can be modified (pieces removed, sugars added)

4. smooth ER
    a. in most cells it packages and transports products of rough ER (sections pinch off and become transport vesicles, move to Golgi complex)
    b. some cells have extensive specialized smooth ER
        (1) lipid synthesis (steroid hormone secreting cells)
        (2) detoxify harmful substances (liver cells)
        (3) store calcium (muscle cells)

- Golgi complex
    1. layers of flattened membranous sacs (cisternae)
    2. processes ER products into final form
    3. sorts and sends products to appropriate place
        a. transport vesicles take products to locations in or outside cell, coating made up of proteins that recognize the product and its destination
        b. secretory vesicles transport products out of specialized cells, fuses with plasma membrane (secretion, exocytosis)

- lysosomes
    1. membranous sacs containing hydrolytic enzymes
    2. digest cellular debris and other substances (old organelles, bacteria)
        a. material from outside cell can be brought in to be digested by lysosome - endocytosis (membrane surrounds substance and vesicle pinches off)
            (1) pinocytosis - fluids, "cell drinking"
            (2) phagocytosis - large particles, "cell eating"
        b. cell can use digested material

- peroxisomes
    1. membranous sacs containing oxidative enzymes
        a. use oxygen to remove hydrogen from molecules (detoxify wastes and other chemicals like alcohol)

- mitochondria
    1. have double membrane
        a. inner membrane has folds called cristae (folds increase surface area)
        b. matrix is gel inside
    2. play a role in apoptosis (programmed cell death)

3. converts energy from food into usable energy for the cell - ATP (adenosine triphosphate)
    a. energy in chemical bonds of food molecules can't be used directly
    b. ATP → ADP +P_i + useful energy
4. three major steps in forming ATP (called cellular respiration)
    a. glycolysis
        (1) in cytosol
        (2) glucose → 2 pyruvic acid (a series of steps)
        (3) yields 2 ATP/glucose (not very efficient by itself)
        (4) attach H to carrier molecules
    b. citric acid cycle (also called Krebs cycle or tricarboxylic acid cycle)
        (1) pyruvic acid is transported to mitochondrial matrix
        (2) pyruvic acid → acetyl CoA
        (3) acetyl CoA enters citric acid cycle, which is a series of reactions
        (4) CO_2 is produced
        (5) hydrogen atoms are attached to carrier molecules (NAD^+, nicotinamide adenine dinucleotide; FAD, flavine adenine dinucleotide; become NADH and $FADH_2$)
        (6) 2 more ATP/original glucose
    c. electron transport chain/oxidative phosphorylation
        (1) occurs on inner mitochondrial membrane which contains electron carrier molecules (each H contains one electron, moving electrons means moving energy)
        (2) NADH and $FADH_2$ from glycolysis and citric acid cycle enter chain, the electron is removed from each H and passed through the series of electron carriers in the membrane, finally ending up on O_2 (the final electron acceptor)
        (3) the energy from the electrons is used to transport H^+ (lost its electron) across the inner membrane; this creates a concentration gradient - more H^+ on one side of the membrane than the other - so H^+ will flow back across the inner membrane
        (4) H^+ can only flow back across at certain points - it flows through channels that contain ATP synthase (the enzyme that makes ATP) which is activated by H^+ flowing by
        (5) yields 28 ATP/original glucose
        (6) steps 3 and 4 are known as the chemiosmotic mechanism (chemical reaction coupled to flow of a substance across a membrane)
        (7) because O_2 is used to make ATP, it is called oxidative phosphorylation

(glycolysis can happen anaerobically - w/o O_2 - but this alone is not very efficient)

(8) H_2O is formed from O_2 and H^+

(9) passing electrons in steps means energy is released slowly (releasing it all at once would create so much heat it would kill the cell)

5. not all the energy in glucose is used to make ATP (no energy transfer is 100% efficient)
6. the building blocks of fats and proteins can be used to make ATP - they can be made into intermediate molecules in the citric acid cycle
7. ATP is used for all the cell's energy needs (making and transporting substances, mechanical work like muscle contraction)

- vaults
    1. non-membranous, octagonal organelle made of protein
    2. probably used to transport molecules from nucleus to other cell locations (mRNA, ribosomes)
    3. may help make cancer cells drug resistant

- Cytosol
    - 55% of cell volume
    - composition varies in different areas of cell
    - involved in several kinds of cell activities
        1. enzymatic regulation of intermediary metabolism
            a. chemical reactions involving synthesizing and breaking down small organic molecules (e.g., sugars, amino acids, fatty acids)
            b. provides raw material for structure and function
        2. ribosome protein synthesis
            a. free ribosomes make enzymes for use in cytosol
        3. storage of fat and glycogen (stored form of glucose)
            a. inclusions - masses of stored nutrients
            b. can be broken down when needed to make ATP

- Cytoskeleton
    - complex protein network running through cytosol
        1. supports and organizes parts of cell
        2. controls movements of cell and within cell

- 3 parts

1. microtubules
    a. largest of cytoskeletal parts
        (1) made mostly of the protein tubulin
    b. maintain shape of cell
        (1) early in cell development
        (2) in asymmetrical cells
    c. transport of vesicles
        (1) special motor proteins (e.g. kinesin) attach to vesicle and microtubule, pulling vesicle along
    d. movement of cilia and flagella
        (1) project from surface of cell
        (2) cilia are shorter, hairlike, many on a single cell; move substances across surface of cell (respiratory tract, oviduct)
        (3) flagella are long, one per human cell; move whole cell (sperm)
        (4) both have same basic structure of grouped microtubules; movement is produced when a motor protein (dynein) displaces tubules relative to one another
    e. formation of mitotic spindle
        (1) formed during mitosis (division of nucleus) and directs movement of chromosomes (DNA)
        (2) centrioles (a pair of microtubule groups) assemble the mitotic spindle

2. microfilaments
    a. one of smaller elements of cytoskeleton
        (1) many made of the protein actin
    b. cellular contractile systems
        (1) muscle cells
        (2) contractile ring that divides a cell - pinches cell together and separates halves
        (3) amoeboid movement - some cells can alternately form and break down actin filaments in order to move the whole cell (e.g., white blood cells)
    c. mechanical support
        (1) support microvilli - extensions of cytoplasm important for increasing surface area of cell

3. intermediate filaments
    a. medium sized
        (1) made of different proteins depending on cell
        (2) very stable in comparison to other cytoskeletal elements
    b. strengthen and stabilize cells
    c. hold together contractile units in muscle cells

4. elements of cytoskeleton are interconnected
    a. supports cell, responsible for rigidity and shape
    b. organizes groups of enzymes
    c. directs transport and movement
    d. may transfer mechanical forces for communication, may influence gene regulation

Chapter 3 **Plasma Membrane & Membrane Potential**

- Basics
  - selectively permeable - controls what gets in and out of cell
  - Membrane Structure
    1. basic membrane structure is a phospholipid bilayer
       a. hydrophilic (water loving) heads are polar, face outward toward water
       b. hydrophobic (water fearing) tails are nonpolar, face inward away from water
          (1) barrier to diffusion - stops water soluble molecules from passing through
          (2) water itself is small enough to get through
       c. responsible for membrane fluidity

    2. cholesterol
       a. between phospholipids
       b. contributes to fluidity and stability

    3. proteins
       a. some span the membrane
          (1) selective channels to transport substances across membrane (e.g., ions), opening filled with water, channel is specific
          (2) carrier proteins also transport specific molecules across membrane
       b. some on one side of membrane
          (1) receptors - bind with molecules on outer surface and initiate changes in cell (chemicals in blood only influence cells with the right receptors)
          (2) membrane bound enzymes – chemical reactions at inner or outer membrane surface
          (3) filamentous meshwork on inner side bind with cytoskeleton to maintain cell shape and for movement
          (4) cell adhesion molecules (CAMs) - stick out from outer surface and secure cell to other cells (caherins “zip” cells together in tissues/organs), also cell communication (growth, defense responses), integrins span the membrane and link cytoskeleton to external environment and relay regulatory signals
          (5) some allow cells to recognize "self" and interact with one another (often glycoproteins)

4. carbohydrates
    a. on outer surface, bound to membrane proteins and lipids (glycoproteins, glycolipids)
    b. important in recognition of cells of same type and tissue organization
    c. involved in tissue growth (cells won't overgrow)

- structure known as fluid mosaic model

- Cell to cell adhesions
  - carbohydrates on membrane surface help arrange cells into groups, which are held together in various ways
    1. CAMs
    2. extracellular matrix (connective tissues)
        a. cells may not be joined directly to other cells, but embedded in matrix of carbohydrates and protein fibers
            (1) collagen - resists tension (e.g., skin)
            (2) elastin - stretch and recoil (e.g., skin, lungs)
            (3) fibronectin - holds cells in position (all over body)
        b. substances diffuse through, going between blood and tissues
        c. important in normal cell functioning
    3. specialized junctions
        a. desmosomes - cells join at particular spots, found all over body, particularly where stretch occurs (e.g., skin, muscle)
        b. tight junctions - impermeable barrier, common in epithelial sheets where they prevent leakage
        c. gap junctions - cells linked by protein tunnels, allows small molecules to pass between cells, important in some cells that transmit electrical activity (e.g., cardiac muscle)

- Membrane Transport (see table Methods of Membrane Transport)
  - two factors influencing transport - solubility of the substance in lipid, and size of substance
    1. small, uncharged or nonpolar molecules move through lipid bilayer (e.g., O_2 CO_2, fatty acids)
    2. ions and small polar molecules (like glucose) can move through channels or by carrier proteins if the right transporter exists
    3. substances too big or without a special protein transporter need special mechanisms to get through the membrane

- Passive Transport (no ATP used)

1. diffusion - molecules move down their concentration gradient (greater → lesser concentration), charged particles move down electrochemical gradients

    a. simple diffusion - substance moves through lipid bilayer or protein channels (e.g., O_2, CO_2, some ions)

    b. osmosis - water moves down its concentration gradient

    c. facilitated diffusion uses a carrier protein that binds to the molecule to be transported and brings it to the other side of the membrane (e.g., glucose)

2. Filtration - water and solutes forced through membrane by pressure (e.g., in kidneys)

- Active Transport (ATP used)

1. carrier proteins transport substance against its concentration gradient (needs ATP to change conformation)

    a. primary active transport - energy from ATP used directly to transport a substance (e.g. Na^+-K^+ pump, in all cells)

    b. secondary active transport - driven by gradients set up by primary active transport

        (1) in the digestive tract glucose and amino acids are "dragged along" with Na^+ diffusing into cell (Na^+ gradient set up by Na^+-K^+ pump)

2. vesicular transport (bulk transport) - large molecules or multimolecular substances enclosed in pieces of membrane

    a. endocytosis (pino/phagocytosis)

        (1) fuse with lysosomes which break down substance and release products to cell (e.g., bacteria)

        (2) vesicle travels to opposite side of cell and releases contents (cells lining capillaries)

    b. exocytosis

        (1) secretion of large polar molecules like hormones and enzymes

        (2) adding components to membrane

- Intercellular communication and signal transduction

- cells must communicate so they can coordinate their activities (maintain homeostasis, control growth and development)

- 3 types of intercellular communication

1. gap junctions

    a. small molecules and ions directly exchanged between cells

b. important in spread of electrical signals (cardiac and smooth muscle, very rarely neurons)

2. signal molecules on cell surface allow direct interaction
    a. phagocytes (body defense cells) recognize and kill invading cells
3. chemical messengers
    a. a specific chemical is made by special cells
        (1) acts on target cells, which then respond appropriately
    b. 4 types
        (1) paracrines - act locally (e.g., histamine in inflammatory response)
        (2) neurotransmitters - act locally; nerve cells release them to other nerve cells, muscles, or glands
        (3) hormones - acts over long distances, released into blood by endocrine glands
        (4) neurohormones - act over long distances, released into blood by special nerve cells (neurosecretory neurons)

- Pathways of chemical messengers

1. specialized protein receptors on plasma membrane bind with a particular messenger
    a. triggers a sequence of events that control a particular cell activity
    b. many possible responses
    c. 3 general ways of eliciting a response
        (1) opening (most commonly) or closing chemically-gated receptor channels in the membrane (regulates movement of ions in/out of cell)
        (2) activating receptor-enzymes
        (3) transferring signal to second messenger (an intracellular chemical messenger) which initiates a series of events inside cell
2. channel regulation
    a. channel proteins have the ability to change shape and thus open/close (act like gates)
    b. receptor binding site is part of the channel, messenger binds → channel opens
    c. eg., neurotransmitters trigger movement of Na^+, K^+, or both across the membrane, which changes the electrical activity of cell (muscle and nerve cells)
3. tyrosine kinase pathway
    a. messenger binds and activates a receptor-enzyme (usually a protein kinase that phosphorylates another protein)
    b. typically a cascade is initiated which ultimately activates a particular protein that brings about the response
    c. eg., insulin and growth factors

4. second messenger systems (most common pathway)
    a. general process
        (1) messenger binds to receptor (G-protein-coupled receptor)
        (2) enzyme on cytoplasmic side of membrane activated by G-protein
        (3) intracellular second messengers are activated, and diffuse through the cell to trigger appropriate response
        (4) typically a cascade is initiated and response accomplished by altering structure/function of particular proteins
    b. cAMP pathway (cyclic adenosine monophosphate, most common)
        (1) messenger binds to receptor
        (2) activates G protein which activates adenylyl cyclase (on cytoplasmic side of membrane)
        (3) ATP → cAMP, which diffuses through cell
        (4) cAMP-dependent protein kinase activated, then phosphorylates a particular intracellular protein (this changes the protein's shape/function, bringing about the appropriate response)
        (5) can switch cellular processes on or off, eg., heart rate changes, formation of sex hormones in typical female, breakdown of stored glucose in liver, water conservation in kidneys
    c. Ca^{2+} pathway
        (1) messenger binds to receptor
        (2) activates G protein which activates phospholipase C (on cytoplasmic side of membrane)
        (3) $PIP_2 \rightarrow DAG + IP_3$
        (phosphatidylinositol bisphosphate, diacylglycerol, inositoltriphosphate)
        (4) IP_3 increases Ca^{2+} in cytosol (from stores in ER), Ca^{2+} diffuses through cell and binds to the protein calmodulin, which in turn activates another protein, bringing about the appropriate response
        (5) pathway important in cell movement such as smooth muscle contraction
    d. the two major second messenger systems can interact, and there are others
    e. very low concentrations of first messengers trigger large responses - one messenger molecule can result in millions of product molecules
    f. receptors can be regulated (number, affinity for messenger)

- Apoptosis
    1. an interesting example of a signal transduction pathway

2. programmed cell death
    a. development
    b. tissue turnover
    c. immune system (infected cells and worn-out phagocytes)
    d. old, damaged or mutated cells
3. cell detaches from neighboring cells and shrinks, killed from the inside by caspases, which take apart DNA, cytoskeleton, etc.
    a. cells normally receive signals for survival, which block the pathway causing apoptosis
        (1) absence of growth factors or detachment from extracellular matrix act as triggers
    b. can receive "death signals" that override life pathway
    c. problems in pathways likely involved in Alzheimer's, Parkinson's and AIDS
    d. not enough apoptosis may play role in cancer
    e. mitochondria play a role (release cytochrome c which activates caspases)
4. does not trigger an inflammatory response

- Membrane Potential
  - separation of charges across a membrane
    1. separated charges have the potential to do work - electrical force of attraction can be harnessed
    2. measured in millivolts (mV) - more charges separated → greater potential
    3. all plasma membranes have potential
    4. due to unequal distribution of a few key ions

  - ions involved
    1. Na^+
    2. K^+
    3. A^- (large anionic intracellular proteins)

  - Na^+-K^+ pump
    1. responsible both directly and indirectly for establishing membrane potential
    2. directly generates about 20% of potential
        a. actively transports 3 Na^+ out for every 2 K^+ in
            (1) leaves cell slightly negative inside
            (2) establishes concentration gradients (Na^+ high outside, K^+ high inside)
            (3) passively, Na^+ → in, K^+ → out

3. indirectly generates other 80% of membrane potential
    a. membrane is more permeable to K^+ than to Na^+ (more K^+ channels open)
    b. K^+ will passively flow out, increasing membrane potential
        (1) K^+ flows out until concentration gradient is balance by electrical gradient (negative charges inside attract K^+)
    c. very little Na^+ leaks back in (closed channels)
4. leads to resting membrane potential of -70mV in a typical nerve cell (sign means more negative inside)

- other effects
1. A^- cannot leave the cell (too large)
    a. contributes to negative charges that balance leakage of K^+ out of cell
2. Cl^- distribution influenced by membrane potential
    a. high outside
    b. negative charge inside cell drives Cl^- out (cells permeable to Cl^-, but most do not actively transport it)

- purpose of membrane potential
1. altering membrane potential results in nerve impulses and muscle contraction
    a. may be involved in activity of secretory cells
    b. significance in other cells not understood

Chapter 4 **Neuronal Physiology**

- Terms
  - excitable tissues: capable of producing electrical signals (transient, rapid changes in membrane potential), nerve & muscle
  - resting membrane potential: the membrane potential that exists when no net changes in potential are occurring
  - graded potentials: local changes in membrane potential that vary in magnitude (flow of ions)
  - action potentials: brief, rapid reversals in membrane potential, which can spread throughout the membrane (flow of ions)
  - voltage-gated channels: membrane channels that open or close in response to changes in potential
  - polarization: a membrane that has potential is polarized
  - depolarization: a decrease in membrane potential (inside becomes more positive)
  - triggering event: event that initiates a depolarization (stimulus like light or touch, chemical messenger)
  - hyperpolarization: an increase in membrane potential (inside becomes more negative)
  - repolarization: return to resting potential after a depolarization

- Graded Potentials
  - magnitude of graded potential related to magnitude of triggering event
    1. stronger trigger → greater magnitude of change in potential
  - current flow (movement of charges)
    1. when a graded potential occurs, a piece of the membrane (called the active area) has a different potential than the rest of the membrane (which is at resting potential, called the inactive area)
       a. current flows between active area and adjacent inactive areas (opposite charges attract)
       b. previously inactive areas become active and more current flow occurs
    2. spread of graded potential is decremental
       a. decreases as it moves along the membrane
       b. current leaks into ECF
       c. function as signals over short distances
    3. usually not an actual reversal of charges - just a reduction in potential (inside becomes less negative than before, small depolarization)
    4. important for nerve and muscle cells (e.g., postsynaptic potentials)

- Action Potentials (AP)
  - can be transmitted over long distances without losing strength
  - Depolarization
    1. triggering event causes depolarization to occur relatively slowly until threshold potential is reached (about -50 to -55 mV)
        a. once threshold is reached, membrane quickly depolarizes to +30 mV
            (1) when triggering event begins depolarization, some of the voltage-gated Na^+ channels open, Na^+ flows into cell (proteins that make up the channel have charged portions, shape change occurs as those charges interact with charges surrounding the membrane)
            (2) this further depolarizes the membrane, causing even more Na^+ channels to open
            (3) at threshold all the Na^+ channels are open and there is an explosive increase in Na^+ permeability (P Na^+)
            (4) at peak depolarization, the Na^+ channels close (the channel is constructed so that the same depolarization that opens them also closes them)

- Repolarization begins
    1. as Na^+ channels close, K^+ channels open (P K^+ increases) due to delayed voltage-gated response to the depolarization, K^+ flows out of cell
    2. this restores internal negativity
    3. as repolarization progresses...
        a. Na^+ channels resume original conformation (closed but capable of opening)
        b. newly opened K^+ channels close
            (1) hyperpolarization occurs before channels close (membrane even more negative than at resting potential)
            (2) resting potential restored

  - AP lasts about 1 millisecond

  - ion gradient restored
    1. Na^+-K^+ pump restores ion gradients
        a. important for long term maintenance of gradient
        b. not necessary between APs
            (1) ion shifts during AP are not so great that they wipe out concentration gradients, so many APs can occur in succession

- Neurons (nerve cells)
  - 3 basic parts
    1. cell body
       a. houses nucleus and organelles
       b. receives signals from other cells (contains receptors for chemical messengers)
    2. dendrites
       a. projections from cell body
       b. increase surface area for receiving signals
    3. axon (nerve fiber)
       a. single elongated projection
       b. conducts APs away from cell body
       c. often has collaterals (side branches)
       d. axon hillock (part of cell body and first part of axon) is area where APs generated in most neurons
       e. ends in branches called axon terminals that release chemical messengers
       f. may be less than a mm or more than a m

- Propagation of an AP
  - Conduction by local current flow (contiguous conduction)
    1. AP at axon hillock
       a. local current flow between this active area and adjacent inactive area causes new AP
       b. AP passed section by section along axon
  - Saltatory conduction
    1. occurs in myelinated fibers
       a. special cells form barrier that is impermeable to ions
          (1) wrap around fiber
          (2) mostly lipids
          (3) formed by oligodendrocytes in central nervous system (CNS), by Schwann cells in peripheral nervous system (PNS)
       b. nodes of Ranvier
          (1) bare spaces between myelin
          (2) contain Na^+ channels
    2. AP "jumps" from node to node
       a. much faster
       b. conserves energy
          (1) fewer ions move so Na^+-K^+ pump uses less ATP restoring gradients

- fiber diameter influences speed of propagation
    1. larger fiber diameter → faster conduction
    2. large myelinated fibers found in areas where information must be transmitted quickly (e.g., fibers innervating skeletal muscle)
    3. smaller unmyelinated fibers found in areas where speed not critical to function (e.g. fibers innervating digestive tract)

- Refractory period
    1. ensures APs propagated in only one direction
    2. membrane that just had AP not very sensitive to further stimulation
        a. absolute refractory period
            (1) no amount of stimulation will induce another AP
            (2) time between when Na^+ gates first opened and when they are in their "ready to open" conformation
        b. relative refractory period
            (1) needs stronger than usual stimulation to produce another AP
            (2) only some Na^+ gates ready to open, some K^+ gates still open
    3. lasts for one to a few msec

- All-or-none law
    1. a membrane responds with a maximal AP or it doesn't respond at all
        a. a stimulus that doesn't reach threshold never initiates an AP
    2. nervous system differentiates between relatively weak or strong stimuli by frequency of APs
        a. stronger stimuli → more APs/sec

• Synapses and neuronal integration
- neuron terminates at...
    1. muscle
    2. gland
    3. another neuron
- Synapse basics
    1. junction between axon terminal of one neuron and dendrites or cell body of next neuron
    2. most neurons have thousands of synaptic inputs
    3. anatomy of a synapse
        a. presynaptic neuron
            (1) conducts APs toward synapse

(2) ends in swelling called synaptic knob, which contains synaptic vesicles that store a specific neurotransmitter

b. postsynaptic neuron

(1) conducts APs away from synapse

(2) portion at synapse called subsynaptic membrane

c. synaptic cleft

(1) space between pre and postsynaptic neurons

4. generally operates in one direction (changes in membrane potential in presynaptic neuron bring changes in membrane potential of postsynaptic neuron)

5. basic synapse function

a. AP reaches presynaptic neuron axon terminal

b. voltage-gated Ca^{2+} channels in synaptic knob open

c. Ca^{2+} influx induces release of neurotransmitter from synaptic vesicles by exocytosis

d. neurotransmitter diffuses across cleft and binds with receptor sites on subsynaptic membrane

e. triggers opening of specific ion channels in subsynaptic membrane (chemically-gated channels)

- Two types of synapses

1. excitatory synapse

a. Na^+ and K^+ channels open

b. net movement of Na^+ in

c. results in small depolarization called an EPSP (excitatory postsynaptic potential), a kind of graded potential

d. takes many EPSPs to bring membrane to threshold and generate an AP (each one brings membrane closer to threshold)

2. inhibitory synapse

a. opens channels for K^+ or Cl^-

b. $K^+ \rightarrow$ out, or $Cl^- \rightarrow$ in

c. results in small hyperpolarization called an IPSP (inhibitory postsynaptic potential)

d. each IPSP moves membrane further away from threshold

3. a given synapse is either always excitatory or always inhibitory

4. the same neurotransmitter is generally released at a given synapse

(1) some nts are always excitatory

(2) some nts are always inhibitory

(3) some nts produce an IPSP at one synapse and an EPSP at another synapse

- Synaptic delay
    1. takes time for signal to cross synapse (.5 - 1 msec)
    2. the more synapses a signal must cross, the longer the time needed for response to occur (total reaction time)

- Removal of nt from the synaptic cleft
    1. as long as the nt is bound to receptor, IPSP or EPSP continues
    2. quickly removed from synapse
        a. diffuses away from synaptic cleft
        b. inactivated by enzymes in subsynaptic membrane
        c. actively transported back to presynaptic neuron

- Neurotransmitters and second messenger systems
    1. most nts change conformation of chemically-gated channels
    2. some use second messenger systems (cAMP), which work in short term and long term changes like memory

- Grand postsynaptic potentials (GPSP)
    1. composite of all EPSPs and IPSPs occurring on a cell at the same time
    2. temporal summation
        a. summation of potentials occurring very close together in time from same synaptic input
    3. spatial summation
        a. summation of potentials from many different synaptic inputs at the same time

- Classical neurotransmitters and neuropeptides
    1. classical neurotransmitters
        a. small, fast-acting
        b. made in axon terminal
        c. amino acids or related compounds
    2. neuropeptides
        a. large (many amino acids)
        b. made in cell body, stored in dense-core vesicles in the axon terminal
            (1) one or more may be released along with a classical nt
        c. some act like classical nts
        d. most are neuromodulators

(1) don't cause EPSPs/IPSPs

(2) cause long term changes in synapse

(3) often use second messenger systems

- Presynaptic inhibition and facilitation
    1. a third neuron may influence the effect of one neuron on another
        a. probably involves Ca^{2+}
        b. can influence inputs from certain neurons while not affecting other inputs

- Convergence and divergence
    1. in convergence a single neuron is influenced by many other neurons synapsing on it
    2. in divergence a single neuron influences many other neurons

- The various types of influences result in a great deal of complexity and ability to control what information is passed on

Chapter 5 **Central Nervous System**

- A "wired" system
  - specific pathways for transmission of signals between areas of body
  - In general, coordinates rapid, precise responses
  - interacts with endocrine system ("wireless")

- Organization of nervous system
  - central nervous system (CNS)
    1. brain and spinal cord
  - peripheral nervous system (PNS)
    1. nerve fibers carry information between CNS and rest of body
    2. afferent (sensory) division
        a. carries information toward CNS
    3. efferent (motor) division
        a. carries information away from CNS to effector organs (muscles, glands)
        b. somatic nervous system
            (1) motor neurons supplying muscles
        c. autonomic nervous system
            (1) innervates smooth and cardiac muscle, glands
            (2) sympathetic division ("fight or flight")
            (3) parasympathetic division ("resting and digesting")
- 3 Classes of neurons
  - afferent
    1. in afferent division of PNS
    2. peripheral end has a sensory receptor
        a. generates APs in response to a stimulus
    3. cell body near spinal cord
    4. synapses with other neurons in spinal cord
  - efferent
    1. in efferent division of PNS
    2. cell body in CNS
    3. terminates at a muscle or gland
  - interneurons (most neurons)
    1. in CNS, between afferent and efferent neurons
    2. interconnect with one another

- Protection /nourishment of the brain
  - glial cells (neuroglia)
    1. astrocytes
       a. hold neurons together
       b. repair of injury and scar formation
       c. induce changes in blood vessels (blood-brain barrier) and participate in transport across barrier
       d. take up and break down some nts (glutamate, GABA)
       e. take up excess K^+ in ECF
       f. enhance synapse formation and modify function, physical and chemical influences
       g. communicate with each other and neurons via gap junctions, nts, and other chemicals
    2. oligodendrocytes
       a. forms myelin sheaths
    3. ependymal cells
       a. line internal cavities of CNS (ventricles of brain, central canal of spinal cord)
       b. help form cerebrospinal fluid (CSF)
       c. serve as stem cells in some areas of brain
    4. microglia
       a. defense cells, can do phagocytosis
       b. secrete nerve cell growth factor

  - blood-brain barrier
    1. capillaries in brain have tight junctions joining cells
       a. only substances that can pass through cells can be exchanged (lipid soluble substances, e.g., O_2, CO_2, alcohol, steroid hormones; substances with specific carriers, e.g., glucose, amino acids, ions)
    2. protects brain from harmful substances
    3. keeps out circulating hormones that act like nts

  - CSF
    1. formed by choroid plexuses, surrounds brain and spinal cord
    2. cushions CNS
    3. it is the interstitial fluid of the CNS
       a. directly contacts CNS cells and exchanges take place
    4. similar to plasma, but lower in K^+ and higher in Na^+

- meninges: connective tissue membranes
    1. dura mater - outer layer
        a. forms dural sinuses and venous sinuses (blood and CSF pool, return to circulation)
    2. arachnoid mater - middle layer
        a. subarachnoid space contains CSF
        b. arachnoid villi reabsorb CSF (return to blood in sinuses)
    3. pia mater - inner layer
        a. well vascularized
        b. important in forming CSF

- bones offer physical protection
    1. cranium (skull) - brain
    2. vertebral column - spinal cord

• brain structure

• Cerebrum
- cortex is outer layer of gray matter (neuron cell bodies and dendrites, glial cells)
- underneath is white matter (tracts of myelinated fibers), which transmits signals between cortical areas, and to other CNS locations
- divided into functional areas (some degree of overlap) specialized for particular activities, but no area acts alone
- 2 hemispheres
    1. connected by corpus callosum
    2. most functional areas occur in both hemispheres (except language areas)
    3. some degree of specialization
        a. left - logical, analytical tasks like language, math; fine motor control
        b. right - nonlanguage skills like spatial perception and art/music
    4. generally involved in functions of opposite side of body (contralateral)
- paired lobes
    1. occipital, temporal, parietal, frontal
    2. functional areas often contained within a lobe
- 3 kinds of functional areas
    1. motor areas - control voluntary motor functions
    2. sensory areas - conscious awareness of sensation
    3. association areas - integrate diverse information

- selected functional areas
    1. primary visual cortex
        a. receives visual information
        b. surrounding higher-order visual cortex interprets
    2. primary auditory cortex
        a. receives information on sound
        b. surrounding higher-order auditory cortex interprets
    3. somatosensory cortex
        a. receives sensory input (somesthetic sensations from skin like touch, temp. and proprioception, etc.)
            (1) localizes source of input, perceives intensity of stimulus, capable of spatial discrimination
            (2) sensory homunculus - a particular region of the brain receives information from a certain part of the body
    4. posterior parietal cortex
        a. integrates somatosensory and visual input
        b. important in complex movement
    5. primary motor cortex
        a. voluntary control of skeletal muscle
            (1) motor homunculus - neurons controlling a particular body part tend to be grouped together
    6. supplementary motor area
        a. helps prepare "programs" for complex patterns of movement
    7. premotor cortex
        a. plans movement based on body orientation, coordination of complex movements
        b. interacts with posterior parietal cortex
    8. Language areas
        a. Broca's area
            (1) important in ability to speak - interacts with motor areas for speech
        b. Wernicke's area
            (1) important in language comprehension (written and spoken) and patterns of speech
        c. Broca's and Wernicke's usually in left hemisphere only, right side has affective language areas, which express and comprehend emotion in speech

9. prefrontal association cortex
    a. plans for voluntary activities
    b. weighing consequences, making choices
    c. personality
    d. complex learning, intellect (cognition), conscience
10. parietal-temporal-occipital association cortex
    a. integrates information from those lobes
11. limbic association cortex
    a. motivation, emotion, memory

- cortex displays plasticity
  1. many areas can change based on need, e.g.:
     a. other areas may take over for damaged areas
     b. use of a particular body part can result in more cortical space being devoted to it

- areas constantly interact

• Subcortical structures
- basal nuclei (basal ganglia)
  1. masses of gray matter within cerebral white matter
  2. functional aggregations of cell bodies
     a. inhibiting muscle tone
     b. maintaining purposeful motor activity and suppressing unnecessary movement
     c. monitor/coordinate muscle contractions in posture/support
     d. complex aspects of motor control
     e. may be involved in cognitive functioning
  3. receives input from all cortical areas
  4. sends feedback via thalamus mainly to prefrontal and premotor areas (no direct connection to motor neurons)

- thalamus
  1. preliminary processing of sensory input
     a. screens out unimportant stimuli and passes on significant input to somatosensory cortex and other brain regions
  2. crude awareness of sensation
  3. reinforces voluntary motor activity

4. some degree of consciousness
5. "gateway" to cerebral cortex - virtually all inputs to cortex pass through
6. contains many nuclei, each with a functional specialty

- hypothalamus
  1. many functionally grouped nuclei
  2. integrating center for homeostasis, links ANS and endocrine system
     a. regulates body T (monitors blood temperature)
     b. regulates water balance (urine output) and thirst (contains osmoreceptors - test concentration of body fluids)
     c. regulates food intake (monitors blood levels of nutrients and hormones)
     d. controls endocrine functioning (produces hormones, regulates pituitary)
     e. role in emotional and behavioral patterns
     f. controls autonomic centers in brain and spinal cord (e.g., activity of smooth and cardiac muscle, exocrine glands)
     g. "biological clock"

- limbic system
  1. parts of cortex, basal nuclei, thalamus, hypothalamus
  2. involved in all aspects of emotion (pleasure, fear, anger, etc.) and physical expressions of emotion (attacking when angered, laughing, crying, etc.)
  3. contains "reward" and "punishment" centers
  4. important in homeostatic drives - hunger, thirst, sex
  5. norepinephrine, dopamine and serotonin important neurotransmitters (precise role unclear, more of these nts associated with pleasure, less with depression)

- Learning and Memory
  - learning: acquisition of knowledge or skills as a consequence of experience, instruction, or both
  - memory: storage of knowledge for later recall
  - remembering: process of retrieving information from storage
  - forgetting: inability to retrieve information
  - memory trace: neural change responsible for storage of information
    1. present throughout brain
    2. particular areas appear to be important in certain kinds of memories
       a. hippocampus - short term memories involving integration of stimuli, consolidation (converting from short-term to long-term), declarative memories (facts and events)

b. cerebellum - procedural memories (a.k.a. skill memories involving motor pathways, e.g., playing piano, typing, riding a bike)

- types of memory
  1. short-term
     a. immediately stored
     b. limited capacity
     c. retrieved rapidly
     d. forgetting is permanent (unless consolidated)
     e. transient changes in preexisting synapses (changes in amount of nt released via modification of Ca^{2+} channels, may involve cAMP pathways)
  2. long-term
     a. longer storage time, enhanced by practice
     b. large storage capacity
     c. more slowly retrieved
     d. quite stable, forgetting usually transient
     e. permanent changes in neurons (formation of new synapses, synthesis of proteins in pre or postsynaptic membranes, changes in amount of nt released)

- factors influencing consolidation
  1. emotional state - transfer better when more alert and motivated
  2. repetition
  3. association of new information with old information

• cerebellum
  - different portions specialize in particular functions (mostly ipsilateral)
    1. maintains balance and equilibrium, important in movement
    3. enhances muscle tone
    4. coordinates voluntary movements
       a. input from cortical motor areas and peripheral receptors (indirect)
       b. ensures smooth, precise movement
    5. plans and initiates voluntary movement
       a. output to cortical motor areas
    6. procedural memories

- brain stem
  - all incoming and outgoing fibers pass through, most synapse here for processing
  - functions
    1. cranial nerve origin
    2. contains nuclei for control of autonomic activities
        a. cardiovascular center (force and rate of heart contraction, blood pressure)
        b. respiratory centers (rate and depth of breathing)
        c. many others such as vomiting, hiccuping, swallowing, coughing, sneezing
    3. modulates pain
    4. regulates equilibrium and posture reflexes
    5. contains reticular formation
        a. receives/integrates all synaptic input
        b. controls cortical alertness (reticular activating system - RAS)
        c. important in ability to direct attention
    6. contains sleep centers

- Sleep
  - an active process in which an individual is not consciously aware of surroundings but can be aroused by external stimuli
  - types of sleep
    1. slow-wave sleep
        a. from light sleep to deep sleep and back
        b. characterized by frequent movement, small decrease in heart and respiratory rate, and blood pressure
    2. paradoxical (REM) sleep
        a. brain activity similar to awake state
        b. characterized by lack of movement (except eyes), irregular heart and respiratory rate and blood pressure, dreaming
  - probably controlled by 3 centers that interact to produce the stages of sleep (arousal system, slow wave center, REM center)
  - functions
    1. time to restore chemical/physiological processes
    2. accomplish changes for learning and memory

- Spinal Cord
  - extends from brain stem

  - has paired spinal nerves
    1. serves a particular body region
    2. both afferent (sensory) and efferent (motor and ANS) fibers

  - gray matter
    1. neuron cell bodies and dendrites, short interneurons, glial cells
    2. dorsal horns
        a. cell bodies of interneurons
        b. afferent neurons terminate
    3. lateral horns
        a. efferent ANS cell bodies
    4. ventral horns
        a. efferent motor neuron cell bodies

  - white matter
    1. fiber tracts
        a. ascending: cord → brain
        b. descending: brain → cord

  - reflexes
    1. response that occurs without conscious effort
        a. simple (basic): built-in, unlearned (e.g., pulling away from a painful stimulus)
        b. acquired (conditioned): learned through practice (e.g., typing , playing sports)
    2. reflex arc: the neural pathway involved
        a. receptor responds to stimulus by generating an AP
        b. afferent pathway relays information to...
        c. integrating center (spinal cord or brain stem for simple reflexes, higher brain levels for acquired reflexes)
        d. efferent pathway transmits information to...
        e. effector (muscle or gland)
    3. spinal reflexes
        a. spinal cord is integrating center (no brain involvement needed)
        b. afferent pathway terminates on three types of neurons:

(1) excitatory interneuron, which stimulates efferent motor neurons (muscle contracts)

(2) inhibitory interneuron, which inhibits efferent motor neurons leading to antagonistic muscle group (called reciprocal inhibition or innervation)

(3) interneurons carrying signal to brain (person becomes aware of stimulus)

c. brain can modify spinal reflex

(1) consciously override by sending inhibitory signals to muscle group that would move, excitatory signals to antagonistic muscle group

Chapter 6 **PNS: Afferent Division**

- Basics
  - information carried toward CNS
    1. from viscera
    2. from surface areas
       a. somatic sensation - includes somesthetic sensation (skin) and proprioception (muscles, joints, inner ear)
       b. special senses - vision, hearing, taste, smell
  - perception: our conscious interpretation of the world created by the brain from a pattern of nerve impulses from sensory receptors

- Receptor Physiology
  - peripheral ends of afferent neurons have receptors that detect stimuli (changes in internal or external environment)
    1. convert stimulus to an AP (transduction)
    2. each kind of receptor is specialized to respond to one kind of stimulus (the adequate stimulus)
       a. receptor may respond to other stimuli as well, but it will lead to the sensation usually detected by that receptor
    3. receptor may be a special cell associated with the peripheral ending of a neuron

  - types of receptors (based on what they respond to)
    1. photoreceptors - light
    2. mechanoreceptors - mechanical stimuli
    3. thermoreceptors - temperature
    4. osmoreceptors - concentration of body fluids
    5. chemoreceptors - chemicals
    6. nociceptors (pain receptors) - tissue damage or distortion (intense stimulation of any receptor perceived as pain)

  - graded receptor potentials
    1. stimulus alters membrane permeability of receptor
       a. opens ion channels - main effect is Na^+ flowing in (depolarization), if summation of depolarizations reaches threshold, AP generated (called a generator potential)

b. if receptor is a separate cell, it releases a chemical messenger that opens chemically-gated Na^+ channels in the nearby neuron, which generates an AP when threshold reached (called a receptor potential)

c. stronger stimuli → greater frequency of APs (frequency code)

d. stronger stimuli often result in stimulation of a larger area → more receptors activated (population code)

- adaptation
  1. continued stimulation does not result in APs
  2. tonic receptors do not adapt or adapt slowly
     a. important when continuous information is useful (posture and balance sensed by proprioceptors, nociceptors)
  3. phasic receptors adapt quickly
     a. useful when more information not necessary (touch)
     b. will exhibit an off response - respond again when stimulus removed
  4. mechanisms not well known, may be inactivation of Na^+ channels

- somatosensory pathways
  1. first-order sensory neuron is an afferent neuron with receptor, synapses with...
  2. second-order sensory neuron in spinal cord or medulla, synapses with...
  3. third-order sensory neuron - in thalamus, and so on
  4. process of sending information through a particular pathway is projection, results in knowledge of type, location and intensity of stimulus

- acuity (discriminative ability)
  1. each sensory neuron has a receptive field (area it responds to)
  2. greater density of receptors results in greater acuity

  3. lateral inhibition also results in greater acuity
     a. areas nearest stimulus stimulated to a greater extent, areas farther away stimulated less
     b. most strongly stimulated pathway inhibits other pathways via inhibitory neurons in CNS

- Pain
  - protective (tissue damage is occurring or about to occur)
  - 3 categories of nociceptors
    1. mechanical
    2. thermal
    3. polymodal

  - sensitized by prostaglandins (fatty acid derivatives from lipid bilayer, act locally)
  - fast pain pathway
    1. from mechanical and thermal nociceptors on large, myelinated fibers
    2. localized, sharp sensation

  - slow pain pathway
    1. from polymodal nociceptors on small, unmyelinated C fibers
    2. dull, aching, poorly localized sensation
    3. activated by chemicals released from damaged tissue(e.g., bradykinin)

  - CNS connections
    1. first-order afferent fibers synapse in spinal cord and release substance P (nt unique to pain fibers)
    2. second-order fibers go to reticular formation (increases overall alertness) and somatosensory cortex via thalamus (localizes stimulus)
        a. signals passed to hypothalamus and limbic system, emotional and behavioral responses occur
    3. abnormal, chronic pain may result from abnormal signaling within pain pathways

  - built-in analgesic system
    1. neural mechanisms can suppress transmission in pain pathways at the spinal cord (presynaptic inhibition of release of substance P)
        a. inhibiting fibers come from periaqueductal gray matter and reticular formation in brain stem
    2. uses opiate receptors on afferent pain fiber terminal
        a. morphine
        b. endogenous opiates (e.g., endorphins, enkephalins, dynorphin)
    3. activation of analgesic system unclear
        a. pain modulators include exercise, acupuncture, hypnosis and some types of stress

Chapter 7 **PNS: Efferent Division**

- Basics
  - autonomic nervous system
    1. involuntary
    2. innervates cardiac and smooth muscle, glands
  - somatic nervous system
    1. voluntary
    2. innervates skeletal muscle
  - two neurotransmitters
    1. acetylcholine (ACh)
    2. norepinephrine (NE)

- ANS
  - pathways typically have a 2 neuron chain extending from CNS to the innervated organ
    1. preganglionic fiber has cell body in CNS, synapses with postganglionic fiber in a ganglion, postganglionic fiber innervates the effector organ
    2. sympathetic
       a. preganglionic fibers originate in thoracic and lumbar regions of the spinal cord
       b. preganglionic fibers are short, synapse in a sympathetic chain ganglion along the spinal cord (release ACh)
          (1) some pass through the ganglion and synapse later in collateral ganglion nearer to the innervated organ
       c. postganglionic fibers are long, terminate on effector organ (release NE)
    3. parasympathetic
       a. preganglionic fibers originate in brain stem or sacral spinal cord
       b. preganglionic fibers are long, synapse in terminal ganglia in or near effector organs (release ACh)
       c. postganglionic fibers are short, end on the effector organ (release ACh)
  - fibers releasing ACh called cholinergic fibers, fibers releasing NE called adrenergic fibers
  - postganglionic fibers terminate in many swelling called varicosities, which release nt over a large area of the organ (influence whole organs)
  - dual innervation
    1. most visceral organs innervated by both sympathetic and parasympathetic fibers
    2. generally have opposite effects
    3. either can be excitatory or inhibitory depending on which organ

4. both systems usually partially active
    a. called sympathetic or parasympathetic tone, or tonic activity
5. when one increases its rate of firing and the other decreases it is called dominance
    a. sympathetic dominance results in increase of oxygen/nutrient rich blood flow to skeletal muscles (vessels dilate), heart beats faster and more forcefully, blood pressure increases, respiratory airways dilate, glycogen and fat stores broken down, digestive and urinary activities inhibited, pupils dilate, sweating
    b. parasympathetic dominance results in normal resting functions like digestion and urinary function being increased, while inhibiting sympathetic activities
6. allows precise control over body functions
7. exceptions...
    a. innervated blood vessels (most arterioles and veins) have only sympathetic fibers (regulated by increasing/decreasing rate from tonic level)
    b. most sweat glands have only sympathetic fibers, and postganglionic fibers release ACh
    c. salivary glands have dual innervation, but both stimulate secretion

- role of adrenal gland
    1. an endocrine gland with cortex and medulla
    2. adrenal medulla secretes hormones when stimulated by sympathetic preganglionic fibers
        a. NE and epinephrine released (reinforce sympathetic activity)

- receptor proteins
    1. response of tissue to nt depends on type of receptor on tissue cells
        a. binding of nt induces response via second messenger

    2. ACh receptors (cholinergic)
        a. nicotinic - on postganglionic cell bodies in all autonomic ganglia and on cells of adrenal medulla (in sympathetic and parasympathetic)
            (1) always excitatory response
        b. muscarinic - on effector cell membranes (parasympathetic)
            (1) excitatory or inhibitory depending on organ

3. adrenergic receptors on effector organs (sympathetic)
    a. alpha (α) receptors - bind with NE and E
        (1) usually an excitatory response (constriction of arterioles in non fight-or-flight organs)
    b. beta (β) receptors
        (1) β_1 binds with NE and E, found mostly in heart, excitatory response (increased rate/force of contraction)
        (2) β_2 bind mostly with E, response inhibitory (e.g., dilation of arterioles and bronchioles)

- ANS regulated by...
    1. medulla in brain stem
    2. hypothalamus
    3. prefrontal association cortex

• Somatic Nervous System

- cell bodies of motor neurons in ventral horn of spinal cord, terminates on skeletal muscle cell (releases ACh)
    1. effects are always excitatory (nicotinic receptors)
    2. inhibition due to presynaptic inhibition
    3. each motor neuron influenced by EPSPs and IPSPs from brain and spinal cord
    4. subject to conscious and subconscious control (posture, balance, stereotypical movements)

- neuromuscular junction
    1. large myelinated fibers branch into many unmyelinated terminals
        a. each terminal is enlarged into a terminal button (or axon terminal), which fits into a groove in the muscle fiber (motor end plate)
        b. cleft (sometimes called synaptic cleft) separates terminal button and motor end plate
    2. electrochemical events
        a. AP reaches terminal button
        b. voltage-gated Ca^{2+} channels open (Ca^{2+} diffuses into terminal button)
        c. ACh released from vesicles in terminal button
        d. ACh diffuses across cleft and binds with receptors on motor end plate
        e. chemically-gated ion channels open, resulting in mainly $Na^{+} \rightarrow$ in muscle fiber (a little $K^{+} \rightarrow$ out)
            (1) causes depolarization known as end-plate potential (EPP)
            (2) similar to EPSP, but greater magnitude (more nt involved, larger surface

area with more receptors, more ion channels open)

(3) a graded potential, magnitude depends on amount of ACh and duration of binding

f. a large enough EPP triggers AP in muscle fiber membrane surrounding motor end plate (typically one EPP enough)

(1) spreads by local current flow throughout muscle fiber, resulting in muscle contraction

g. an enzyme in motor end plate breaks down ACh to end APs

(1) acetylcholinesterase (AChE)

(2) allows control of movement

Chapter 8 **Muscle Physiology**

- Basics
  - 3 types of muscle
    1. skeletal (striated, voluntary, multinucleate)
       a. movement of whole body or parts
    2. cardiac (striated, involuntary, one nucleus)
       a. pump blood
    3. smooth (unstriated, involuntary, one nucleus)
       a. movement of substances through hollow organs
- Skeletal muscle
  - functional anatomy
    1. whole muscle
       a. made up of long cells bundled with connective tissue
       b. connective tissue extends to form tendons attaching muscle to bone
    2. muscle cell (fiber)
       a. contains myofibrils (specialized organelles) which are made up of protein filaments (myofilaments)
       b. thick filaments
          (1) made of myosin molecules, each of which has a head and tail end
          (2) heads form cross bridges, have an actin binding site and ATPase site
       c. thin filaments
          (1) made mostly of actin molecules, each of which has a myosin binding site (cross bridge binding site)
          (2) tropomyosin blocks binding sites when cell at rest
          (3) troponin holds tropomyosin in place, has Ca^{2+} binding site
       d. thick and thin filaments arranged into sarcomeres (functional units that contract) this arrangement results in striations
       e. plasma membrane also called sarcolemma
          (1) forms T tubules, which project into cell (continuous with surface membrane, allowing electrical activity at cell surface to be transmitted throughout cell)
       f. sarcoplasmic reticulum is modified smooth ER
          (1) network of tubules surrounding myofibrils
          (2) ends of each portion expand into sacs called terminal cisternae (a.k.a. lateral sacs, stores Ca^{2+})

- Contraction (excitation-contraction coupling and the sliding filament mechanism)
    1. EPP at motor end plate results in AP
        a. spreads throughout cell surface and T tubules by local current flow
    2. triggers release of Ca^{2+} from terminal cisternae
    3. Ca^{2+} binds to troponin, changing its shape so that it moves tropomyosin out of the way of the binding sites
    4. cross bridge attachment - myosin heads bind to actin
    5. power stroke - myosin had uses energy of ATP to pivot and pull thin filaments toward the center of sarcomere
    6. cross bridge detachment - a new ATP molecule binds to myosin head, cross bridge releases
    7. "cocking" of the myosin head - ATP → ADP + P_i by ATPase, myosin head returns to original position (high energy conformation)
    8. steps 3-7 repeat until full contraction reached and Ca^{2+} used up (called cross bridge cycling)
        a. once AP is over (1-2 msec) Ca^{2+} no longer released
        b. Ca^{2+} -ATPase pump transports Ca^{2+} back into SR
        c. troponin and tropomyosin again cover binding sites
        d. muscle cell is relaxed
    9. other important points
        a. during contraction, at any given time, only some cross bridges are attached - as they release others attach so thin filaments don't slide backward
        b. latent period is time between AP and contraction
        c. contraction and relaxation last about 100 msec
        d. contraction of an individual cell is an all-or-none response

- Skeletal muscle mechanics
    - gradation of whole muscle tension
        1. a single AP to a muscle fiber results in a weak contraction (twitch) - muscle cells work together to produce more force
        2. recruiting more motor units → more tension (more force, stronger contraction)
            a. a motor unit is a motor neuron plus all the fibers it innervates (fibers spread throughout muscle)
            b. smaller motor units in muscles needing precise control (eyes, fingers), larger motor units in muscles designed for power (legs)
            c. asynchronous recruitment of motor units prevents fatigue - alternate motor units (e.g., postural muscles, holding a heavy object)

3. influencing tension in each fiber
    a. increased frequency of stimulation → increased tension
        (1) twitch summation occurs when fiber does not relax completely between APs, greater cross bridge cycling from prolonged availability of Ca^{2+}
        (2) if there is no relaxation between APs, tetanus occurs (a smooth, sustained contraction of maximal strength)
    b. length-tension relationship (optimal length → increased tension)
        (1) maximal force possible at optimal length - myosin cross bridges have maximal access to actin binding sites
    c. less fatigue → increased tension
    d. thicker fibers → increased tension
        (1) more myofilaments in cell

- types of contraction
    1. isotonic
        a. tension constant, muscle changes length
            (1) concentric contraction - muscle shortens (lifting a load)
            (2) eccentric contraction - muscle lengthens (lowering load)
    2. isometric
        a. tension develops, length stays the same (trying to lift too heavy a load, pushing against a wall)

- muscles accomplish work (force x distance), but most of the energy muscles use (about 75%) converted to heat

- lever systems
    1. muscles provide force to move bones (levers) around joints (fulcrum)
    2. depending on construction of system, allows a given effort to move a heavier load, or to move it farther and faster

• Skeletal muscle metabolism
- muscle cells have enough ATP reserves to last 4-6 seconds of strenuous activity
- 3 ways to form ATP
    1. creatine phosphate
        a. contains high energy phosphate group
            CP + ADP → creatine + ATP (with enzyme creatine kinase)

b. very fast

c. enough stores to last 15-20 sec

2. oxidative phosphorylation

a. in mitochondria, needs O_2

(1) fueled by fatty acids (during rest or light exercise, slow) or glucose (during more intense exercise, from blood and glycogen stores)

b. high yield of ATP but relatively slow

c. constant supply of O_2 facilitated by myoglobin (stores O_2, increases O_2 transfer from blood)

d. good for long term (endurance)

3. anaerobic glycolysis

a. fast but not as efficient as with O_2, pyruvic acid → lactic acid, which contributes to soreness and fatigue

b. good for short term (high intensity)

- fatigue

1. muscle fatigue: muscle no longer responds with same degree of contraction

a. increase in P_i from the breakdown of ATP is primary cause (interferes w/power stroke, decreases sensitivity of regulatory proteins to Ca^{2+}, decrease amount of Ca^{2+}released)

b. depleted Ca^{2+} levels (leaks from cell after periods of intense exercise)

c. depleted glycogen reserves

2. neuromuscular fatigue

a. ACh synthesis too slow to keep up with high intensity exercise

3. psychological fatigue

a. CNS does not activate motor neurons due to pain or tiredness

- oxygen debt

1. oxidative phosphorylation allows restoration of energy reserves

a. breaks down lactic acid, replenishes stores of creatine phosphate and glycogen

b. takes minutes to whole day

• Fiber types

- most muscles have varying percentages of fiber types

1. slow-oxidative

a. small, contract slowly (low ATPase activity)

b. use oxidative phosphorylation (lots of mitochondria, myoglobin, capillaries)

c. good for low intensity endurance, resist fatigue (postural muscles in back and legs)

2. fast-glycolytic
    a. large (more myofilaments), contract quickly (lots of force, high ATPase activity)
    b. use anaerobic glycolysis (few mitochondria, little myoglobin, lots of glycogen & glycolytic enzymes)
    c. good for short duration high intensity movement (arms for lifting)
3. fast-oxidative
    a. medium sized, contract quickly (lots of force)
    b. mostly oxidative phosphorylation, some anaerobic glycolysis (characteristics of slow-ox and fast-gly)
    c. good for intermediate activities

- training can lead to changes in fiber type
    1. endurance exercise converts fast-glycolytic to fast-oxidative, weight lifting does the opposite
        a. changes in amount of mitochondria, blood supply, size, etc.
    2. typically cannot convert between slow and fast fibers
        a. depends on nerve supply

• Control of skeletal muscle
- 3 levels of input
    1. spinal cord (spinal reflexes)
    2. corticospinal (pyramidal) motor system
        a. from primary motor cortex
        b. activity planned by premotor and supplementary motor areas, and cerebellum
        c. mainly precise movements, especially of hands/fingers, face
    3. multineuronal (extrapyramidal) motor system
        a. complex pathways including primary motor cortex, reticular formation, cerebellum, basal nuclei, thalamus, premotor and supplementary motor areas
        b. mainly regulation of posture and large muscle groups (subconscious)

- afferent signals
    1. necessary for coordinated activity
    2. muscle proprioceptors sense changes in length and tension
        a. inform brain
        b. local spinal reflexes

3. muscle spindles
    a. in middle of muscle, monitors muscle length and speed of stretching
    b. when whole muscle stretched, afferent fibers sense stretch in spindle fibers (respond with increased AP frequency)
        (1) in spinal cord, synapse on alpha motor neuron supplying that muscle, causing stretch reflex (muscle contracts) which resists passive changes in muscle length
    c. when whole muscle contracts, gamma motor neurons signal ends of intrafusal fibers to contract (takes up slack so receptors maintain sensitivity to stretch)
4. Golgi tendon organs
    a. in tendons, monitor tension
    b. when whole muscle contracts, afferent fibers fire in response to the stretch of the tendon (increased APs directly related to amount of tension)
    c. can inhibit alpha motor neurons of that muscle to prevent damage

- Smooth muscle
  - functional anatomy
    1. small cells arranged in sheets
    2. thick and thin filaments
        a. no troponin
        b. tropomyosin does not block binding sites
    3. no myofibrils or sarcomeres (no striations)

  - contraction
    1. Ca^{2+} enters mostly from ECF (voltage-gated Ca^{2+} channels), then some from sarcoplasmic reticulum
    2. Ca^{2+} acts as second messenger, activating myosin kinase, which phosphorylates myosin
    3. cross bridge cycling occurs until Ca^{2+} no longer available (actively pumped back to ECF and SR)

  - multiunit smooth muscle
    1. groups of cells function independently
    2. innervated by ANS, which initiates contractions
    3. large blood vessels, large airways, eye, hair follicles

- single-unit smooth muscle (most)
    1. cells electrically linked (gap junctions)
    2. clusters of cells are self-excitable and pass activity to rest of cells (myogenic activity)
        a. no resting potential - cells gradually depolarize with automatic changes in channel permeability
        b. ANS controls gradation of contraction by influencing amount of intracellular Ca^{2+}

- smooth muscle designed for sustained contractions with low energy use and no fatigue
    1. a single contraction can be 3 sec long (cross bridge cycling and Ca^{2+} removal slow)
    2. uses oxidative phosphorylation
        a. ATP use slow
        b. can use anaerobic glycolysis if needed
    3. can develop tension even when stretched to about 2.5 times resting length (filaments still overlap)

    see table Comparison of Muscle Types

Chapter 9 **Cardiac Physiology**

- Basics of cardiovascular system and heart
  - function of CV system is transport
    1. heart is the pump
       a. establishes a pressure gradient (flow occurs from greater → lesser pressure)
    2. blood vessels are passageways
    3. blood is the transport medium

  - heart is a double pump
    1. pulmonary circuit
       a. heart → lungs and back (at lungs, picks up O_2, releases CO_2)
       b. right side is pump
    2. systemic circuit
       a. heart → body tissues and back (at tissues, picks up CO_2, releases O_2)
       b. left side is pump

  - valves prevent backflow of blood
    1. AV valves attached by chordae tendinae to papillary muscles so that they open in one direction only
    2. semilunar valves are shaped like cups, this structure prevents them from opening backward

  - fibrous skeleton
    1. provides attachment for valves and muscle
    2. separates atria from ventricles (important so they contract at different times)

  - heart wall is 3-layered
    1. endocardium (epithelial lining)
    2. myocardium (muscle)
    3. epicardium (thin fibrous connective tissue layer)

  - pericardial sac
    1. fibrous covering continuous with epicardium
       a. anchors heart
       b. filled with fluid to prevent friction

- Electrical activity of heart
  - autorhythmic cells
    1. specialized cells that initiate and conduct APs
    2. display pacemaker activity (no resting potential, changes in potential due to voltage-gated Na^+, K^+ and Ca^{2+} channels)
       a. decreased flow of K^+ out and increased inward flow of Na^+ through "funny" channels results in slow depolarization
       b. near threshold, voltage-gated transient Ca^{2+} channels open and bring membrane to threshold (Ca^{2+} flows in)
       c. at threshold voltage-gated long-lasting Ca^{2+} channels open, more Ca^{2+} flows in (this is the AP)
       d. at peak of depolarization, voltage-gated K^+ channels open and repolarization occurs
    3. locations
       a. SA node (sinoatrial)
          (1) right atrium
          (2) fastest rate of autorhythmicity, it's the pacemaker of the heart (under usual conditions initiates APs)
          (3) interatrial pathway extends to left atrium (spreads AP, atria contract)
          (4) internodal pathway extends to next node
       b. AV node (atrioventricular)
          (1) electrical connection between atria and ventricles
          (2) signal slightly delayed (.1 sec) to allow atria to finish contracting - more efficient blood pumping
       c. AV bundle (bundle of His)
          (1) branch into ventricles
       d. Purkinje fibers
          (1) branch throughout ventricular myocardium (ventricles contract)

  - contractile cells
    1. APs spread from cell to cell
       a. adjacent cells joined by intercalated discs
          (1) desmosomes resist mechanical stress
          (2) gap junctions allow spread of electrical signals
    2. cardiac muscle APs
       a. cell depolarized by autorhythmic activity

b. voltage-gated Na^+ channels open, $Na^+ \rightarrow$ in, cell depolarized to +30 mV

c. at the peak of depolarization, Na^+ channels close, voltage-gated slow Ca^{2+} channels open (Ca^{2+} flows in - results in plateau, the channels are a "slow" version of the long-lasting Ca^{2+} channels in autorhythmic cells)

d. at the end of the plateau, Ca^{2+} channels close, voltage-gated K^+ channels open ($K^+ \rightarrow$ out, repolarization)

3. excitation-contraction coupling

a. AP travels down T tubules, voltage-gated Ca^{2+} channels open, $Ca^{2+} \rightarrow$ in from ECF

b. Ca^{2+} influx triggers further release of Ca^{2+} from sarcoplasmic reticulum

c. Ca^{2+} binds with troponin-tropomyosin complex, cross bridge cycling occurs

d. Ca^{2+} actively pumped back to ECF and SR

e. extent of cross bridge cycling depends on amount of Ca^{2+} that enters cytosol (unlike in skeletal muscle, where enough Ca^{2+} for maximum contraction is always released)

4. long contractions due to lots of Ca^{2+} from ECF and SR
5. long refractory period

a. due to inactivation of Na^+ channels during plateau

b. tetanus does not occur (no summation)

c. keeps cardiac functioning efficient

- Cardiac cycle

- systole (contraction) and diastole (relaxation) occur in atria and ventricles - most often refers to ventricles

1. diastole

a. AV valves open

b. blood fills ventricles (amount at end of diastole is called end-diastolic volume, EDV is about 135 ml)

c. atria contract

2. systole

a. ventricles contract, closing AV valves

b. semilunar valves open

c. blood ejected (amount of blood still in ventricles is end-systolic volume, ESV is about 65 ml)

- Cardiac output (CO)
  - CO is the volume of blood pumped by each ventricle in one minute (left and right normally equal)

    CO = heart rate (beats/min) x stroke volume (ml/beat)

    1. typically about 5 liters/min at rest (entire blood volume)
    2. can increase to 20-25 l/min
        a. difference between CO at rest and maximum CO is cardiac reserve

  - factors influencing heart rate (HR)
    1. parasympathetic effects (ACh, decrease HR)
        a. primarily supplies atria (SA and AV nodes)
        b. acts on SA node
            (1) increases PK^+ by slowing K^+ channel closure, resulting in hyperpolarization, takes longer to reach threshold
        c. also increases PK^+ at AV node, lengthening delay
        d. acts on atrial contractile cells, weakening contraction
            (1) shortens the plateau phase, by decreasing Ca^{2+} influx
        e. little effect on strength of ventricular contraction
    2. sympathetic effects (NE and E, increase HR)
        a. acts on SA node
            (1) decreases PK^+ by speeding up inactivation of K^+ channels, resulting in "hypopolarization", threshold reached more quickly
        b. reduces delay at AV node, probably by enhancing influx of Ca^{2+}
        c. speeds spread of AP throughout nodal system by enhancing Ca^{2+} influx

  - factors influencing stroke volume (SV)
    1. intrinsic control
        a. resting cardiac muscle is at less than optimal length - stretching fibers by increasing EDV (increasing venous return) results in a more forceful contraction (increases SV)
        b. important to match SV to venous return
            (1) automatically equalizes flow through pulmonary and systemic circuits (blood does not "back up")
    2. increasing contractility (increasing SV)
        a. sympathetic stimulation increases Ca^{2+} influx (atria and ventricles) resulting in greater cross bridge cycling and more forceful contraction
            (1) also enhances venous return by constricting veins, squeezing more blood toward heart

- Coronary circulation

  - heart receives O_2 and nutrients from coronary arteries branching off the aorta (coronary veins empty into right atrium)

    1. most blood flow occurs during diastole
    2. uses oxidative phosphorylation
        a. uses mostly free fatty acids, but can use glucose
    3. during exercise, increased demands for O_2 met by vasodilation (dilation of blood vessels)
        a. adenosine (formed from breaking down ATP) released from muscle cells
            (1) during O_2 deficit
            (2) during increased activity (using more ATP)
            (3) induces dilation of vessels (smooth muscle relaxes)

- Homeostatic imbalances

  - heart failure (heart can't keep up with demands of body)

    1. 2 main reasons
        a. damage from heart attack or impaired circulation to cardiac muscle
        b. prolonged pumping against increased afterload (stenotic semilunar valve or chronically elevated blood pressure)
    2. contractility of heart is decreased
        a. SV decreased for a given EDV (Frank-Starling curve shifts down to right)
        b. body compensates with increased sympathetic activity and retaining salt and water to expand blood volume and increase EDV
        c. eventually body can't compensate
            (1) backward failure - blood pools in venous system (congestive heart failure)
            (2) forward failure - inadequate supplies to tissues
            (3) left-sided failure worse
            backward - fluid accumulates in lungs (pulmonary edema), forward - kidney function depressed and they retain even more water and salt

- atherosclerosis and its effects on the heart (called coronary artery disease when it occurs in coronary vessels)

1. complications of disease are leading cause of death in US
2. can lead to myocardial ischemia (insufficient O_2 to heart), factors causing ischemia:
    a. vascular spasm - decreased O_2 triggers platelet activating factor (PAF) release from vessels, causing spastic constriction, further decreasing O_2 to heart
    b. atherosclerotic plaques - accumulation of lipid and overgrown smooth muscle reduce blood flow, in later stages Ca^{2+} accumulates ("hardening of the arteries")
    c. thromboembolism - plaque breaks through lining of blood vessels and platelets form abnormal clots (thrombus) if clot breaks free (embolus) it can block small vessels (complete blockage causes myocardial infarction - heart attack)
3. transient ischemia causes angina pectoris (chest pain)
    a. usually during physical or emotional stress
    b. may be due to accumulation of lactic acid as heart makes ATP anaerobically
4. risk factors - genetics, obesity, old age, smoking, high blood pressure, diabetes, lack of exercise, nervous tension, high blood cholesterol levels
5. specific indicators of risk
    a. high blood levels of homocysteine (promotes smooth muscle growth and causes oxidation)
    b. high blood levels of C-reactive protein (an indicator of inflammation)
6. cholesterol
    a. carried in blood as lipoprotein complexes
    b. low density lipoproteins (LDL) transport to cells ("bad cholesterol")
    c. high density lipoproteins (HDL) transport to liver and some excreted from body ("good cholesterol")
    d. cholesterol needed for cell membranes, hormones, bile salts - but high levels of LDL associated with atherosclerosis

Chapter 10 **Blood Vessels and Blood Pressure**

- Basics
  - exchanges between blood and tissue cells take place through the interstitial fluid

  - all organs receive fresh blood
    1. amount to each organ adjusted based on need

  - the blood is constantly "reconditioned" so its composition is relatively constant
    1. reconditioning organs receive a high proportion of cardiac output (digestive system, kidneys)

  - organization "vascular tree"
    1. arteries (carries blood from heart toward tissues)
    2. arterioles (adjusts blood flow to tissues)
    3. capillaries (exchanges made)
    4. venules (carries blood to veins)
    5. veins (carries blood from tissues toward heart)

  - flow rate (volume of blood passing through a particular segment of vascular tree per unit time)
    1. directly proportional to pressure gradient
    2. inversely proportional to resistance (hindrance to flow from friction)
       *a. vessel radius - smaller vessels → more resistance
       b. viscosity of blood - thicker blood → more resistance
       c. length of vessel - longer vessel → more resistance

- Arteries
  - fast transport
    1. large

  - pressure reservoir
    1. walls contain endothelial lining surrounded by smooth muscle and connective tissue fibers (collagen and elastin), which allow walls to stretch to contain pumped blood
    2. when the heart is relaxing the arteries recoil and keep the blood flowing

- arterial pressure fluctuates
    1. blood pressure is the force exerted by blood on vessel walls
        a. depends on blood volume and distensibility of vessel
        b. systolic pressure is the maximum pressure during systole (should be <120 mmHg)
        c. diastolic pressure is the pressure during diastole (should be <80 mmHg)
        d. systolic - diastolic = pulse pressure (the pressure felt in arteries near the body surface)
    2. mean arterial pressure is the main driving force for blood flow to tissues

MAP = diastolic pressure + 1/3 pulse pressure

- Arterioles
    - major resistance vessels (small radii)

    - radii adjusted by smooth muscle
        1. vasoconstriction and vasodilation (narrowing and enlarging)
        2. normally partially constricted (vascular tone)
            a. myogenic activity
            b. sympathetic innervation

    - local control of arteriolar radius matches blood flow to tissue needs
        1. chemical influences
            a. metabolic factors causing vasodilation
                (1) decreased O_2
                (2) increased CO_2
                (3) increased acid (from CO_2 and lactic acid)
                (4) increased K^+ (APs outpacing Na^+-K^+ pump in brain or skeletal muscle)
                (5) increased osmolarity (more solutes formed during times of elevated metabolism)
                (6) release of adenosine (in cardiac muscle)
                (7) release of prostaglandins (not well understood)
            b. local metabolic factors probably act by causing release of chemical mediators from endothelial cells (called vasoactive mediators), e.g.,
                (1) endothelial-derived relaxing factor (EDRF), also known as nitric oxide (NO) inhibits Ca^{2+} influx in smooth muscle - vasodilator
                (2) endothelin – vasoconstrictor

2. physical influences
    a. application of heat (vasodilation) or cold (vasoconstriction)
    b. myogenic responses to stretch (vasoactive substances probably contribute)
        (1) tone increases in response to increased stretch (resists stretch) - important to keep flow to tissues constant as MAP changes (pressure autoregulation)
        (2) tone decreases in response to decreased stretch - important in restoring flow to previously deprived tissue (reactive hyperemia)

- extrinsic control of arteriolar radius helps regulate arterial BP
    1. sympathetic activity produces generalized vasoconstriction, increasing resistance and BP (don't vasoconstrict brain)

$$MAP = CO \times \text{total peripheral resistance}$$

    a. NE at α receptors causes vasoconstriction
    b. E at β_2 receptors causes vasodilation (heart, skeletal muscles)
    2. other hormones
        a. vasopressin - important in fluid balance, vasoconstrictor
        b. angiotensin II - important in fluid balance, vasoconstrictor
    3. local control mechanisms can override

- Capillaries

- responsible for exchanges between plasma and interstitial fluid (solute exchange mainly by diffusion)
    1. thin-walled, narrow vessels
    2. highly branched
    3. blood flows slowly through individual vessels
    4. lipid soluble substances pass through cells (O_2, CO_2)
    5. water soluble substances pass through pores (ions, glucose, amino acids)
    6. some vesicular transport (hormones)
    7. degree of "leakiness" may change due to actin-myosin in capillary cells

- precapillary sphincters
    1. rings of smooth muscle can block flow through capillaries in less active tissues
        a. sensitive to local metabolic changes

- fluid shifts and bulk flow
    1. important in distribution of fluids between plasma and interstitial fluid
        a. fluid (not proteins) pushed out through pores at arteriolar end (ultrafiltration)
            (1) capillary blood pressure exceeds plasma-colloid osmotic pressure (oncotic pressure - force drawing water toward plasma proteins)
        b. fluid reabsorbed at venular end
            (1) capillary BP lower than plasma-colloid osmotic pressure
    2. and, ultrafiltration occurs in open capillaries, reabsorption in closed capillaries
    3. fluid shifts occur as needed
        a. loss of blood, shifts to plasma
        b. excess fluid in blood, shifts to interstitial fluid
        c. keeps plasma volume relatively constant (temporary)

- extra fluid picked up by lymph vessels (initial lymphatics) in capillary beds
    1. large valvelike openings allow in fluid and any leaked proteins (lymph)
    2. around larger lymph vessels, surrounding smooth muscle pushes fluid to larger and larger vessels, which contain one-way valves
    3. skeletal muscles help squeeze lymph through
    4. eventually empty into thoracic veins

- edema (accumulation of excess interstitial fluid, reduces exchange between blood and cells)
    1. low plasma proteins
        a. more fluid filtered out, less reabsorbed
        b. kidney or liver disease, diet deficient in protein, burns
    2. increased permeability of capillaries
        a. loss of proteins
        b. injuries, allergic responses
    3. increased venous pressure
        a. also increased capillary pressure
        b. congestive heart failure, pregnancy
    4. blocked lymph vessels
        a. lymph node removal, parasite

- Veins
  - transport back to heart
  - blood reservoir
    1. stretchable with little recoil
    2. venous storage decreases effective circulating volume
        a. can be altered based on need
  - factors influencing venous return
    1. sympathetic activity
        a. vasoconstriction drives more blood toward heart
        b. still low resistance vessels (large radius)
    2. skeletal muscle activity
        a. acts as pump
    3. valves
        a. one-way valves every few centimeters allow flow toward heart only
    4. respiratory activity
        a. acts as pump due to decreased pressure in thoracic cavity
    5. cardiac suction
        a. blood "sucked in" as ventricles relax

- Blood Pressure
  - MAP is main driving force
    1. high enough to get blood to tissues
    2. not too high or extra work for heart, increased risk of vascular damage

  - short term regulation (seconds)
    1. baroreceptor reflex
        a. pressure sensors in carotid sinus and aortic arch sense changes in MAP and pulse pressure
            (1) rate of firing increases with increasing pressure, decreases with decreasing pressure
        b. integrating center is cardiovascular control center in medulla of brain stem
            (1) adjusts sympathetic/parasympathetic activity

  - long term regulation (minutes to days)
    1. adjustments in total blood volume via salt/water balance - urinary system and thirst (volume receptors in left atrium, osmoreceptors in hypothalamus)

- other contributing factors
    1. chemoreceptors in carotid and aortic arteries
        a. sense low O_2 and high acid
            (1) increase respiratory activity but also increase BP (signals CV center)
    2. cerebral cortex - hypothalamic pathway influence emotional/behavioral responses
    3. exercise
        a. may be unidentified "exercise centers"
    4. hypothalamic temperature regulation
        a. overrides baroreceptor reflex for skin vessels
    5. vasoactive substances from endothelial cells
    6. neurotransmitter effects in brain (poorly understood)

- Hypertension
    1. BP above 140/90 (high-normal is 135/85)
    2. cause identified in about 10% of cases (secondary hypertension)
        a. include atherosclerosis, endocrine disorders, nervous system defects
    3. primary hypertension causes may include...
        a. kidney salt regulation
        b. excessive salt intake
        c. diet low in fruit, vegetables, dairy (low in $K^+$and Ca^{2+})
        d. defects in Na^+-K^+ pumps
        e. abnormal local vasoactive substances
        f. excess vasopressin
    4. baroreceptors reset at higher level
    5. stresses heart and blood vessels
        a. congestive heart failure from increased afterload
        b. rupture of vessels - stroke, heart attack
        c. damage to vessels may cause accumulation of lipids and lead to atherosclerosis
        d. kidney failure due to damaged vessels
        e. loss of vision from damaged vessels

- hypotension
    1. BP below 100/60
    2. transient
        a. standing up - gravity decreases venous return
        b. in some people emotional stress decreases sympathetic activity (may be adaptive)
    3. when blood flow to tissues inadequate its called circulatory shock
        a. many causes
            (1) loss of blood volume (hemorrhage, diarrhea)
            (2) weakened heart
            (3) vasodilation (septic or anaphylactic)
            (4) loss of sympathetic tone (extreme pain as in crushing injury)
        b. may become irreversible

Chapter 11 **Blood**

- Basics
  - 8% of body weight, 5-5.5 liters
  - connective tissue
    1. formed elements
       a. erythrocytes (RBCs)
       b. leukocytes (WBCs)
       c. platelets
    2. matrix is plasma

- Plasma
  - 90% water
  - contains proteins, ions, buffers, respiratory gases, nutrients, wastes, hormones
  - proteins are functionally important
    1. establish osmotic pressure (holds water)
    2. 3 types
       a. albumins - bind substances for transport
       b. globulins - bind substances for transport, blood clotting, inactive precursors, antibodies
       c. fibrinogen - blood clotting

- Erythrocytes
  - carry oxygen

  - contain hemoglobin
    1. carries most of O_2 (4 O_2/molecule)
    2. carries some CO_2
    3. helps buffer blood

  - no nucleus or organelles

  - contains glycolytic enzymes for making ATP

  - contain carbonic anhydrase, which converts CO_2 to its transported form (HCO_3^-, bicarbonate)

- erythropoiesis (production of RBCs)
    1. RBCs live about 120 days and most old, fragile cells die in spleen capillaries
    2. occurs in red bone marrow (in adults - sternum, vertebrae, ends of long bones, ribs, base of skull)
        a. contains undifferentiated cells that give rise to all blood cells(pluripotent stem cells)
        b. controlled by hormone erythropoietin
            (1) released by kidneys in response to decreased O_2
            (2) restoring normal O_2 levels is negative feedback
        c. maturing cells eject nucleus/organelles
        d. process takes days to weeks depending on how many cells needed

- Leukocytes (WBCs)
    - body defense
    - originally made in red marrow in response to stimulating factors
        1. found in blood and in tissues

- Platelets
    - cell fragments produced from megakaryocytes in red marrow
        1. live about 10 days
        2. produced in response to the hormone thrombopoietin (control unknown)
        3. can be stored in spleen (as are RBCs)
        4. no nucleus, but do have organelles

    - hemostasis (stopping blood flow)
        1. vascular spasm
            a. blood flow through a break minimized by vasoconstriction (vascular response and sympathetically induced)
        2. formation of platelet plug seals break
            a. platelets stick to exposed collagen of damaged connective tissue
                (1) platelets release chemicals like ADP and thromboxane A_2 that cause more platelets to become "sticky" and build up
                (2) normal endothelium releases prostacyclin which inhibits platelet aggregation (plug does not spread beyond damaged area)
            b. actin-myosin complex in platelets contracts and strengthens plug
            c. plug releases vasoconstrictors (serotonin, epinephrine, thromboxane A_2)

3. blood clotting needed to plug larger holes
    a. clotting cascade initiated by exposure of plasma precursors to damaged vessel
        (1) series of reactions resulting in clotting
        (2) thrombin converts fibrinogen to fibrin, which forms meshwork that traps RBCs
        (3) thrombin also activates factor XIII which stabilizes meshwork
b. clot retraction
        (1) platelets contract and squeeze serum from clot
4. long term healing begins as fibroblasts from connective tissue form a scar
    a. as healing occurs plasmin dissolves clot

Chapter 12 Body Defenses

- External Defenses (first line of defense)
  - Skin (integument)
    1. physical barrier
       a. keratinocytes form barrier, also influence immune cells
    2. skin-associated lymphoid tissue (SALT)
       a. contain specialized immune cells
    3. chemical barrier
       a. secretions of sweat and oil (sebaceous) glands are toxic to bacteria

  - Mucous membranes and associated structures (line cavities open to outside of body)
    1. digestive tract
       a. salivary enzymes kill bacteria
       b. acid in stomach kills bacteria
       c. secretions contain antibodies
       d. normal intestinal bacteria outcompete pathogens (disease causing organisms)
       e. gut-associated lymphoid tissue (GALT) a.k.a. Peyer's patches contain immune cells
       f. appendix contains immune cells
    2. genitourinary tract
       a. acidic urine
       b. acidic vaginal secretions
       c. sticky mucus in genitourinary tract traps pathogens & has antibodies
          (1) swept out as organ empties
          (2) engulfed by phagocytes
    3. respiratory tract
       a. large particles filtered by hairs in nasal passages
       b. tonsils and adenoids contain immune cells
       c. sticky mucus traps pathogens in airways
          (1) cilia sweeps mucus upward (swallowed, or coughing, sneezing or expectorating removes it from body)
          (2) antibodies secreted in mucus
       d. alveolar (air sac) macrophages engulf pathogens

- Defense Cells
  - WBCs
    1. neutrophils: highly mobile phagocytes
    2. eosinophils: secrete chemicals that kill parasitic worms, involved in allergic reactions
    3. basophils: release histamine and heparin (inflammatory response) involved in allergic reactions
    4. lymphocytes: can reproduce outside bone marrow (in lymphoid tissues like lymph nodes)
        a. B lymphocytes: secrete antibodies
            (1) probably mature in bone marrow
        b. T lymphocytes: destroy virus infected and cancer cells
            (1) mature in thymus
    5. monocytes: become macrophages - large phagocytes in tissues

  - most in tissues, some circulate in blood
    1. lymphocytes (and some others) found in lymphoid tissues
        a. store, produce or process lymphocytes
        b. lymph nodes, spleen, thymus, tonsils, adenoids, appendix, SALT, GALT
        c. located to catch invaders and decrease their spread

- Nonspecific defenses (general defenses or innate immunity)
  - responses that defend against any invader or abnormal material
  - triggered by general molecular patterns associated with pathogens or other dangers
  - Inflammation (Inflammatory Response)
    1. designed to bring phagocytes and plasma proteins to injured area
        a. destroy/inactivate invaders
        b. clean up debris
        c. prepare for healing
        d. characteristics include redness, heat, swelling and pain
    2. resident macrophages begin phagocytosis
    3. histamine released from mast cells (similar to basophils, present in connective tissues) causes...
        a. vasodilation → increased blood flow (redness, heat)
        b. increased capillary permeability → plasma proteins flow out, → edema (swelling, pain)
    4. "walling off" of area due to fibrin forming interstitial fluid clots (inhibits spread of invader)
    5. neutrophils and monocytes migrate to area

a. margination - CAMs on capillary cells cause leukocytes to stick to capillary walls
b. move to tissues by diapedesis
c. leukocytes follow chemical trail to damaged tissue (chemotaxis)
d. phagocytosis occurs to recognized substances
    (1) rough surfaces of damaged cells
    (2) opsonins - chemical placed on non-self cell by immune system, links it to phagocyte (antibodies, complement)
e. phagocyte secretions (cytokines) enhance response
    (1) nitric oxide (toxic to bacteria)
    (2) lactoferrin (binds iron so bacteria can't use it to reproduce)
    (3) histamine
    (4) clotting triggers
    (5) enzymes that trigger kinin production (stimulate complement, reinforce histamine effects, activate pain receptors, act as chemotaxins)
    (6) endogenous pyrogen (EP) which causes fever and encourages inflammatory response
    (7) interleukin 1 (IL-1) enhances lymphocyte production

- Interferon
    1. released by virus-infected cells, triggers production of virus-blocking enzymes in nearby cells
    2. enhances role of phagocytes and other immune cells on virus-infected and cancer cells

- Natural killer cells
    1. similar to a type of lymphocyte, lyse virus-infected cells and cancer cells

- Complement system
    1. plasma protein precursors activated by exposure to pathogen or antibodies
        a. lyses non-self cells
            (1) membrane attack complex (MAC) inserts into bacterial membrane and pokes holes
        b. serve as chemotaxins and opsonins
        c. promote vasodilation and histamine release
        d. activate kinins

- Specific Immune Responses (adaptive immunity)
  - act on particular invaders
    1. B lymphocytes specialize in recognizing free-existing invaders like bacteria, bacterial toxins, some viruses (antibody-mediated or humoral immunity)
    2. T lymphocytes specialize in killing virus-infected and cancer cells (cell-mediated immunity)
    3. during maturation each B and T cell becomes capable of responding to a particular invader (only one specific kind of invader for each individual cell)
        a. which invaders we can respond to is genetically determined
    4. recognize antigens - large, complex molecule that the immune system can respond to
        a. usually proteins, or large polysaccharides
        b. may be on cell surface or individual molecules secreted by the pathogen
    5. self-antigens are plasma membrane glycoproteins
        a. major histocompatibility complex (MHC) is a group of genes that determines which MHC glycoproteins an individual has
        b. lymphocytes do not harm these cells under normal conditions

  - antibody mediated immunity
    1. B cells display antibodies on their surfaces and secrete them
        a. antibodies are also called gamma globulins or immunoglobulins (Ig)
        b. each antibody molecule has 2 binding sites for a specific antigen
    2. When a B cell clone is exposed to the right antigen the cells reproduce and...
        a. some become plasma cells, which secrete antibodies
        b. some become memory cells, which launch a more powerful attack if the body is exposed to that antigen again (secondary response)
    3. antibodies enhance immune responses
        a. neutralization - bind to free floating antigens and stop them from causing harm
        b. most powerful activator of complement system (so enhance inflammation)
        c. act as opsonins, enhancing phagocytosis
        d. cause agglutination of cells with antigen
        e. stimulate killer cells to lyse bacteria (similar to natural killer cells but require antibodies)
    4. active immunity occurs when an individual's B cells make antibodies
        a. infections, vaccines
    5. passive immunity is when antibodies come from a donor who is immune
        a. breast milk, snake bite/rabies/tetanus shots

- Cell-mediated immunity
  - macrophages "present antigen" to T cells (often to B cells also)
    1. macrophage phagocytizes antigen and places it on its surface
    2. appropriate type of T cell binds and is activated to reproduce and differentiate

  - T cells require both non-self and self antigen to bind and destroy a cell

  - types of T cells
    1. cytotoxic T cells (killer cells or CD8 cells)
        a. destroy virus-infected, cancer or transplanted cells
            (1) direct killing by releasing perforin to poke holes and lyse cell
            (2) indirect by signaling for apoptosis (programmed cell death)
    2. helper T cells (CD4)
        a. secrete cytokines that regulate nearly all aspects of immune response, including...
            (1) B cell growth factor
            (2) T cell growth factor (interleukin 2)
            (3) chemotaxins
            (4) macrophage-migration inhibiting factor keeps macrophages in area and makes them more powerful
    3. suppressor T cells
        a. do not need presented antigen to be active
        b. limit responses of other immune cells
        c. reproduce more slowly than other immune cells and shut down immune responses after they've served their purpose

  - Cells that blur the boundaries of innate and adaptive immunity
    1. innate lymphoid cells (ILCs) similar duties as T cells but faster and less powerful
    2. innate response activator cells (IRA) B cells recognize bacteria and produce cytokines to activate other innate cells (not typical of B cells)

Chapter 13 **Respiratory System**

- Terminology (different from text)
  - pulmonary ventilation: breathing
  - external respiration: gas exchange between the blood and alveoli (air sacs)
  - gas transport: blood transports gases to tissues (CV system)
  - internal respiration: gas exchange between the blood and tissues (CV/tissues)
  - cellular respiration: use of O_2 to produce ATP (cells)

- Functions
  - obtain O_2, eliminate CO_2
  - nonrespiratory functions
    1. route for water and heat loss
    2. enhance venous return
    3. acid-base balance (CO_2)
    4. vocalization
    5. defense against inhaled invaders
    6. sense of smell
    7. alters blood composition

- Functional anatomy
  - airways
    1. smallest bronchioles have no cartilage; smooth muscle regulates air flow (bronchoconstriction and bronchodilation)

  - alveoli (air sacs)
    1. thin walled and surrounded by capillaries
       a. large surface area for gas exchange
       b. type I cells - simple squamous epithelium
       c. type II cells - secrete surfactant
       d. macrophages fight invaders

  - pleural sacs
    1. each lung is separate
    2. intrapleural fluid lubricates surfaces and helps lungs stick to thoracic wall

- Respiratory mechanics
  - in ventilation air flows down a pressure gradient
    1. 3 important pressures
       a. atmospheric pressure (760 mmHg at sea level)
       b. intra-alveolar a.k.a. intrapulmonary pressure (varies)
       c. intrapleural pressure a.k.a. intrathoracic pressure is within the pleural sac (756 mmHg at rest)
    2. lungs will always expand to fill the thoracic cavity
       a. intrapleural fluid (sticky)
       b. transmural pressure gradient
          (1) intra-alveolar pressure always equilibrates with atmospheric pressure
          (2) greater pressure outward than inward
    3. inspiration
       a. inspiratory muscles contract (diaphragm and external intercostals)
       b. volume of thoracic cavity and lungs increases
       c. intra-alveolar pressure decreases
       d. air flows in
    4. expiration
       a. inspiratory muscles relax (quiet breathing)
       b. volume of thoracic cavity and lungs decreases
       c. intra-alveolar pressure increases
       d. air flows out
    5. forced expiration
       a. expiratory muscles contract (abdominal wall muscles and internal intercostals)

  - airway resistance
    1. adjusted to meet the body's needs
       a. parasympathetic stimulation → bronchoconstriction → increased resistance → decreased airflow
       b. sympathetic stimulation/epinephrine → bronchodilation → decreased resistance → increased airflow
  - matching airflow to blood flow (ventilation-perfusion coupling)
    1. local controls act on bronchiolar smooth muscle and on arteriolar smooth muscle
    2. bronchioles
       a. increased CO_2 → bronchodilation → increased airflow
       b. decreased CO_2 → bronchoconstriction → decreased airflow

3. arterioles
    a. decreased O_2 → vasoconstriction → decreased blood flow
    b. increased O_2 → vasodilation → increased blood flow
4. simultaneous adjustments mean air and blood not wasted
    a. examples:
        (1) if blood flow > airflow, increased CO_2 and decreased O_2 in alveoli, so bronchodilation and vasoconstriction
        (2) if airflow > blood flow, decreased CO_2 and increased O_2 in alveoli, so bronchoconstriction and vasodilation

- elastic behavior of lungs

1. healthy lungs recoil after stretching and are compliant (easy to inflate)
2. two main factors
    a. elastin fibers in lung connective tissue
    b. alveolar surface tension
        (1) water molecules lining alveoli attract each other, creating surface tension
        (2) surfactant decreases surface tension (without it lungs would collapse)
        (3) surfactant also increases compliance and reduces work needed to breathe
        (4) surfactant may also enhance phagocytosis
3. in healthy lungs breathing requires little energy
    a. 3% of total energy at rest
    b. 5% during exercise
    c. up to 30% at rest with obstructive lung disease

• Gas Exchange

- gases diffuse down partial pressure gradients (pressure exerted by a particular gas in a mixture of gases or dissolved in a body fluid)

1. alveolar PO_2 is lower than atmospheric PO_2 and alveolar PCO_2 is higher than atmospheric PCO_2
    a. water vapor in lungs dilutes gases
    b. newly inspired air mixes with old air (15% new air with inspiration)
2. CO_2 requires a smaller gradient for efficient transfer because it is more soluble (usually about equal amounts of O_2 /CO_2 exchanged)
3. at lungs
    a. PO_2 always higher in alveoli, O_2 → blood
    b. PCO_2 always higher in blood, CO_2 → alveoli

4. at tissues
    a. PO_2 always higher in blood, O_2 → tissues
    b. PCO_2 always higher in tissues, CO_2 → blood

- other factors influence the rate of gas transfer
    1. during exercise...
        a. more pulmonary capillaries open, increasing surface area for exchanges
        b. greater stretching of alveolar membranes increases surface area and thins membrane (decreased distance for diffusion)
    2. disease thickens membrane and increases distance for diffusion (pulmonary edema, pulmonary fibrosis, pneumonia

- Gas transport

  - O_2
    1. 1.5% dissolved in blood
    2. 98.5% on hemoglobin (Hb)

$$\underset{\text{(reduced Hb)}}{Hb} + O_2 \leftrightarrow \underset{\text{(oxyhemoglobin)}}{HbO_2}$$

    3. Hb saturation
        a. primary influence is PO_2
            (1) pulmonary capillaries - increased PO_2 leads to formation of HbO_2 at lungs
            (2) systemic capillaries - decreased PO_2 leads to O_2 dissociation from HbO_2 at tissues
        b. Hb-O_2 dissociation curve
            (1) plateau portion means that blood can carry nearly maximum amounts of O_2 at varying PO_2 levels (safety margin on low O_2 environments)
            (2) steep portion means that small decreases in PO_2 at active tissues allow more O_2 to be released
        c. curve shifts to the right in active tissues (more O_2 is released at active tissues at a given PO_2)
            (1) Bohr effect - increased PCO_2
            (2) increased acid (from increased CO_2 and lactic acid)
            (3) increased temperature
            (4) increased 2,3-bisphosphoglycerate (BPG), produced inside RBCs in increasing amounts when HbO_2 levels below normal

- CO_2

1. 10% dissolved in blood
2. 30% as $HbCO_2$ (carbaminohemoglobin)
    a. removal of O_2 from HbO_2 at tissues increases the affinity of Hb for CO_2 (Haldane effect)
3. 60% as HCO_3^- (bicarbonate, more soluble than CO_2)
    a. $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
    b. can occur in plasma, but more efficient in RBCs because of enzyme carbonic anhydrase
    c. HCO_3^--Cl^- carrier in RBC membrane
        (1) HCO_3^- out of RBCs at tissues, in at lungs
        (2) Cl^- into RBCs down electrical gradient at tissues, out at lungs (chloride shift)
    d. most of the accumulated H^+ binds to Hb (helps buffer the blood)

- Control of Respiration

- medullary respiratory center

1. pattern probably established by pacemaker activity in rostral ventromedial medulla (Pre-Botzinger complex)
2. dorsal respiratory group (DRG) responsible for quiet breathing
    a. inspiratory neurons terminate on motor neurons in spinal cord which supply inspiratory muscles
    b. quiet expiration begins when neurons stop firing
3. ventral respiratory group (VRG) important when demands for ventilation increase
    a. not active in quiet breathing
    b. stimulate motor neurons supplying expiratory muscles

- pons respiratory centers

1. pneumotaxic and apneustic centers "fine tune" medullary centers to produce smooth inspirations and expirations

- Hering-Breuer reflex

1. pulmonary stretch receptors in airways are activated at large tidal volumes
    a. inhibit inspiratory neurons

- Influencing factors
    1. mainly
        *a. central chemoreceptors in medulla sense increased PCO_2 (via increased H^+ in CSF) and signal respiratory centers to increase ventilation
        b. peripheral chemoreceptors known as carotid bodies and aortic bodies sense increased H^+ and signal to increase ventilation
    2. PO_2 important only at very low O_2 levels
        a. peripheral chemoreceptors signal to increase ventilation

- exercise
    1. precise triggers to increase ventilation unknown (ventilation increases before significant changes in PCO_2 and PO_2)
    2. may be...
        a. proprioceptors in muscles and joints stimulating respiratory centers
        b. increase in body temperature
        c. epinephrine
        d. input from cerebral cortex

- other factors
    1. reflexes like coughing/sneezing
    2. pain
    3. emotion
    4. swallowing

Chapter 14 **Urinary System**

- The Kidney is the major functional organ, other organs carry urine out of the body
  - basic functions
    1. water balance and osmolarity
    2. electrolyte (ion) balance
    3. maintain plasma volume, long term regulation of blood pressure
    4. acid/base balance
    5. excrete wastes (urea, uric acid, creatinine) and other materials
    6. secrete erythropoietin
    7. secrete renin (Na^+ balance)
    8. converts vitamin D to its active form

  - nephron is the functional unit of the kidney
    1. arrangement forms cortex and medulla
    2. glomerulus
       a. tuft of capillaries that filters blood
       b. renal artery branches to form afferent and efferent arteriole for each nephron
          (1) efferent arteriole divides to form peritubular capillaries (supply renal tissue with blood)
    3. tubule
       a. glomerular capsule surrounds glomerulus and collects filtrate
       b. proximal convoluted tubule (PCT)
       c. loop
       d. distal convoluted tubule (DCT)
       e. collecting duct/tubule - drains fluid from several nephrons to renal pelvis
    4. juxtaglomerular apparatus
       a. regulates kidney function
       b. macula densa - specialized cells of DCT as it passes by glomerulus
       c. granular cells (juxtaglomerular cells or JG cells) are specialized smooth muscle cells of arterioles
    5. 2 types of nephrons
       a. cortical - lie mainly in cortex (80%)
       b. juxtamedullary - loops dip to end of medulla (important in urine concentration/conserving water)
          (1) vasa recta are blood vessels that run near long loop

- 3 renal processes
    1. glomerular filtration
        a. about 20% of plasma entering glomerulus is filtered
        b. entire plasma volume filtered 65 times/day
        c. nonselective process - everything but cells and plasma proteins are filtered
    2. tubular reabsorption
        a. selective recovery of filtered substances
    3. tubular secretion
        a. selective transfer of materials from plasma in peritubular capillaries to filtrate

• Glomerular Filtration

- filtered substances pass through highly permeable filtration membrane
    1. glomerular capillaries are 100x more permeable than other capillaries
    2. basement membrane (collagen for strength and glycoproteins with a negative charge that repels plasma proteins)
    3. inner layer of glomerular capsule
        a. podocytes wrap around capillaries and form filtration slits

- glomerular capillary blood pressure forces fluid through filtration membrane
    1. higher than in other capillaries
        a. diameter of afferent arteriole larger than efferent arteriole, blood dams up and filtration occurs throughout glomerulus
    2. glomerular filtration rate (GFR)
        a. GFR = K_f x net filtration pressure
        (K_f= filtration coefficient, collective properties of filtration membrane)
        b. autoregulation
            (1) allows GFR to remain constant despite changes in BP
                (vasoconstriction/dilation of afferent arteriole)
            (2) myogenic mechanism - arteriolar smooth muscle constricts when stretched, relaxes with decreased pressure
            (3) tubuloglomerular feedback mechanism - macula densa detects changes in rate of filtrate flow or osmotic changes and signals granular cells to release vasoactive substances
                increased flow → vasoconstriction → decreased GFR
                decreased flow → vasodilation → increased GFR

(4) sufficient in MAP 80-180 mmHg range

c. extrinsic sympathetic control

(1) GFR changed based on need (override autoregulation to reg BP)

(2) baroreceptor reflex

decreased plasma volume → generalized vasoconstriction, including afferent arteriole → decreased GFR → conservation of fluids

increased BP → vasodilation → increased GFR → eliminate more fluids

(3) can alter K_f by closing off part of capillaries and filtration slits

- Tubular Reabsorption
  - typically nephrons reabsorb 99% of the water, 100% of the sugar, 99.5% of the salt that is filtered
  - different portions of tubule specialize in particular substances
  - most substances pass through tubule cells (transepithelial transport)
  - can be active or passive
    1. if <u>any</u> step is active, reabsorption of that substance is considered active

  - Na^+ reabsorption
    1. occurs via Na^+-K^+ ATPase in the basolateral membrane
       a. creates gradients for diffusion
       b. tied to reabsorption of other substances (glucose, amino acids, water, Cl^-, urea)
       c. occurs in PCT and loop - automatically reabsorb most Na^+ (92%)
       d. DCT and collecting tubule - hormonal control, reabsorption according to need
    2. renin-angiotensin-aldosterone system
       a. in response to decreased NaCl/dec. ECF volume/dec. BP, macula densa signals granular cells to release renin (an enzyme)
       b. angiotensinogen → angiotensin I
       c. angiotensin I → angiotensin II in lungs
          (1) vasoconstriction of arterioles
          (2) stimulates thirst
          (3) stimulates vasopressin release (H_2O reabsorption)
          (4) adrenal cortex releases aldosterone - promotes insertion of more Na^+ channels and Na^+-K^+ pumps into cells of DCT and collecting tubule (Cl^- and H_2O follow Na^+)

3. atrial natriuretic peptide (ANP) inhibits Na^+ reabsorption
    a. released from atria in response to increased stretch from inc ECF/inc BP
    b. decrease Na^+ reabsorption → decrease ECF and BP

- Glucose and amino acids
    1. cotransport systems driven by Na^+-K^+ pumps in PCT

- Water reabsorption
    1. passively reabsorbed throughout most of nephron (not ascending limb of loops)
    2. 80% osmotically follows solute reabsorption (water flows through channels into cells or through leaky tight junctions)
    3. 20% reabsorbed according to need in DCT and collecting tubule (hormonal control-vasopressin)

- urea reabsorption
    1. only waste product reabsorbed
    2. as H_2O reabsorbed in PCT, urea becomes more concentrated and then moves down its concentration gradient (50% reabsorbed)

• Tubular Secretion
- enhances removal of some substances
- transepithelial transport (opposite of reabsorption)

- H^+ secretion
    1. important in acid/base balance
    2. actively secreted in PCT, DCT and collecting tubules according to need (inc H^+ → increased secretion of H^+)
    3. can be coupled to Na^+ reabsorption instead of K^+ (basolateral pump in distal nephron)

- K^+ secretion
    1. reabsorption in PCT is automatic (active)
    2. controlled secretion of K^+ in DCT and collecting tubule
        a. Na^+-K^+ pump creates gradient
        b. inc plasma K^+ → inc aldosterone → inc K^+ secretion
        dec plasma K^+ → dec aldosterone → dec K^+ secretion
        c. important in maintaining membrane potential

- organic anion and cation secretion
    1. special carriers for each in PCT
    2. prostaglandins and other chemical messengers
    3. other substances like drugs or pollutants
        a. liver must convert substance to anionic form

see table Summary of Transport across Proximal and Distal Portions of the Nephron

- Variations in urine solute concentration (controlling amount of H_2O excreted)
    - countercurrent mechanism (medullary countercurrent system)
        1. long loops of juxtamedullary nephrons establish a vertical osmotic gradient in interstitial fluid of medulla
        2. vasa recta prevent loss of gradient
        3. water can be reabsorbed from collecting tubules as it flows through gradient (under control of vasopressin)

    - establishing the gradient (countercurrent multiplication) - by loop
        1. descending limb permeable to H_2O but not Na^+
        2. ascending limb pumps out Na^+ but is impermeable to H_2O
        3. as Na^+ is pumped out of ascending limb, water leaves descending limb by diffusion
            a. leads to gradient of 300-1200 mosm/L in medulla
            b. urea also contributes to gradient

    - variable H_2O reabsorption
        1. filtrate in DCT very dilute
        2. without vasopressin (antidiuretic hormone or ADH, from hypothalamus/posterior pituitary) DCT and collecting duct impermeable to H_2O
            a. H_2O not reabsorbed, urine dilute
        3. when vasopressin present (released as hypothalamus detects increased osmolarity/decreased H_2O) DCT and collecting ducts become permeable to H_2O
            a. cAMP second messenger system - results in insertion of H_2O channels in tubule
            b. water reabsorbed as it flows through medullary gradient
    - countercurrent exchange in vasa recta
        1. medullary gradient does not dissipate because of the construction of the blood supply
        2. vasa recta follow loop and exchanges of NaCl and H_2O occur so that the blood equilibrates with the surrounding interstitial fluid

- Micturition (urination)
  - urethra has two sphincter muscles that prevent leaking of urine
    1. internal urethral sphincter made of smooth muscle (involuntary)
    2. external urethral sphincter made of skeletal muscle (voluntary)
  - micturition reflex occurs when stretch receptors in bladder are activated and parasympathetic fibers stimulated
    1. occurs at 250-400 ml urine
    2. parasympathetic stimulation causes bladder to contract, opening internal sphincter and inhibiting motor neurons to external sphincter
       a. we become conscious of having to urinate, but we can temporarily override reflex until it's convenient

Chapter 16 **Digestive System**

- Basics
  - function: transfer nutrients, H_2O and electrolytes from food to body
    1. food is an energy source and contains basic building blocks of body tissues
  - 4 digestive processes
    1. motility
       a. muscular contractions that move food through digestive tract (propulsive) and mix food
    2. secretion
       a. digestive juices (enzymes, bile, mucus, hormones)
    3. digestion
       a. breaking down large molecules into smaller units
    4. absorption
       a. substances moved from digestive tract to blood or lymph

  - major and accessory organs

  - layers of digestive tract wall

  - intrinsic nerve plexuses
    1. network of nerves in digestive tract wall (enteric nervous system)
    2. influence all digestive tract activity
       a. mainly coordinate activities
    3. influenced by extrinsic nerves

  - extrinsic nerves (ANS)
    1. influences motility and secretion
       a. modify activity of intrinsic plexuses
       b. act directly on glands and smooth muscle

  - receptors and reflexes
    1. digestive tract contains
       a. chemoreceptors
       b. mechanoreceptors
       c. osmoreceptors

2. stimulation of receptors initiates reflexes
    a. short reflexes - entirely within intrinsic nerves
    b. long reflexes - also involve ANS

- gastrointestinal hormones
    1. produced in mucosa, released to blood in response to local chemical changes or nerve stimulation

- Mouth
    - mastication (chewing)
        1. mixes and breaks down food
    - saliva produced by salivary glands
        1. begins digestion of carbohydrate with salivary amylase
        2. moistens food with mucus for easy swallowing
        3. lysozyme lyses bacteria
        4. produced in response to stimulation from chemoreceptors and pressure receptors in mouth, or seeing/smelling food

- Pharynx and Esophagus
    - pathways to stomach

- Stomach
    - 3 major functions
        1. store food and release to duodenum at the appropriate rate
        2. secrete HCl and enzymes to begin protein digestion (continue carbohydrate digestion with salivary enzymes)
        3. mix food with gastric secretions to make chyme

    - 4 aspects of motility
        1. gastric filling
            a. plasticity - stomach can stretch without increasing tension
            b. receptive relaxation - eating triggers reflex relaxation
        2. gastric storage
            a. food stored mainly in body of stomach
        3. gastric mixing
            a. mostly in antrum (thicker muscle layer)

b. peristaltic contractions

4. gastric emptying

a. peristaltic waves push some chyme into duodenum

b. influencing factors (stomach)

(1) amount of chyme - more chyme increases emptying via direct effect on smooth muscle, intrinsic and extrinsic neurons, hormone gastrin

*c. influencing factors (duodenum)

(1) stimuli such as fat, acid, increased osmolarity and distention in duodenum trigger slowing of gastric emptying via neural and hormonal responses

(2) neural response - short and long reflexes (enterogastric reflex)

(3) hormonal response - enterogastrones released to blood act on stomach (secretin, cholecystokinin or CCK, gastric inhibitory peptide or GIP)

- gastric secretions come from gastric pits/gastric glands

1. oxyntic mucosa (body and fundus)

a. surface epithelial cells secrete thick alkaline mucus that protects stomach from acid and digestive enzymes

b. mucous neck cells produce watery, lubricating mucus, also divide rapidly and differentiate into other cell types (entire mucosa replaced every 3 days)

c. parietal cells secrete HCl and intrinsic factor

(1) HCl activates digestive enzymes and produces optimal pH for protein digestion; breaks down connective tissue and muscle; kills bacteria

(2) intrinsic factor allows absorption of vitamin B_{12}

d. chief cells secrete pepsinogen (inactive so cells won't be digested), which is converted to protein digestive enzyme pepsin

2. pyloric gland area (antrum)

a. secretes mucus and some pepsinogen (not HCl)

*b. G cells secrete hormone gastrin

(1) stimulates parietal and chief cells

(2) stimulates growth of mucosa in stomach and small intestine

3. control of gastric secretions

a. cephalic phase

(1) thinking about food and eating increases gastric secretion via parasympathetic stimulation

b. gastric phase

(1) protein, distention, caffeine and alcohol initiate both short and long reflexes that trigger gastrin secretion

c. intestinal phase

(1) protein stimulates release of intestinal gastrin (excitatory component)

*(2) enterogastric reflex and enterogastrones suppress secretory activity (inhibitory component)

- Small Intestine
  - major organ of digestion and absorption

  - motility: segmentation
    1. mixes chyme and exposes chyme to absorptive surfaces
    2. slowly moves chyme forward
    3. duodenum segments in response to distention
    4. ileum segments in response to gastrin when chyme is in the stomach (gastroileal reflex)

  - pancreas secretes digestive enzymes and protective alkaline fluid ($NaHCO_3$) into duodenum
    1. control
       a. cephalic phase - parasympathetic stimulation
       b. gastric phase - gastrin
       *c. intestinal phase - secretin → $NaHCO_3$, CCK → enzymes
    2. proteolytic enzymes
       a. secreted in inactive forms
       b. trypsinogen → trypsin, with enterokinase in luminal border of mucosa
       c. trypsin digests protein and converts other enzymes to active forms

          chymotrypsinogen → chymotrypsin

          procarboxypeptidase → carboxypeptidase
       d. each enzyme breaks different peptide bonds
    3. pancreatic amylase (secreted in active form)
       a. polysaccharides → disaccharides
    4. pancreatic lipase (active)
       a. triglycerides → monoglycerides + fatty acids

- liver's digestive function is to produce bile that can be stored in gall bladder until needed in the duodenum
    1. bile salts, cholesterol and lecithin are produced by hepatocytes (other fluids come from bile duct cells)
        a. bile salts emulsify fats - break up fat into droplets to expose more surface area for digestion
        b. form micelles that carry non-water soluble products of fat digestion to absorption sites on mucosa
        c. released in response to parasympathetic stimulation, secretin, *bile use
    2. other liver functions
        a. hepatic portal circulation brings venous blood from digestive tract directly to liver
            (1) processing/storage of nutrients
            (2) detoxification of wastes, drugs, etc.
        b. makes plasma proteins
        c. activates vitamin D
        d. macrophages (Kupffer cells) eat bacteria and old RBCs
        e. excretes cholesterol
        f. excretes bilirubin (from breakdown of Hb)

- small intestine adapted for absorption (lots of surface area)
    1. secretes mucus, but digestive enzymes are in epithelial cell membranes (brush border)
    2. absorbs most nutrients to its full ability (iron and Ca^{2+} regulated)
    3. Na^+
        a. active and passive
        b. Na^+-K^+ pump at basolateral side establishes gradients for passive movement
        c. H_2O and Cl^- follow
        d. also involved in secondary active transport of sugars and amino acids
    4. products of fat digestion

- Large Intestine
    - actively absorbs Na^+, H_2O and Cl^- follow
    - no digestion except bacteria digest cellulose for themselves
        1. bacteria also synthesize vitamin K, which we absorb (important in clotting)
        2. bacteria can't go backward to small intestine (ileocecal valve and sphincter)

    - secretes alkaline, lubricating mucus

- motility
    1. haustral contraction (similar to segmentation but slower)
        a. mostly short reflex control
    2. mass movements (gastrocolic reflex)
        a. strong contractions move contents to rectum for storage until defecation reflex occurs (triggered by distention)

- Hormones and other factors involved in digestive function

  - Leptin: made by fat cells, tells hypothalamus you have enough energy stored and suppresses appetite (molecular satiety signal)
  - Ghrelin: made by stomach, signals hunger and activates reward system
  - PYY: released by intestines as food moves through (satiety signal)
  - Fiber
    1. insoluble helps food move faster and generate satiety signal sooner
    2. soluble delays stomach emptying making you feel more full

Chapters 18/19 **Endocrine System**

- Basics
  - "slow" control system
  - many interactions among endocrine glands
  - interacts with nervous system (neuroendocrine reflexes)

  - acts via hormones
    1. chemical secreted into the blood that acts on target cells elsewhere in the body
        a. only target cells have receptors for a particular hormone
    2. function at very low concentrations
    3. prolonged effects
    4. includes neurohormones
    5. tropic hormones regulate hormone secretion of other glands

  - general functions
    1. regulate metabolism
    2. H_2O and electrolyte balance
    3. coping with stress
    4. growth and development
    5. reproduction
    6. RBC production
    7. digestion/absorption

  - 3 categories of hormones
  - most hormone systems operate with negative feedback
  - diurnal (circadian) rhythms
    1. hormone secretion varies throughout time (a day-days-months)
        a. set point changed by CNS
    2. negative feedback maintains level at set point for that time
    3. external cues like light/dark or activity/inactivity

  - endocrine disorders
    1. hyposecretion (genetic, dietary, toxins, immune disorder)
    2. hypersecretion (tumors)
    3. abnormality of target cell (lack of receptors or lack of enzymes for reactions)

- responsiveness of receptors
    1. action of hormone depends on number of receptors
        a. hormone influences number of its own receptors
            (1) down-regulation (more hormone → fewer receptors)
        b. other hormones influence receptors of a different hormone (number of receptors or affinity)
            (1) permissiveness - enhances response of another hormone
            (2) synergism - both hormones enhance each others response
            (3) antagonism - inhibits response of another hormone

- Pineal Gland
    - melatonin
        1. regulates biological clock
            a. cued by light/dark sensed by eyes
        2. may also...
            a. induce sleep
            b. inhibit sex hormones
            c. enhance immunity
            d. slow aging (antioxidant)

- Hypothalamus and Posterior Pituitary (neurohypophysis)
    - Hypothalamus produces hormones that are stored in posterior pituitary
        1. hypothalamus signals release with APs

    - Vasopressin (ADH)
        1. conserves H_2O (when osmolarity increased)
        2. vasoconstrictor (when ECF/BP decreased)

    - Oxytocin
        1. uterine contractions during childbirth
            a. estrogen has permissive effects
            b. triggered by neuroendocrine reflexes (baby's head pushing against cervix)
        2. milk ejection
            a. triggered by baby nursing

- Hypothalamus and Anterior Pituitary (adenohypophysis)

  - Anterior pituitary produces hormones and releases them in response to hormones from hypothalamus

    1. hypothalamus secretes tropic hormones (releasing and inhibiting hormones)
    2. anterior pituitary tropic hormones act on other endocrine glands
        a. thyroid stimulating hormone (TSH, thyrotropin)
            (1) growth and secretion of thyroid gland
            (2) thyrotropin releasing hormone (TRH)
        b. adrenocorticotropic hormone (ACTH, adrenocorticotropin)
            (1) growth and secretion of adrenal cortex (cortisol)
            (2) corticotropin releasing hormone (CRH)
        c. gonadotropins
            (1) secretion of sex hormones by gonads
            (2) gonadotropin releasing hormone (GnRH)
        d. growth hormone (GH, somatotropin)
            (1) regulates growth and metabolism
            (2) growth hormone releasing hormone (GHRH) and growth hormone inhibiting hormone (GHIH)
    3. nontropic anterior pituitary hormone
        a. prolactin (PRL)
            (1) breast development and milk production in typical female
            (2) prolactin releasing factor (PRF) and prolactin inhibiting hormone (PIH)

  - Growth Hormone

    1. stimulates production of IGF-1 (somatomedins) mainly in liver that then act on target cells (most cells) to promote growth
        a. growth of cells in size/number
            (1) stimulates protein synthesis and cellular uptake of amino acids
            (2) inhibits protein breakdown
        b. growth of bones in length/thickness
    2. conserves glucose (for brain) and use fat stores
        a. increases blood fatty acids for muscle use
        b. triggered by exercise, stress, changes in blood nutrient levels such as increase in amino acids, decrease in fatty acids
        c. maintains body during fasting

- Thyroid Gland
  - Thyroid Hormone (many effects)
    1. mix of T_3 and T_4
    2. acts on most cells
    3. increases overall metabolic rate
    4. permissive effects on E and NE
    5. critical for normal nervous system activity
    6. critical for growth, increases GH secretion and has permissive effects
    7. disorders among most common in endocrine system
        a. hypothyroidism - decreased MR, cold intolerant, gain weight, fatigue, slow reflexes
        b. hyperthyroidism - increased MR, perspiration, loss of weight, weakness, palpitations, irritability, bulging eyes

  - Calcitonin
    1. involved in Ca^{2+} balance
        a. inhibits breakdown of bone
        b. protects bones when there's high Ca^{2+} demand (pregnancy, breast feeding)

- Adrenal Cortex (steroid hormones)
  - Mineralocorticoids
    1. influence mineral balance (e.g., aldosterone)

  - sex hormones
    1. similar or identical to gonadal hormones

  - Glucocorticoids
    1. cortisol (stress response; makes energy and building blocks available)
        a. increases blood glucose
            (1) inhibits uptake by most tissues, sparing it for brain
            (2) gluconeogenesis by liver (aa → glucose)
        b. increases blood aa and fatty acids
            (1) stimulates breakdown of protein and fat
        c. permissive actions on hormones of adrenal medulla (catecholamines)
        d. important in adaptation to stress
        e. alters mood and behavior (mechanisms unclear)
        f. anti-inflammatory

- Adrenal Medulla
  - secretes both NE and E (E more important)

  - Epinephrine
    1. sympathetic effects
       a. inc HR and CO, vasoconstrictor → inc BP (α and β_1)
       b. vasodilation in skeletal muscle and heart (β_2)
       c. bronchodilation (β_2)
       d. also increases alertness, sweating, dilates pupils
    2. metabolic effects (stress response makes energy and building blocks available)
       a. increases blood glucose
          (1) stimulates gluconeogenesis and glycogenolysis in liver, glycogenolysis in skeletal muscle
          (2) inhibits secretion of insulin, simulates secretion of glucagon
       b. increases blood fatty acids
          (1) breakdown of fats
       c. increases overall metabolic rate

- Pancreas
  - Insulin
    1. stores energy as body absorbs nutrients (absorptive state)
       a. decreases blood glucose
          (1) glucose → cells (increases transporters)
          (2) glycogenesis in liver (glucose → glycogen)
          (3) inhibits glycogenolysis and gluconeogenesis in liver
       b. decreases blood fatty acids
          (1) glucose → adipose tissue to form fatty acids and glycerol
          (2) fatty acids → cells
          (3) inhibits lipolysis
       c. decreases blood amino acids
          (1) aa → cells and made into proteins
          (2) inhibits protein breakdown
    2. diabetes most common endocrine disorder

- Glucagon

1. maintains levels of blood nutrients (postabsorptive state, opposite of insulin), major effects are on liver

a. increases blood glucose

(1) decreases glycogenesis

(2) increases glycogenolysis and gluconeogenesis

b. increases blood fatty acids

(1) increases lipolysis

(2) decreases lipid synthesis

- Parathyroid

- Parathyroid Hormone (PTH)

1. involved in Ca^{2+} balance (opposite of calcitonin)

a. increases plasma Ca^{2+}

(1) breaks down bone

(2) stimulates reabsorption by kidneys

(3) helps activate vit D, which enhances absorption of Ca^{2+} from diet

2. also involved in PO_4^{3-} balance

a. decreases plasma PO_4^{3-}

(1) increases excretion by kidneys (in bone, would ppt in blood w/ Ca^{2+})

Chapter 20 **Reproductive System**

- Basics
  - Primary reproductive organs (gonads)
    1. major functions
       a. produce gametes (gametogenesis)
          (1) sperm in typical male
          (2) ova in typical female
       b. secrete sex hormones (androgens & estrogens)
          (1) mainly testosterone (male)
          (2) mainly estrogen & progesterone (female)
          (3) important in the development of secondary sex characteristics (hair distribution, body shape, voice change) as well as major reproductive functions and development

  - essential reproductive functions in the typical male
    1. spermatogenesis
    2. delivery of sperm to female

  - essential reproductive functions in the typical female
    1. oogenesis
    2. receive sperm and transport for fertilization
    3. maintain fetus
    4. parturition and nourishment of infant

  - sex differentiation

- Spermatogenesis
  - begins at puberty

  - parts of sperm
    1. head contains DNA
       a. acrosome has enzymes to penetrate egg
    2. midpiece has mitochondria
    3. tail is for movement

- control of spermatogenesis
    1. an increase in GnRH from hypothalamus occurs at puberty
        a. probably due to a decrease in melatonin
    2. anterior pituitary hormones secreted (gonadotropins)
        a. luteinizing hormone (LH a.k.a. ICSH) → testosterone from interstitial cells → mitosis/meiosis of germ cells
        b. follicle stimulating hormone (FSH) → spermiogenesis (sperm remodeling)

- Semen
    - produced by different glands
        1. seminal vesicles (about 70%)
            a. fructose for energy
            b. prostaglandins for smooth muscle contraction in male and female reproductive tracts (transport)
            c. fibrinogen for clotting
        2. prostate (about 30%)
            a. alkaline fluid neutralizes acidic female reproductive tract
            b. enzymes activate clotting
            c. enzymes break down clot (fibrinolysin)
        3. bulbourethral glands
            a. neutralize acidic male urethra

- Oogenesis
    - begins during fetal development
        1. arrested during meiosis
        2. will not complete meiosis unless fertilized
        3. lots of cytoplasm, organelles

- Ovarian cycle
    - increase in GnRH occurs at puberty
        1. due to decrease in melatonin and increase in % body fat
    - follicular phase
        1. LH → thecal cells make androgen (DHEA)
        2. FSH → granulosa cells make estrogen from androgen
        3. developing follicle makes low levels of estrogen (negative feedback)

- ovulation
    1. LH surge triggers release of ovum
        a. due to high estrogen levels from developed follicle (positive feedback)

- luteal phase
    1. high LH level triggers development of corpus luteum
        a. secretes progesterone (powerful negative feedback on LH) and some estrogen
        b. LH declines → corpus luteum degenerates → progesterone decreases
    2. if pregnancy occurs developing zygote produces human chorionic gonadotropin (hCG) that acts like LH and maintains corpus luteum

• Uterine cycle
- proliferative phase
    1. estrogen stimulates growth of endometrium and synthesis of progesterone receptors in endometrium

- secretory phase
    1. progesterone further prepares endometrium (loosens connective tissue, blood vessel growth, secretes glycogen, decreases contractility of uterus)

- menstrual phase
    1. endometrium breaks down from lack of estrogen and progesterone (due to neg feedback effects of progesterone on LH)