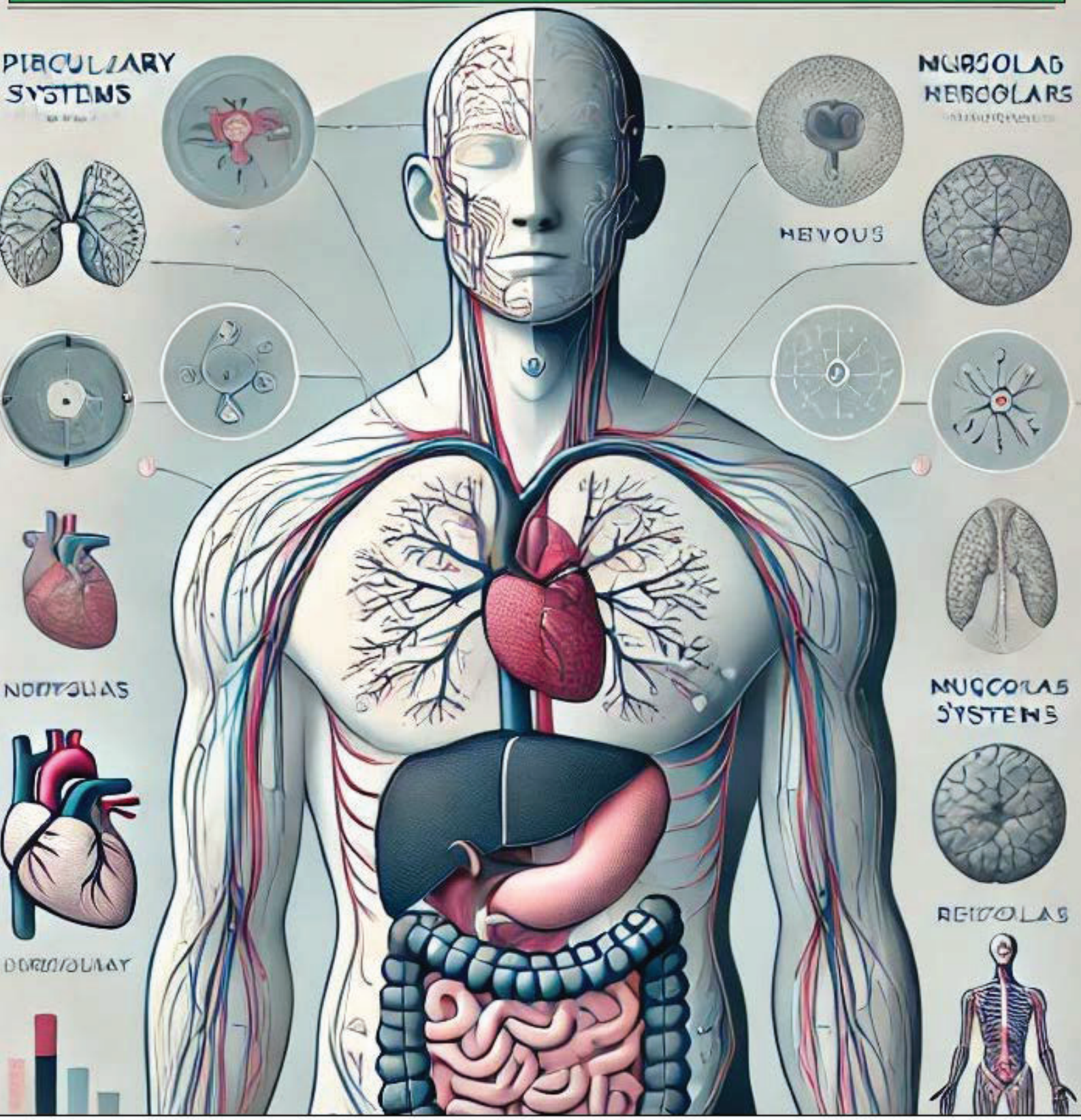
Constantin Munteanu

Basic Physiology



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Preface

This book, Basic Physiology, by Constantin Munteanu, emerges from a deep commitment to expanding the understanding of physiological principles and their pivotal role in the broader field of biomedical sciences. In a time marked by rapid advancements in health sciences, this work serves as a foundational text for students entering the field and a detailed reference for professionals seeking to revisit or deepen their knowledge.

Physiology, as a discipline, explores the mechanisms that govern the function and regulation of living organisms, bridging knowledge from molecular interactions within cells to complex systemic functions that sustain life. The author approaches this task with a structured framework integrating classical physiology concepts with current advancements and practical insights. The book provides a thorough grounding in cellular and molecular physiology, explaining the cellular components and bioelectric properties that underlie nerve impulse propagation, muscle contractions, and the orchestration of metabolic pathways.

Divided into key thematic sections, this book offers an in-depth examination of human physiological systems, from neural and cardiovascular to respiratory and endocrine, detailing the regulatory mechanisms that maintain homeostasis under varied physiological demands. Emphasis is placed on the body's adaptive responses to internal and external stressors, underscoring the relevance of physiological knowledge in fields such as sports science, rehabilitation, and clinical medicine.

In preparing Basic Physiology, the author has drawn on contemporary literature and empirical findings, making it a comprehensive reference that aligns with the educational needs of students and the research needs of professionals. With clear language, illustrative examples, and practical applications, this book is poised to significantly contribute to physiological education and professional practice, enhancing the reader's ability to understand and apply physiological principles in varied biomedical contexts.

As the reader journeys through this text, they are invited to acquire knowledge and appreciate the interconnectedness of physiological processes and the elegance of regulatory mechanisms in sustaining life. This work aspires to cultivate an appreciation for the human body's complexity and resilience and an understanding of how knowledge in physiology can be leveraged to promote health and well-being across diverse fields of application.

October 2024, Iași
Assoc. Prof. Constantin Munteanu

Constantin Munteanu

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Course 1 / Practical Session 1: Introduction to Medical Physiology. Elements of Cellular and Molecular Physiology. Sub-topic: Electrical Membrane Phenomena and Ionic Channels

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1. Introduction to Cellular and Molecular Physiology

- Definitions: Cellular and molecular physiology.
- Functional levels of organization: chemical, cellular, tissue, organ, and organism.
- Concepts of homeostasis and feedback mechanisms (negative and positive feedback loops).

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2. Electrical Membrane Phenomena

- Resting membrane potential: concept and measurement.
- Ion distribution across the cell membrane (Na+, K+, Cl-) and its influence on membrane potential.
- Mechanisms of maintaining the resting potential: Na+/K+ ATPase pump.
- Concept of action potential: depolarization, repolarization, and hyperpolarization phases.

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3. Ionic Channels: Types and Functions

- Classification of ion channels:
  - Voltage-gated channels (Na+, K+, Ca2+, Cl-).
  - Ligand-gated channels.
  - Mechanosensitive and temperature-sensitive ion channels.
- Gated vs. non-gated channels: regulation of ion flow.
- Functional roles of ion channels in different tissues: neurons, muscle fibers, cardiac cells.
- Clinical relevance: ion channelopathies.

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4. Action Potential and Signal Propagation

- Threshold stimulus and initiation of an action potential.
- Phases of action potential: depolarization, repolarization, refractory periods.
- Saltatory conduction in myelinated axons and continuous conduction in unmyelinated axons.
- Propagation of action potentials in neurons and muscle fibers.

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5. Synaptic Transmission and Neuromuscular Junction

- Structure and function of synapses (chemical vs electrical).
- Role of neurotransmitters: acetylcholine, dopamine, and others in synaptic transmission.
- Neuromuscular junction: transmission of signals from motor neurons to skeletal muscles.

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6. Signal Transduction Pathways Involving Ion Channels

- Overview of G-protein coupled receptors (GPCR) and ion channel regulation.
- Phospholipase C activation, IP3, and calcium signaling.
- Role of second messengers such as cAMP and Ca2+ in regulating ion channels.

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7. Practical Applications and Clinical Implications

- Clinical relevance of membrane potential and action potentials in cardiac arrhythmias.
- Channelopathies: diseases caused by dysfunctional ion channels (e.g., epilepsy, cystic fibrosis).
- Pharmacological modulation of ion channels: calcium channel blockers, sodium channel inhibitors.

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8. Review and Case Studies

- Case studies on muscle fatigue, nerve injuries, and cardiac abnormalities.
- Integration of ionic channel functions with clinical diagnostics.

Examination and Assessment

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1. Introduction to Cellular and Molecular Physiology

Definitions: Cellular and Molecular Physiology

- Cellular physiology explores how cells function, interact, and maintain internal stability.
- Molecular physiology focuses on molecular mechanisms, including protein function, gene expression, and molecular interactions in maintaining cell function and homeostasis.

Approaches to Physiology

- **Teleological approach**
  - –Is thinking about the " why "
    - Why do RBCs transport oxygen?
      - –" because cells need oxygen and RBCs bring it to them"
- **Mechanistic approach**
  - –Thinking about physiological processes - the " how "
    - How do RBCs transport oxygen?
      - – "Oxygen binds to hemoglobin molecules contained in RBCs"

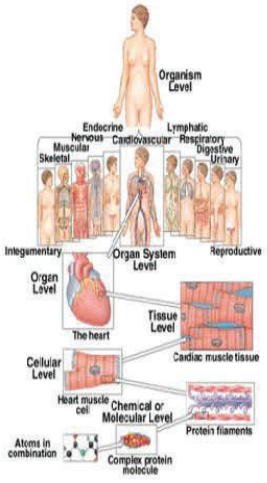
The Specialties of Physiology

- Cellular physiology
- Special physiology
  - –(e.g. ergophysiology)
- Systemic physiology
  - –(e.g. cardiovascular Physiology)
- Pathological physiology - Pathophysiology

Functional Levels of Organization

1. Chemical Level: This includes atoms and molecules like proteins, lipids, nucleic acids, and carbohydrates that are essential to cellular structure and function.
2. Cellular Level: The cell is the basic unit of life, consisting of organelles that carry out specific functions (e.g., mitochondria for ATP production, the nucleus for genetic information storage).
3. Tissue Level: Groups of similar cells performing a common function. There are four primary types: epithelial, connective, muscle, and nervous tissue.
4. Organ Level: Organs consist of different types of tissues working together for a common function (e.g., the heart, liver).
5. Organism Level: All organ systems functioning cohesively to sustain life and maintain homeostasis.

Functional levels of organization



* **Whole body level** • Organism — *Homo sapiens*
* **Body system level** • *Organ systems* — Integumentary, Nervous, Skeletal, Endocrine, Muscular, Cardiovascular, Lymphatic, Urinary, Respiratory, Digestive, Reproductive
* **Organ level** • *Organ* — Contain various tissue types; Heart, lung, pancreas, stomach, brain, etc....
* **Tissue level** • *Tissues* — Comprised of various cell types; Connective, muscle, nervous, epithelium
* **Cellular level** • *Cellular* — Comprised of many macromolecular complexes; The most basic functional unit of any multicellular organism
* **Chemical or molecular level** • *Chemical* — *Molecules*: Complex proteins comprised of atoms (DNA); *Atoms*

Physiological Variables

- Gender, age, diet, weight, physical activity
- Typical physiological values
  - –reference male
    - *22 years old, 80 kg, light physical activity*
    - *consumes 2800 kcal/day*
  - –reference female
    - *21 years old, 60 kg and 2000 kcal/day*
- *Overmedication of elderly*

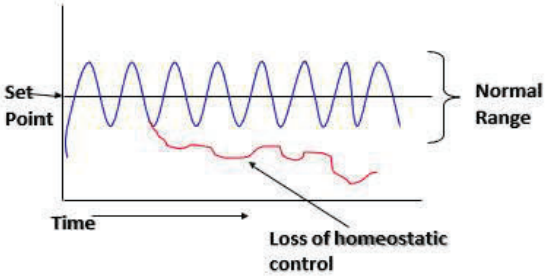
Concepts of Homeostasis and Feedback Mechanisms

- Homeostasis is the process of maintaining a stable internal environment. It is vital for the proper function of enzymes, membrane potentials, and the balance of bodily fluids.
- Negative feedback loops (e.g., body temperature control, blood glucose regulation) work by counteracting changes to bring conditions back to a set point. This is the most common regulatory mechanism.
- Positive feedback loops (e.g., blood clotting, childbirth) amplify changes, leading to more rapid or intense responses.

Homeostasis

"The process of maintaining a relatively constant internal environment within an organism"

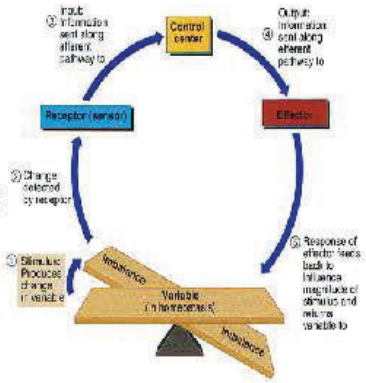
(body temperature, heart rate, blood glucose levels, etc..)



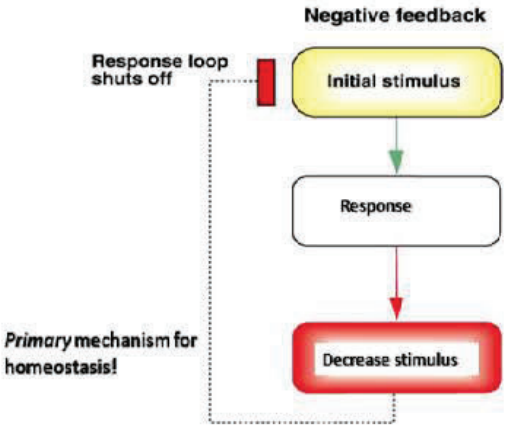
The term homeostasis is used by physiologists to mean the maintenance of nearly constant conditions in the internal environment. Essentially all organs and tissues of the body perform functions that help maintain these relatively constant conditions. For instance, the lungs provide oxygen to the extracellular fluid to replenish the oxygen used by the cells, the kidneys maintain constant ion concentrations, and the gastrointestinal system provides nutrients.

Homeostatic regulation involves

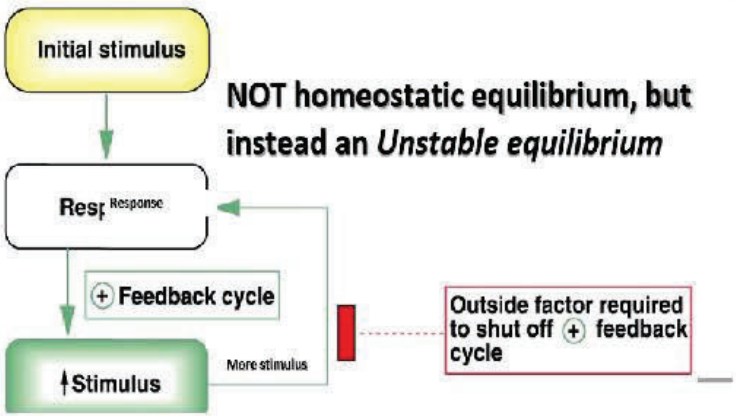
- A receptor (*input signal*)
- A control center
- An effector (*output/efferent signal*)



Negative Feedback



Positive feedback



NOT homeostatic equilibrium, but instead an *Unstable equilibrium*

Harmful Positive Feedback Loop

- Fever >36°Celsius
  - –metabolic rate increases
  - –body produces heat even faster
  - –body temperature continues to rise
  - –further increasing metabolic rate
- Cycle continues to reinforce itself
- Becomes fatal at 45 °Celsius
  - – Damage to brain occurs around 41.6°Celsius degrees

2. Electrical Membrane Phenomena

Resting Membrane Potential: Concept and Measurement

- The resting membrane potential (RMP) is the electrical potential difference across the plasma membrane when the cell is not sending signals. It is usually around -70 mV in neurons, with the inside of the cell being negative relative to the outside.
- This potential arises from the uneven distribution of ions, particularly Na^+, K^+, Cl^-, and negatively charged proteins (A^-), as well as selective membrane permeability.

Ion Distribution Across the Cell Membrane

- Na^+: High concentration outside the cell (~145 mM) and low inside (~12 mM).
- K^+: High concentration inside the cell (~150 mM) and low outside (~5 mM).
- Cl^-: Higher outside the cell, contributing to the charge difference.
- Large Anions (A^-): These negatively charged molecules, including proteins, are trapped inside the cell, helping to maintain the negative interior charge.

Mechanisms of Maintaining the Resting Potential

- The Na^+/K^+ ATPase pump plays a vital role in maintaining the RMP by actively pumping 3 Na^+ out of the cell and 2 K^+ in, utilizing ATP. This pump prevents Na^+ and K^+ equilibrium, ensuring a negative intracellular environment.
- K^+ leakage channels allow K^+ to move out of the cell more easily than Na^+ enters, creating a negative charge inside the cell relative to the outside.

Concept of Action Potential: Depolarization, Repolarization, and Hyperpolarization Phases

- Depolarization: Triggered when a stimulus causes Na^+ channels to open, allowing Na^+ to enter the cell and making the inside more positive.
- Repolarization: K^+ channels open, allowing K^+ to exit, restoring the negative membrane potential.
- Hyperpolarization: K^+ channels stay open longer than necessary, causing the membrane potential to dip below its resting value before stabilizing.

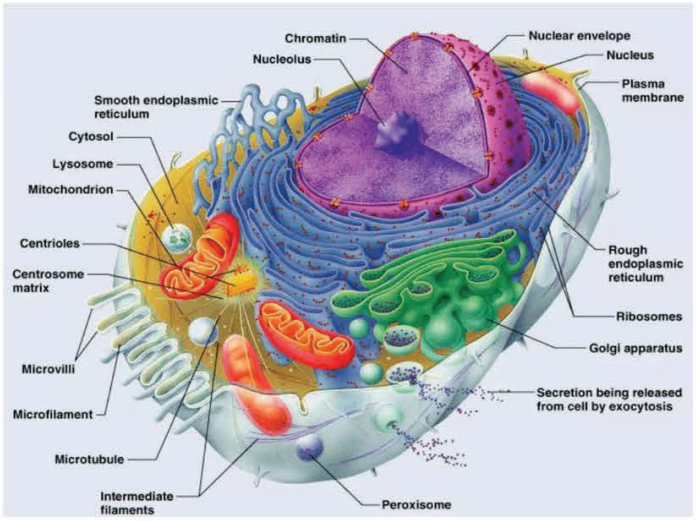
Typical cell & variation

Structure : - Limiting membranes

Cell Organelles

– membrane bound

– without membrane



- **Is surrounded by extracellular fluid, which is the interstitial fluid of the tissue**
- **Has an outer boundary called the *cell membrane, plasma membrane, or plasmalemma***

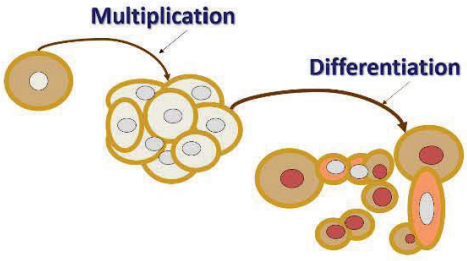
Structure & functions of Organelles

Functions of the cell as a whole

- **Obtaining O2 & nutrients from the environment**
- **Performing chemical reactions**
- **Elimination of waste products**
- **Synthesis of proteins for structure, growth**
- **Controlling exchange of material**
- **Intracellular movement of materials**
- **Sensitiveness &response to the environment**
- **Reproducing**

Transition

unicellular organism → multicellular organism



Other functions

-Endocytosis
- Pinocytosis
- Receptor mediated
- Phagocytosis

- Exocytosis

- Intercellular junctions
  - Tight junctions
  - Gap junctions
  - Desmosomes

- Movement of cilia, flagella

Intercellular communication

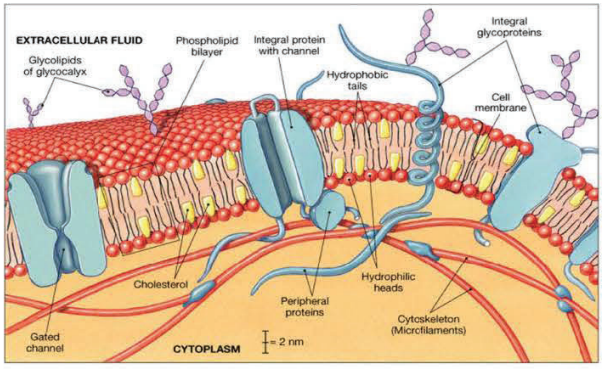
- Paracrine
- Endocrine
- Neurocrine

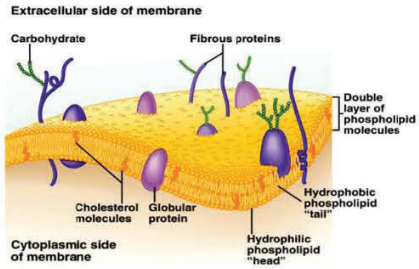
Intercellular communication

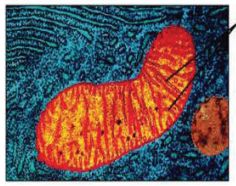
transport of substances across the cell membrane

Cell Membrane

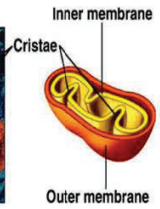
- Where does most "physiology" occur?
  - Cell membrane
- Cell membrane composition
  - Lipids
    - » *phospholipid bilayer*
    - » Cholesterol
  - Carbohydrates (sugars)
  - *Proteins*







A



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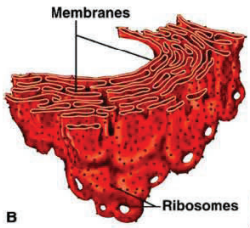

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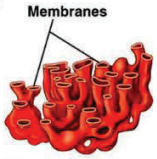

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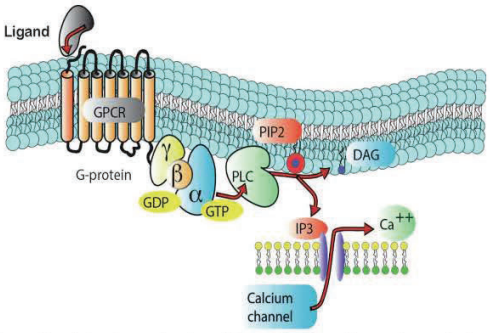
Cell membrane functions

1. Forms physical boundary of the cell
2. *Selectively permeable* – regulates transport across the membrane
3. Structural support
4. *Motility*– facilitated by the presence of cilia (moves EC fluid, flagellum (moves cell), etc.
5. *Signal Transduction- movement of a stimulus from one form to another*
6. Cellular recognition- autoimmune conditions



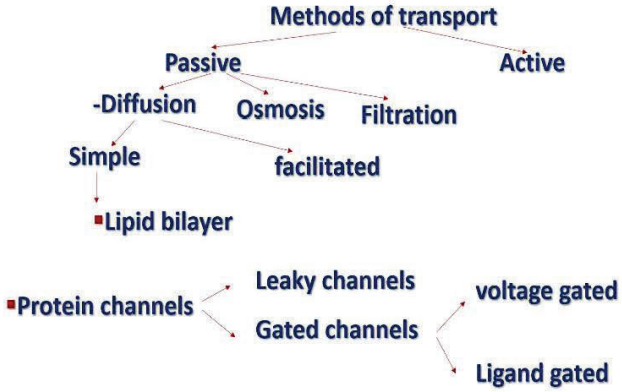
G protein-mediated signal transduction. A ligand binds to a G protein-coupled receptor (GPCR) in the membrane. This, in turn, activates a phospholipase C, which hydrolyzes phosphatidylinositol biphosphate (PIP_2) to form diacylglycerol (DAG) and inositol triphosphate (IP_3). IP_3 acts to increase cytosolic calcium as part of a signal transduction cascade.

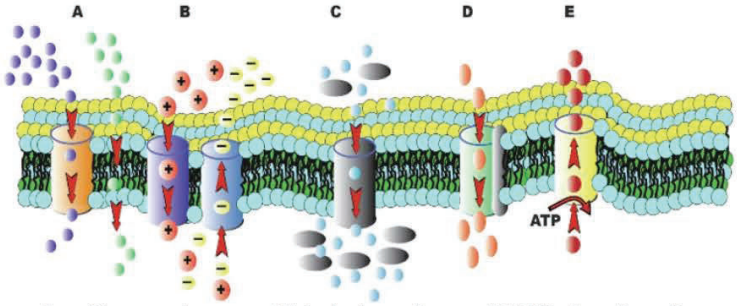
Membrane Proteins

1) Integral membrane protein
   - normally spans membrane - "transmembrane" protein
   - Crosses the membrane
2) Peripheral membrane protein
   - bound to the inner or outer surface (two com together to make tight junctions
3) *Anchoring proteins (junction proteins)*
   - attach cell membrane to *structures* : cytoskeleton
   - attach cell membrane to other membranes: *intercalated discs*
   - *These proteins can degrade when metabolized*
4) Enzymatic Proteins (help break down other substances)
   - Binds enzymes to catalyze intracellular or extracellular reactions
   Example: *peptidases*
5) Receptor proteins
   Bind to *ligands* , causes cells to respond
   Ex: Insulin, antigen, glucose, neurotransmitters, serotonin, epinephrine, ect.
6) Carrier proteins *transport* solutes across membranes
   - Includes uniport, symport, and *antiport*
   'ATP dependent' - *Na+ K*- exchange protein
   'ATP independent'- neurotransmitter transporters
   NEVER FORMS AND OPEN CHANNEL

7a) Non gated ion channel proteins
- "Non-gated"- *always open*
  - Leak Channel or pores (Cl^- channel, K^+ channel, etc.)
  - Selectivity determined by channel diameter and electrical charge of amino acids

7b) Gated ion channels
- "gated" = *opening/closing*
  - "gated" by voltage change (Na^+, K^+, Ca^{2+} channels)
  - "gated" by *chemical ligand (chemical binds to receptor)* (acetylcholine receptor)
  - "gated" by physical change (physical distortion of membrane) (*temperature*, force)

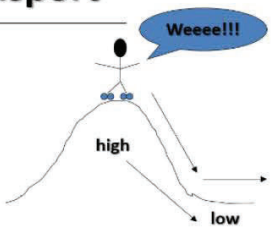




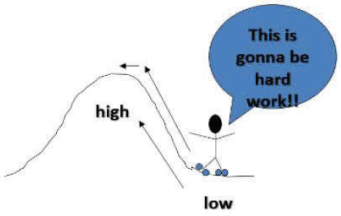
Examples of transport across a biological membrane. (A) Diffusion of small hydrophilic or hydrophobic particles driven by a concentration gradient. (B) Diffusion of hydrophilic or charged particles driven by a voltage gradient. (C) Osmosis, diffusion of solute driven by a concentration gradient of a nonpermeable compound. (D) Facilitated diffusion. (E) Active transport against a concentration gradient.

Types of Cellular Transport

- **Passive Transport**
  cell doesn't use energy
  1. Diffusion
  2. Facilitated Diffusion
  3. Osmosis



- **Active Transport**
  cell does use energy
  1. Protein Pumps
  2. Endocytosis
  3. Exocytosis



Types of Passive Transport

Diffusion

Facilitative Diffusion – diffusion with the help of transport proteins

Osmosis – diffusion of water

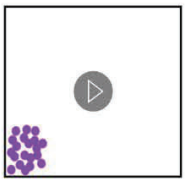
Passive Transport: 1. Diffusion

1. Diffusion: random movement of particles from an area of high concentration to an area of low concentration.

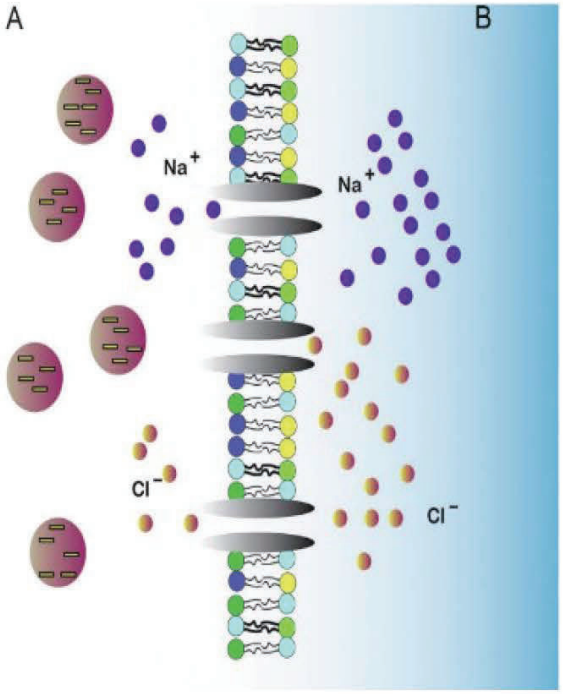
   (High to Low)

- Diffusion continues until all molecules are evenly spaced (equilibrium is reached)-*Note:* molecules will still move around but stay spread out.

Simple Diffusion Animation

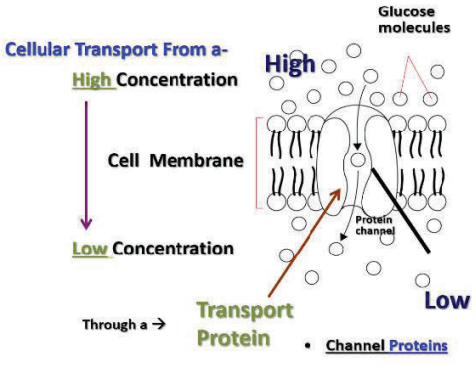


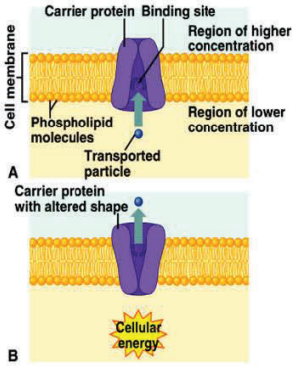


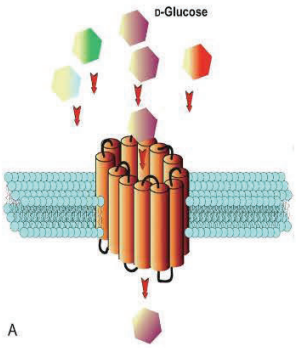


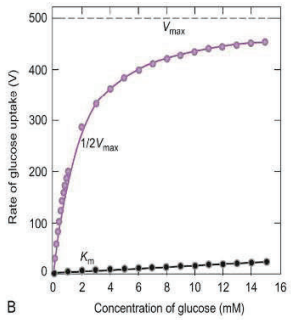
The Donnan effect. A semipermeable membrane will allow the diffusion of Na^+ and Cl^- ions, but not the negatively charged protein, in chamber A. Initially, there is an equal number of cations and anions in chambers A and B, which means that the Cl^- is at much greater concentration in B than in A to balance the anionic charge of the impermeable protein. With time, Cl^- will flow down its concentration gradient from B to A. To maintain electroneutrality, Na^+ would also move from B to A. However, this would cause the osmotic concentration to be greater in chamber A than in chamber B; therefore water moves from B to A.

Passive Transport: 2. Facilitated Diffusion



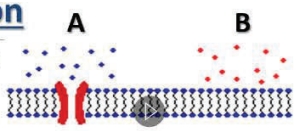






Glucose transport into red blood cells: facilitated diffusion. (A) A glucose transport protein (permease) for glucose. (B) Glucose moves down its concentration gradient into red blood cells at a rate much faster than would be predicted by simple diffusion through the lipid bilayer *(black line)*. The plot for rate of glucose uptake versus external glucose concentration is hyperbolic *(red line)*. The rate increases with external glucose concentration until it reaches a maximal velocity (V_{max}). The K_m is the concentration of external glucose at which half maximal velocity is reached.

Passive Transport: 2. Facilitated Diffusion



2. Facilitated diffusion: diffusion of specific particles through transport proteins found in the membrane
   a. Transport Proteins are specific – they "select" only certain molecules to cross the membrane
   b. Transports larger or charged molecules

Facilitated diffusion (Channel Protein)

Diffusion (Lipid Bilayer)

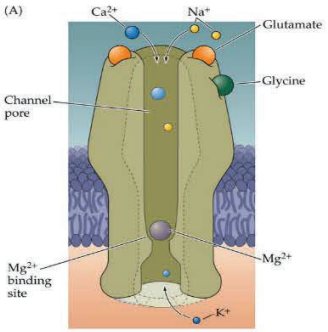


Carrier Protein

Types of ion channels

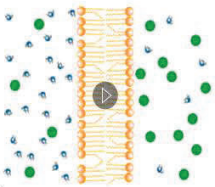
NMDA receptors

N-methyl-D-aspartate receptor

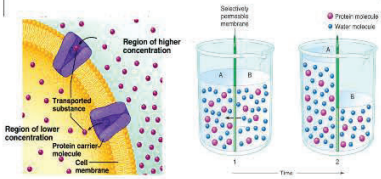


Passive Transport: 3. Osmosis

Osmosis animation



• 3.Osmosis: diffusion of *water* through a selectively permeable membrane
• Water moves from high to low concentrations

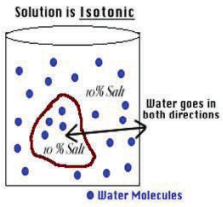


•Water moves freely through pores.
•Solute (green) to large to move across.

Isotonic Solution

• Osmosis Animations for isotonic, hypertonic, and hypotonic solutions

***Isotonic*: The concentration of solutes in the solution is equal to the concentration of solutes inside the cell.**



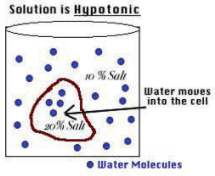


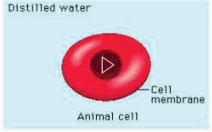
Result: Water moves equally in both directions and the cell remains same size! (Dynamic Equilibrium)

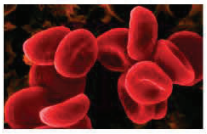
Hypotonic Solution

• Osmosis Animations for isotonic, hypertonic, and hypotonic solutions

***Hypotonic*: The solution has a lower concentration of solutes and a higher concentration of water than inside the cell. (Low solute; High water)**





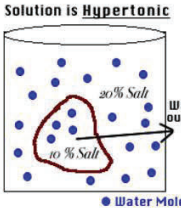


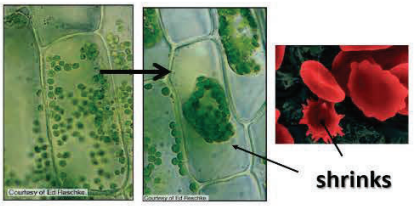
Result: Water moves from the solution to inside the cell): Cell Swells and bursts open (*cytolysis*)!

Hypertonic Solution

• Osmosis Animations for isotonic, hypertonic, and hypotonic solutions

***Hypertonic*: The solution has a higher concentration of solutes and a lower concentration of water than inside the cell. (High solute; Low water)**





Result: Water moves from inside the cell into the solution: Cell shrinks (*Plasmolysis*)!

Active transport

- Primary active transport
- Secondary active transport

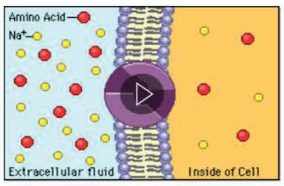
Types of transporters

Uniport | Synport | Antiport

Types of Active Transport

1. Protein Pumps - transport proteins that require energy to do work

- **Example: Sodium / Potassium Pumps are important in nerve responses.**

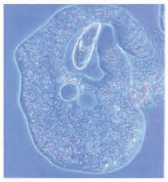


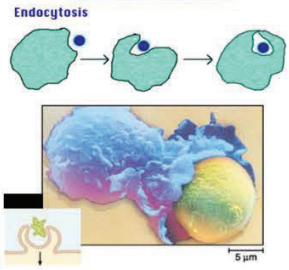
Protein changes shape to move molecules: this requires energy!

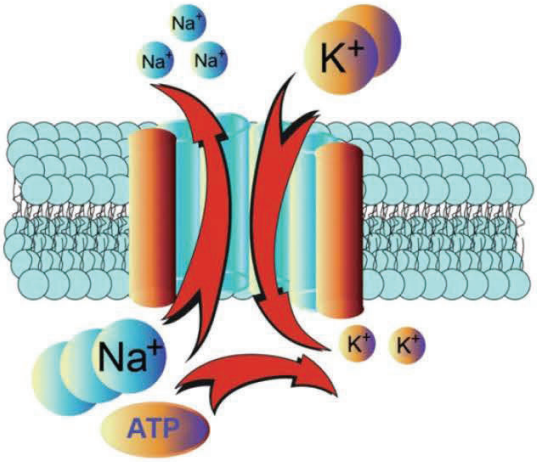
Types of Active Transport

2. Endocytosis: taking bulky material into a cell

- Uses energy
- Cell membrane in-folds around food particle
- *"cell eating"*
- forms food vacuole & digests food
- This is how white blood cells eat bacteria!







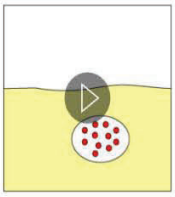
The Na/K-ATPase is an electrogenic pump. It moves three Na^+ ions out of the cell and two K^+ ions into the cytoplasm at the expense of ATP hydrolysis to ADP and inorganic phosphate.

Types of Active Transport

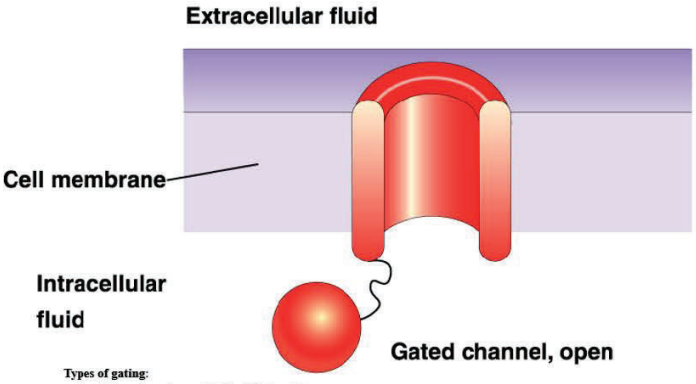
3. Exocytosis: Forces material out of cell in bulk

- membrane surrounding the material fuses with cell membrane
- Cell changes shape – requires energy
- EX: Hormones or wastes released from cell

Endocytosis & Exocytosis animations

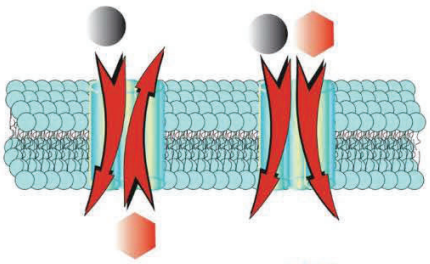


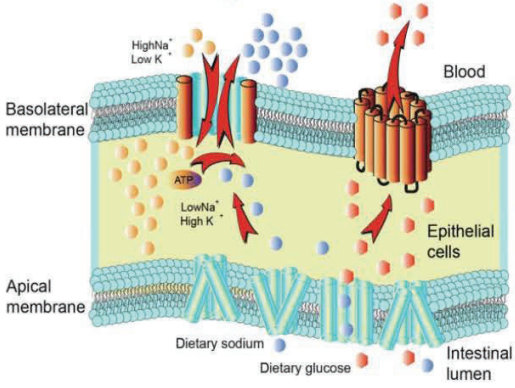
Gated Channel Proteins



Types of gating:

- "gated" by voltage change (Na^+, K^+, Ca^{2+} channels)
- "gated" by *chemical ligand (chemical binds to receptor)* (acetylcholine receptor)
- "gated" by physical change (physical distortion of membrane) (*temperature*, force)





Coupled transport. The transport of one molecule across a biological membrane can be coupled by the transport protein to the movement of another molecule. If the movement of both molecules is in the same direction, the cotransport is referred to as *symport*. If the molecules are being moved in opposite directions, the cotransport is referred to as *antiport*.

Transport of glucose into and out of intestinal epithelial cells. Glucose enters from the intestinal lumen through the apical membrane of the epithelial cells by a glucose Na^+ symport transporter. The binding of one Na^+ molecule and one glucose molecule to separate sites on the extracellular domain of a glucose Na^+ symport protein causes the transporter to change conformation. The change of conformation creates a channel through which Na^+ and glucose can be transported into the cytosol. The symport protein then returns to its original conformation. The Na^+ ions are pumped back out of the cell by Na/K-ATPase, located on the basolateral membrane. Glucose then exits the cell by facilitated diffusion, by permeases located in the basolateral membrane.

3. Ionic Channels: Types and Functions

Classification of Ion Channels

1. Voltage-Gated Channels: These open in response to changes in membrane potential. Examples:
    - Na^+ channels initiate depolarization during an action potential.
    - K^+ channels help repolarize the membrane.
    - Ca^{2+} channels play a crucial role in muscle contraction and neurotransmitter release.
2. Ligand-Gated Channels: These open in response to the binding of a chemical messenger (e.g., neurotransmitters such as acetylcholine binding to receptors on muscle cells to trigger contraction).
3. Mechanosensitive and Temperature-Sensitive Channels: These respond to mechanical stress or temperature changes, playing a role in processes like touch, hearing, and thermoregulation.

Gated vs. Non-Gated Channels

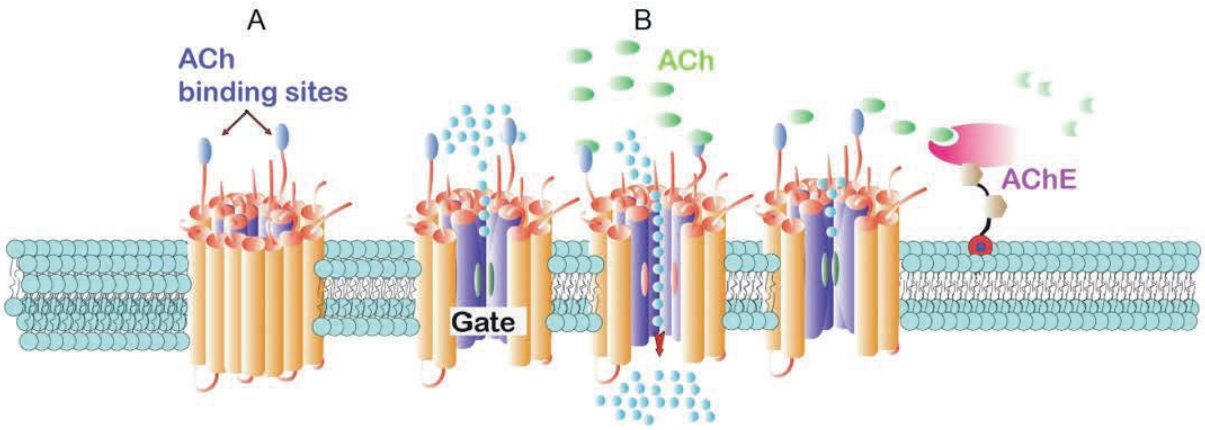
- Gated channels are regulated by voltage, ligands, or mechanical forces and open only in response to specific stimuli.
- Non-gated (leakage) channels are always open, allowing continuous passive movement of ions according to concentration gradients.

Functional Roles of Ion Channels in Different Tissues

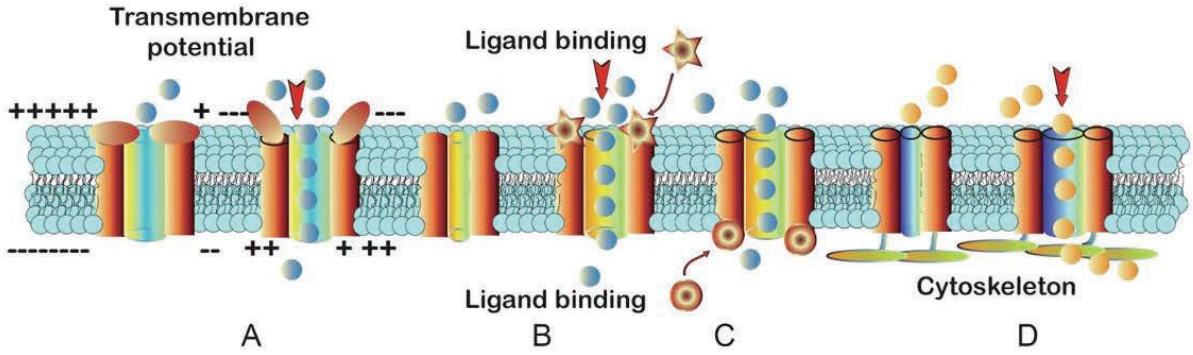
- Neurons: Voltage-gated Na^+ and K^+ channels propagate action potentials.
- Muscle Fibers: Ca^{2+} channels in the sarcoplasmic reticulum release Ca^{2+} to trigger muscle contraction.
- Cardiac Cells: The interaction of Na^+, K^+, and Ca^{2+} channels governs the rhythmic contraction of the heart.

Clinical Relevance: Ion Channelopathies

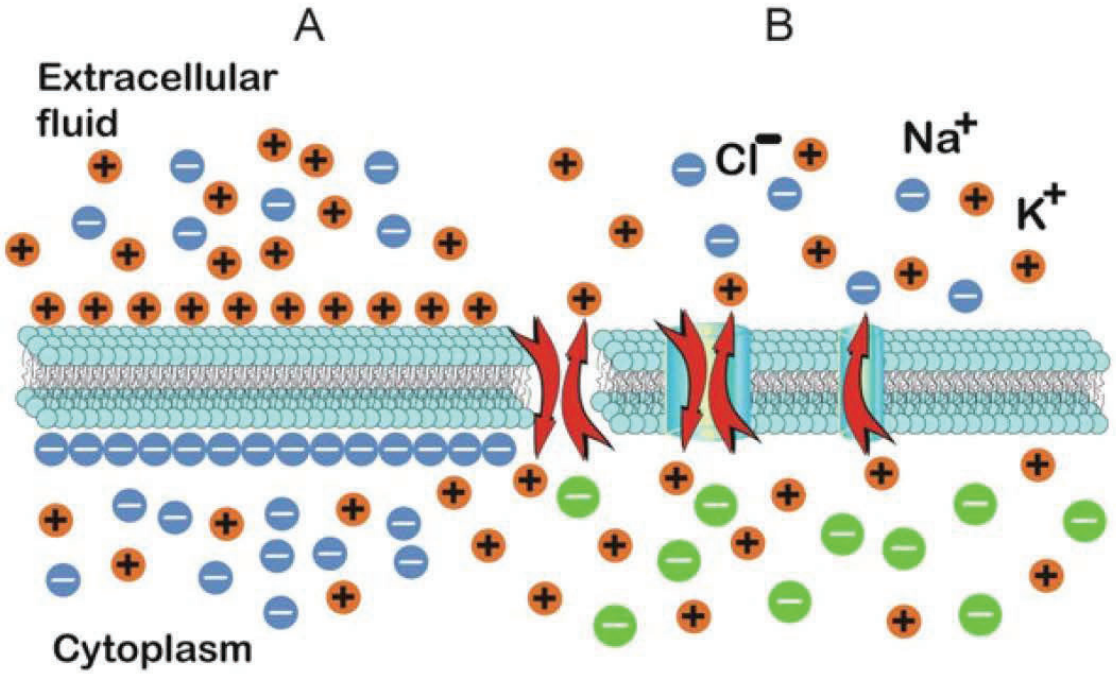
- Ion channelopathies are diseases caused by dysfunction in ion channel proteins. Examples include:
    - Epilepsy: Mutations in Na^+ or K^+ channels cause hyperexcitability in neurons.
    - Cystic Fibrosis: A defect in the CFTR Cl^- channel impairs chloride and water transport, affecting mucus clearance.



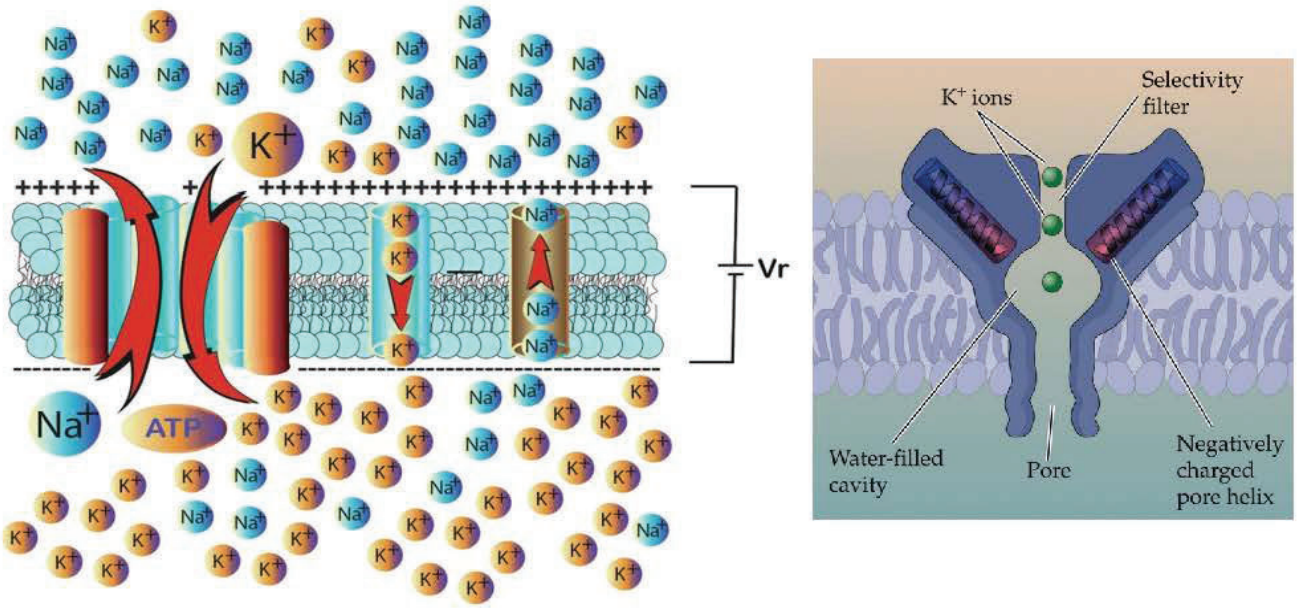
A model of the acetylcholine receptor. (A) The pentameric configuration of the receptor is typical of many other members of the ligand-gated ion channel family. Two of the subunits are identical, and three are different; each of the two α-subunits contains an extracellular binding site for acetylcholine (ACh). (B) Three conformational states of the acetylcholine-gated ion channel. In the absence of ACh, the gate is closed. ACh is released, and the binding of two acetylcholine molecules alters the protein conformation to open the channel pore. However, the effect is only transient; the pore soon closes with acetylcholine still bound to the receptor sites. Once the ligand dissociates from the receptor, the channel can return to a closed but receptive conformation, and ACh is rapidly degraded by acetylcholinesterase (AChE), a GPI-anchored protein that can move very rapidly to scavenge its substrate.



Classes of ion channels stimulated by different gating mechanisms. Ion channels are distinguished according to the signal that opens them. (A) Voltage-gated channels require a deviation of the transmembrane potential. (B,C) Ligand-gated receptors respond to the binding of a specific ligand, either an external neurotransmitter molecule or an internal mediator such as a nucleotide or ion. (D) Mechanically gated channels can sense movement of the cell membrane linked by cytoskeletal filaments to the channel protein. Each effector causes an allosteric change that opens the channel, thereby causing an ion flux across the membrane.

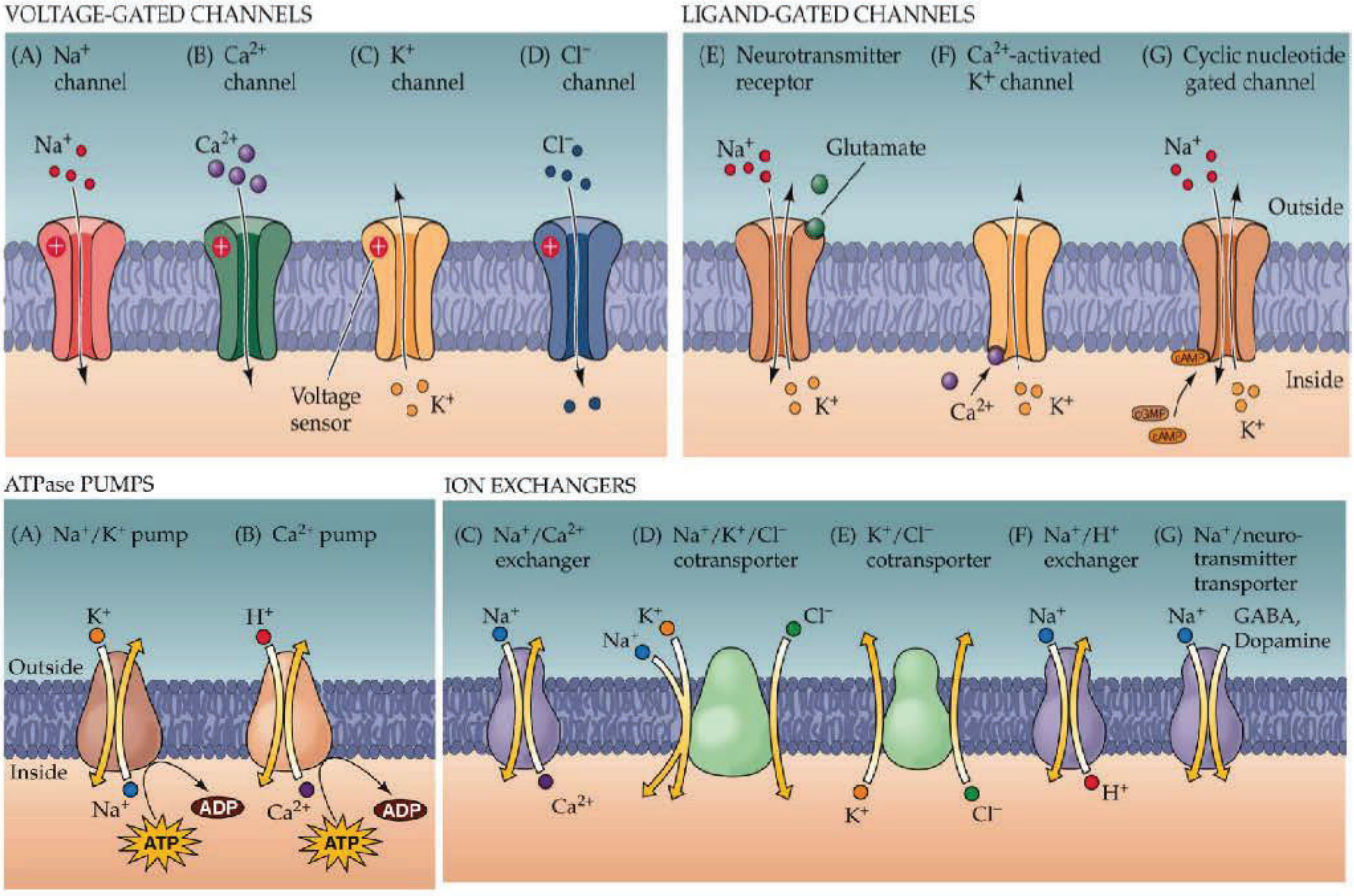


The separation of charge across the cell membrane forms a membrane potential. (A) A net excess negative charge inside the membrane and a matching net excess positive charge outside the membrane form a transmembrane potential difference that is maintained across an impermeable lipid bilayer. Charge on either side of the membrane is concentrated in a thin layer (1 nm thick) and formed by an extremely small percentage of the total ions in the cell. (B) Opposing forces regulate K^+ flux across the plasma membrane. Membrane potential is primarily based on four ion species: K^+, Na^+, Cl^-, and organic anions (−), such as amino acids and other metabolites. The resting membrane potentia of a cell permeable only to K^+ depends on the passive diffusion of K^+ out of the cell down its concentration. If left unchecked, K^+ efflux would eventually create an excess negative charge in the cell (an overbalance of organic anions) and a buildup of $[K^+]_o$, were it not for an electrical driving force moving K^+ in the opposite direction. An equilibrium results when these two opposing forces counterbalance each other.



Passive and active fluxes maintain the resting membrane potential. The cell at rest maintains a steady state whereby Na^+ influx and K^+ efflux defined by passive diffusion are balanced by active transport of these ions in the opposite direction by Na/K-ATPase.

Types of ion channels



4. Action Potential and Signal Propagation

Threshold Stimulus and Initiation of an Action Potential

- An action potential is triggered when the membrane is depolarized to a threshold level (usually ~-55 mV). This opens voltage-gated Na^+ channels, initiating rapid depolarization.

Phases of Action Potential

1. Depolarization: Na^+ channels open, allowing Na^+ influx, making the inside of the cell more positive.
2. Repolarization: K^+ channels open, allowing K^+ efflux, restoring the negative membrane potential.
3. Refractory Periods:
    - Absolute Refractory Period: No action potential can be generated because Na^+ channels are inactivated.
    - Relative Refractory Period: A stronger-than-usual stimulus can trigger an action potential as some Na^+ channels have reset.

Saltatory Conduction in Myelinated Axons

- In myelinated axons, the action potential jumps between Nodes of Ranvier, increasing conduction speed. Myelin acts as an insulator, preventing ion leakage along the axon.

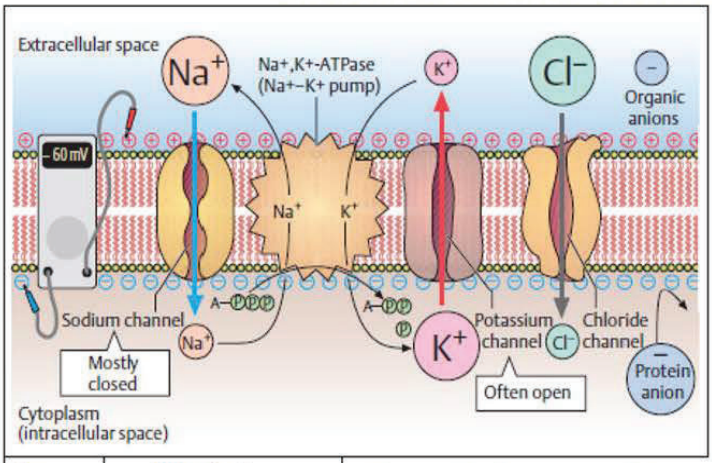
Continuous Conduction in Unmyelinated Axons

- In unmyelinated axons, the action potential travels along every part of the membrane in a slower, continuous fashion.

Propagation of Action Potentials in Neurons and Muscle Fibers

- Neurons: Action potentials propagate down the axon, leading to the release of neurotransmitters at synaptic terminals.
- Muscle fibers: Action potentials trigger the release of Ca^{2+} from the sarcoplasmic reticulum, leading to muscle contraction.

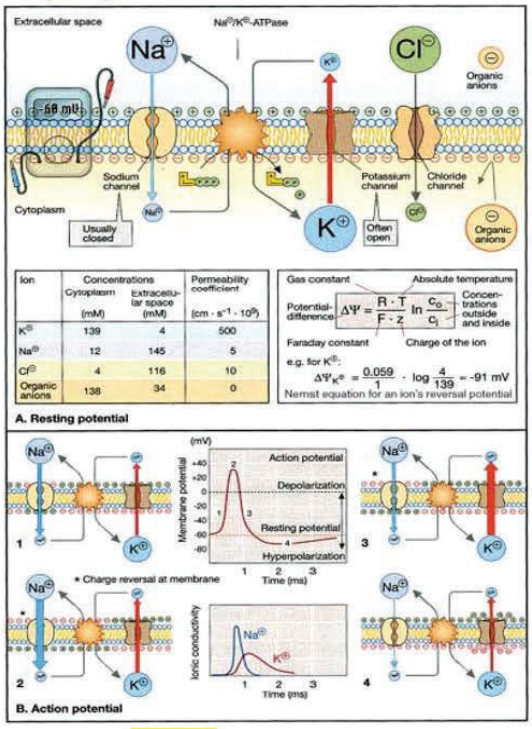
Electrochemical Gradient (EG)



Ion	Concentration	
	Cytoplasm (mM)	Extracellular space (mM)
K^+	139	4
Na^+	12	145
Cl^-	4	116
Organic anions	138	134

Fig. 1.13 **Membrane potential of a cell.** (After Koolman and Röhm)

- **The EG is the foundation of all electrical phenomena in neurons.**
- **It is also what starts the Action Potential.**



Excitability is the property of living matter to react through specific manifestations (synthesis, secretion, contraction, elaboration of the nervous influx) to the action of a stimuli from the internal and external environment.

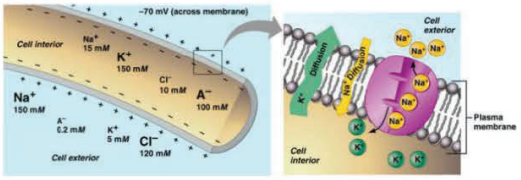
- Depending on the response to the stimulus we can classify the biological structures in:
  - Excitable (most cells and tissues)
  - Non-excitable (bone cell, connective cell, liver cell, RBC)
- Depending on the type of energy conveyed we can classify stimuli into:
  - Physical stimuli – mechanical, vibration, pressure, electricity, light;
  - Chemical stimuli – acidity, alkalinity, pH;
  - Biological stimuli – molecular structures that exchange information with the cell membrane (coupling with receptors, immunomodulators).

Membrane potentials and action potentials

- The resting potential (RP) is the difference in potential that can be recorded on the two sides of the membrane of a cell under the conditions of electrical and functional rest.
- When an effective stimulus is applied, a sufficient number of ion channels are opened to reach the critical level (threshold) locally.
- This will cause the explosive opening of all ion channels, followed by the intracellular invasion of sodium ions, which will lead to the reversal of the membrane potential.
- The action potential (PA) is the modification of the resting potential after supraliminal stimulation of the cell.

Resting Membrane Potential (V_r)

- The potential difference (-70 mV) across the membrane of a resting neuron
- It is generated by different concentrations of Na^+, K^+, Cl^-, and protein anions (A^-)
- The cytoplam inside a cell is negative and the outside of the cell is positive. (Polarized)

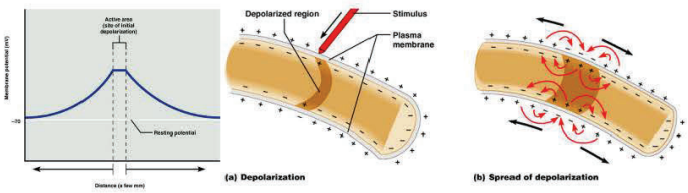


Changes in Membrane Potential

- Changes are caused by three events
  - Depolarization – the inside of the membrane becomes less negative
  - Repolarization – the membrane returns to its resting membrane potential
  - Hyperpolarization – the inside of the membrane becomes more negative than the resting potential

Graded Potentials

- Short-lived, local changes in membrane potential
- Decrease in intensity with distance
- Their magnitude varies directly with the strength of the stimulus
- Sufficiently strong graded potentials can initiate action potentials



GENERAL LAWS OF EXCITABILITY:

I. The response reaction occurs only if the stimulus has a threshold / linear intensity;

i. Subliminal stimulation produces local membrane changes that can generate the excitation state only if repeated at short intervals.

ii. The increase of the stimulus intensity is followed by an amplification proportional to the response reaction, up to a maximum manifestation.

II. The cellular response occurs after a period of time from the moment of the excitatory action (latency period), necessary to produce the physico-chemical changes capable of translating the stimulus into the response.

III. The stimuli must act with a certain abruptness and persist for a minimum time to produce cell stimulation.

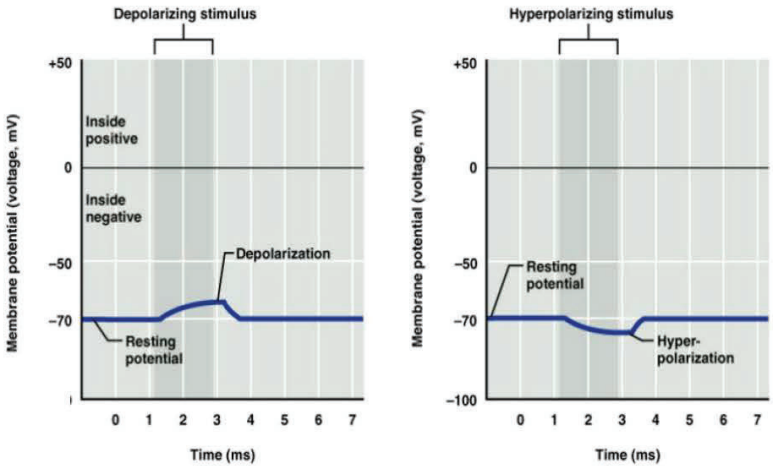
IV. The stimulation process produces excitability changes in the living structure, which will behave differently under the conditions of a new impact with energy variations in the environment.

Role of Ion Channels

- Types of plasma membrane ion channels:
  - Passive, or leakage, channels – always open
  - Chemically gated channels – open with binding of a specific neurotransmitter
  - Voltage-gated channels – open and close in response to membrane potential (change in charge)
  - Mechanically gated channels – open and close in response to physical deformation of receptors

Membrane Potentials: Signals

- Used to integrate, send, and receive information
- Membrane potential changes are produced by:
  - Changes in membrane permeability to ions
  - Alterations of ion concentrations across the membrane
- Types of signals – graded potentials and action potentials

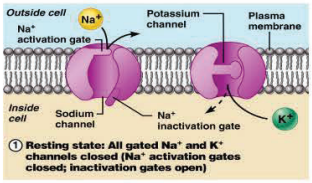


Action Potentials (APs)

- A brief change in membrane potential from -70mV(resting) to +30mV (hyperpolarization)
- Action potentials are only generated by muscle cells and neurons
- They do not decrease in strength over distance
- An action potential in the axon of a neuron is a nerve impulse

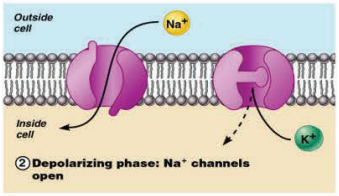
Action Potential: Step 1 Resting State

- Na^+ and K^+ channels are closed
- Leakage accounts for small movements of Na^+ and K^+
- Each Na^+ channel has two voltage-regulated gates
  - Activation gates - closed in the resting state
  - Inactivation gates - open in the resting state



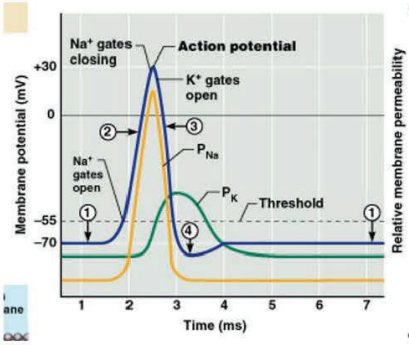
Action Potential: Step 2 Depolarization Phase

- The local depolarization current flips open the sodium gate and Na^+ rushes in.
- Threshold: when enough Na+ is inside to reach a critical level of depolarization (-55 to -50 mV) threshold, depolarization becomes self-generating.



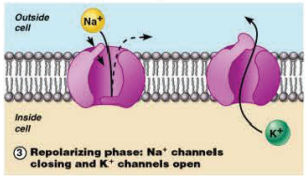
Action Potential: Step 2 Cont.

- Na + will continue to rush in making the inside less and less negative and actually overshoots the 0mV (balanced) mark to about +30mV.



Action Potential: Step 3 Repolarization Phase

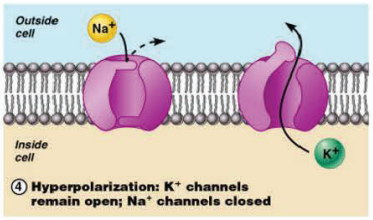
- After 1 ms enough Na+ has entered that positive charges resist entering the cell.
- Sodium inactivation gates close and membrane permeability to Na^+ declines to resting levels
- As sodium gates close, voltage-sensitive K^+ gates open
- K^+ exits the cell and internal negativity of the resting neuron is restored



- 1 - resting state
- 2 - depolarization phase
- 3 - repolarization phase
- 4 - hyperpolarization

Action Potential: Step 4 Hyperpolarization

- Potassium gates are slow and remain open, causing an excessive efflux of K^+
- This efflux causes hyperpolarization of the membrane (undershoot).
- The neuron is insensitive to stimulus and depolarization during this time



Action Potential: Role of the Sodium-Potassium Pump

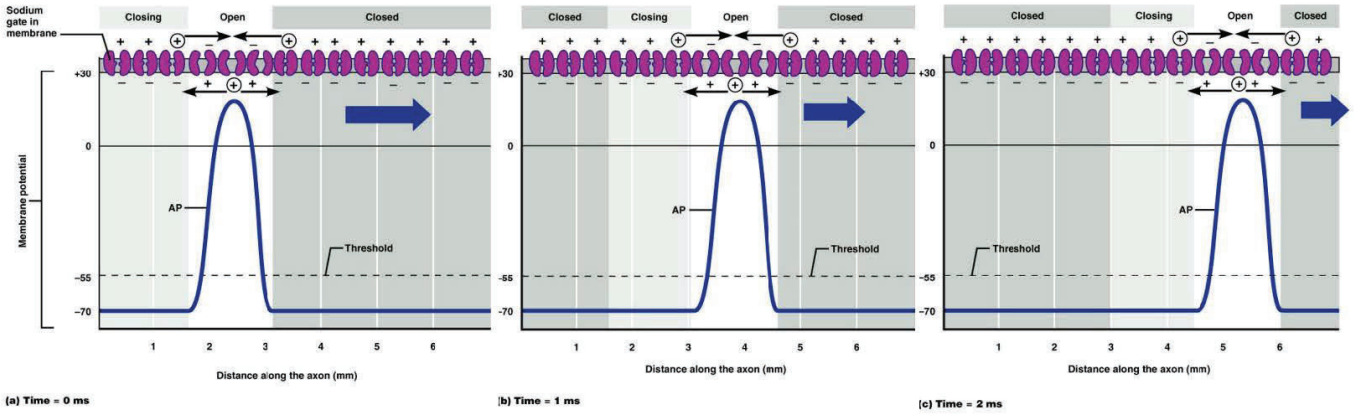
- Repolarization
  - Restores the resting electrical conditions of the neuron
  - Does not restore the resting ionic conditions
- Ionic redistribution back to resting conditions is restored by the sodium-potassium pump

Propagation of an Action Potential

- When one area of the cell membrane has begun to return to resting the positivity has opened the Na+ gates of the next area of the neuron and the whole process starts over.
- A current is created that depolarizes the adjacent membrane in a forward direction
- The impulse propagates away from its point of origin

Coding for Stimulus Intensity

- All action potentials are alike and are independent of stimulus intensity
- Strong stimuli can generate an action potential more often than weaker stimuli
- The CNS determines stimulus intensity by the frequency of impulse transmission



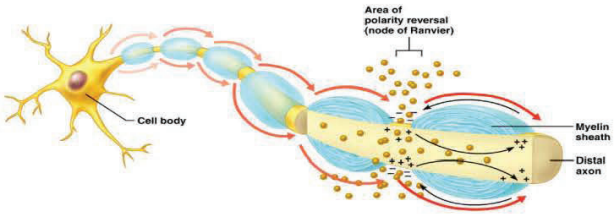
Conduction Velocities of Axons

- Conduction velocities vary widely among neurons
- Rate of impulse propagation is determined by:
  - Axon diameter - the larger the diameter, the faster the impulse
  - Presence of a myelin sheath - myelination dramatically increases impulse speed

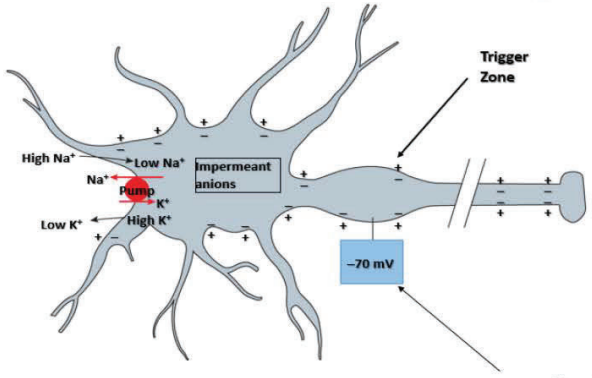
Saltatory Conduction

- Current passes through a myelinated axon only at the nodes of Ranvier
- Voltage-gated Na^+ channels are concentrated at these nodes and Action potentials jump from one node to the next
- Much faster than conduction along unmyelinated axons where the entire axon has continuous conduction.

Saltatory Conduction



The Membrane Potential of the Resting Neuron

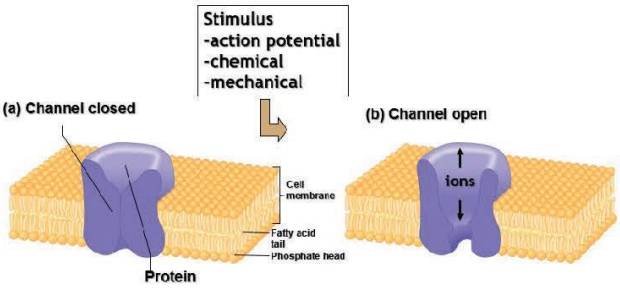


-70 millivolts

Membrane Potential = unequal distribution of + and - ions on either side of a cell membrane

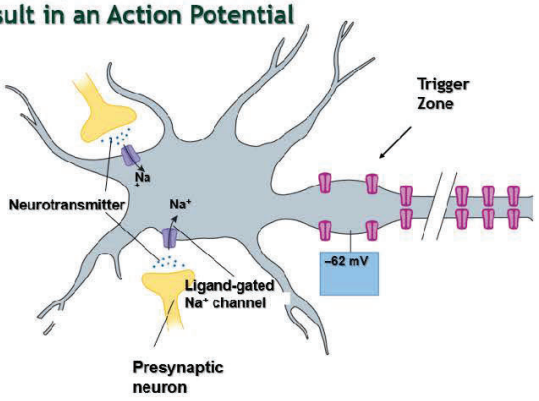
1 mV= 0.001Volts

Gate-like Mechanism of Ion Channels

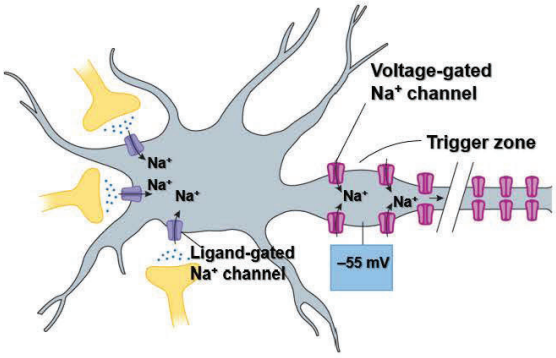


Membrane potential changes due to movement of ions when channels are open

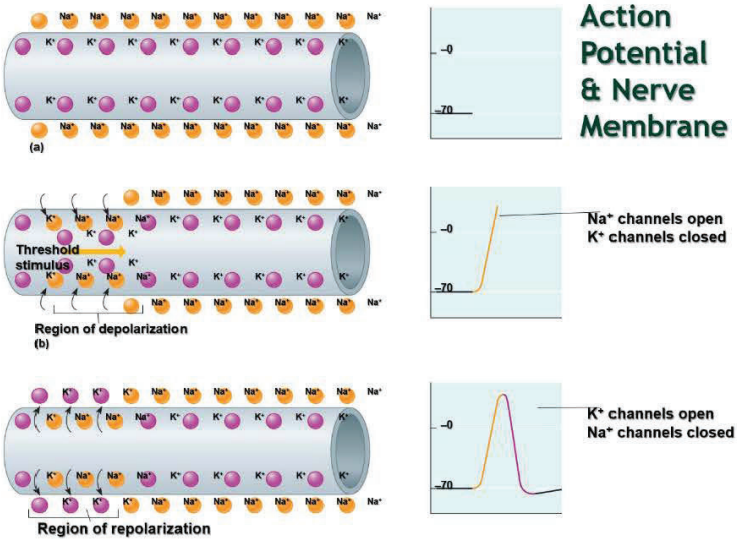
Sub-threshold Depolarization Does not Result in an Action Potential



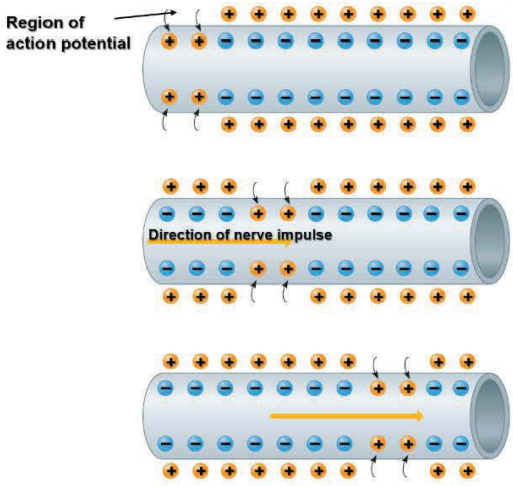
An Action Potential is Generated When Depolarization Reaches ~55mV



Action Potential & Nerve Membrane



A Nerve Impulse = moving Zone of Depolarization



5. Synaptic Transmission and Neuromuscular Junction

Nerve impulses pass from neuron to neuron at synapses, moving from a pre-synaptic neuron to a post-synaptic neuron. Neurotransmitters are released when the impulse reaches a synaptic knob.

Structure and Function of Synapses

- Chemical Synapses: Neurotransmitters are released from the presynaptic neuron and bind to receptors on the postsynaptic cell.
- Electrical Synapses: Allow direct electrical coupling between neurons through gap junctions, enabling faster transmission.

Role of Neurotransmitters

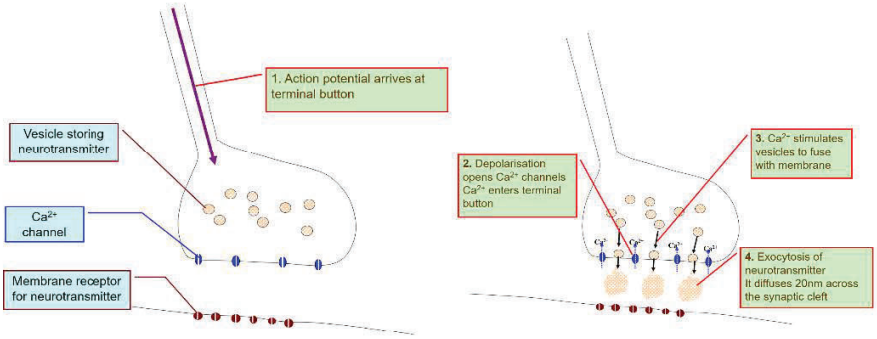
- Acetylcholine (ACh): Binds to receptors on skeletal muscle to initiate contraction.
- Dopamine: Involved in reward pathways and motor control.
- Other neurotransmitters include serotonin, glutamate, and GABA, each playing unique roles in the nervous system.

Neuromuscular Junction

- At the neuromuscular junction, the motor neuron releases acetylcholine, which binds to receptors on the muscle cell membrane (sarcolemma). This triggers an action potential in the muscle, leading to contraction.

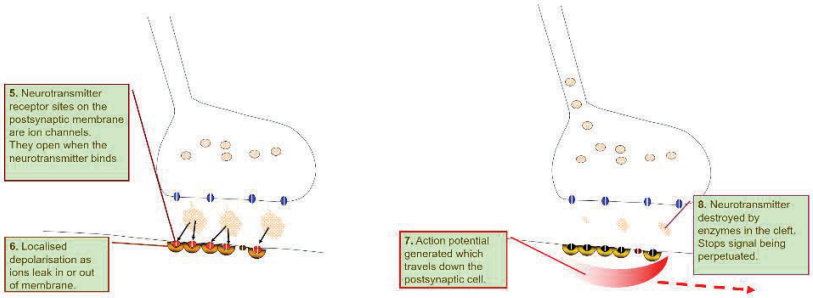
The synapse

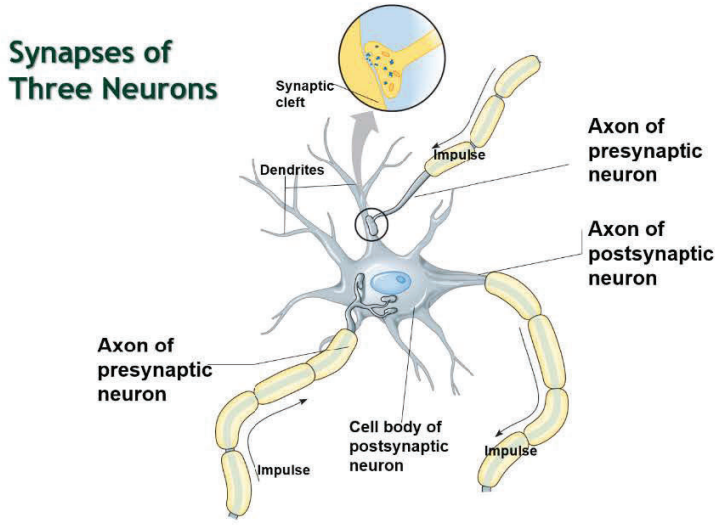
- A gap (about 20nm)
- Where the nerve impulse passes from one cell to the next
- The electrical signal (the action potential) → a chemical signal to cross the gap between the cells
- Neurotransmitter
- The neurotransmitter crosses by diffusion
- This creates a small delay.



The passage across the synapse

- An action potential travels down an axon to the terminal buttons
- The membrane of a terminal button depolarises
- Voltage-gated Ca^{2+} channels to open
- Ca^{2+} ions flood into the terminal button
- This stimulates hundreds of synaptic vesicles, packed with neurotransmitter, to fuse with the membrane of the terminal button
- Exocytosis
- The Ca^{2+} ions are then pumped out again.
- Neurotransmitter diffuses across cleft to postsynaptic membrane
- Neurotransmitter molecules bind with specific receptor sites on postsynaptic membrane
- The receptor sites are ligand-gated ion channels
- These channels let Na^{+} ions in or K^{+} ions out causing localised depolarisation of the membrane.





6. Signal Transduction Pathways Involving Ion Channels

Overview of G-Protein Coupled Receptors (GPCRs)

GPCRs are a large class of receptors that, upon ligand binding, activate intracellular G-proteins. These proteins then influence ion channels or enzymatic pathways, leading to cellular responses.

Phospholipase C Activation and Calcium Signaling

- Phospholipase C (PLC) cleaves phosphatidylinositol bisphosphate (PIP_2) into inositol triphosphate (IP_3) and diacylglycerol (DAG).
- IP_3 releases Ca^{2+} from intracellular stores, increasing cytosolic Ca^{2+} levels, modulating processes like muscle contraction, secretion, and metabolism.

Role of Second Messengers (cAMP and Ca^{2+})

- cAMP: Activates protein kinase A (PKA), which phosphorylates various target proteins, altering their activity.
- Ca^{2+}: Acts as a ubiquitous second messenger in muscle contraction, neurotransmitter release, and many other processes.

7. Practical Applications and Clinical Implications

Clinical Relevance of Membrane Potential and Action Potentials in Cardiac Arrhythmias

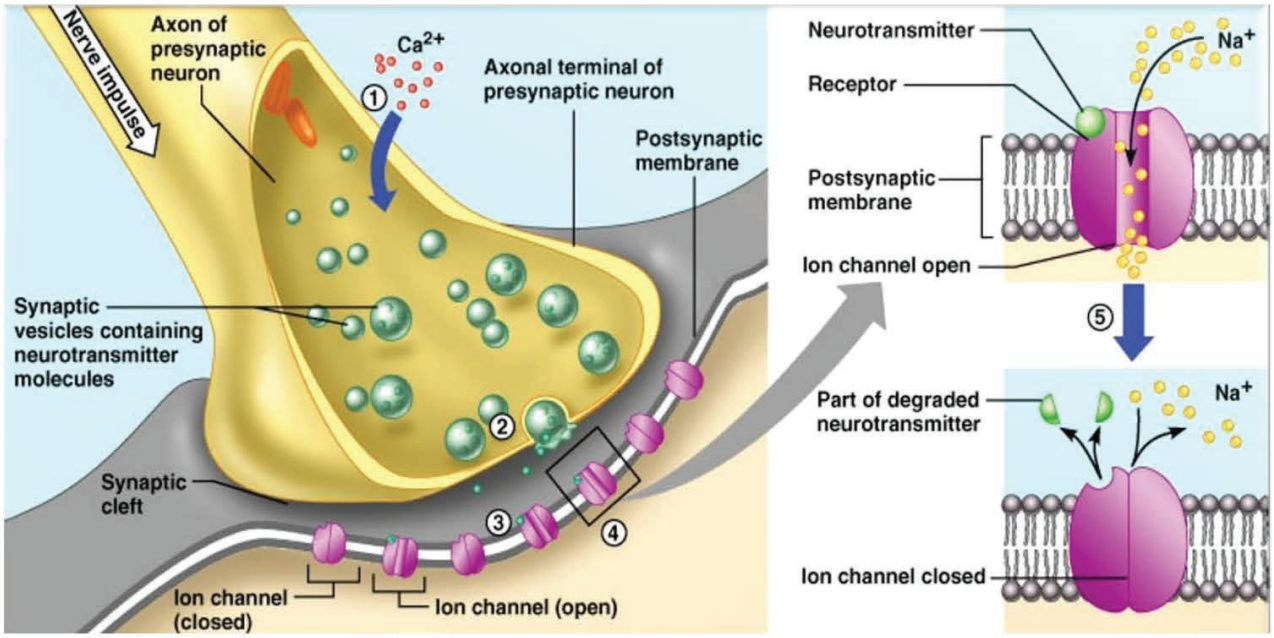
- Cardiac arrhythmias result from abnormal ion channel function, disrupting the normal sequence of action potentials in the heart, leading to irregular heartbeats.

Channelopathies

- Epilepsy: Caused by mutations in ion channels leading to excessive neuronal excitability.
- Cystic Fibrosis: Caused by a defective CFTR Cl^- channel, impairing ion transport and fluid regulation.

Pharmacological Modulation of Ion Channels

- Calcium channel blockers (e.g., verapamil) are used to treat hypertension by reducing Ca^{2+} influx in vascular smooth muscle cells, leading to vasodilation.
- Sodium channel inhibitors (e.g., lidocaine) block Na^+ channels to prevent action potential generation, often used as local anesthetics.



Examination and Assessment

1	Physiology is the branch of knowledge that studies:	
a.	how structures of a living organism function in order to maintain life	True
b.	the function of organisms	True
c.	the mechanism of life at the organ, tissue, cellular and molecular levels	True
d.	contribution of organ - system to homeostasis	True
e.	the function of the body	True
f.	the mechanism of nuclear fusion	False
g.	electricity transport and distribution	False
h.	psychological aspects of life	False
i.	theory and practice of human life	False
j.	the mechanism of spatial integration	False

2	Teleological approach in physiology means:	
a.	thinking about the " why " regarding different functions	True
b.	explaining " why " various functions are happening	True
c.	for example - Why do red blood cells transport oxygen?	True
d.	what need the physiological process fills	True
e.	reason for something which serves as a function of its end	True
f.	thinking about the " how " regarding different functions	False
g.	explaining " how " various functions are happening	False
h.	for example - How do red blood cells transport oxygen?	False
i.	How physiological processes are happening	False
j.	reason for something which serves as a function of its cause	False

3	Mechanistic approach in physiology means:	
a.	thinking about the " how " regarding different functions	True
b.	explaining " how " various functions are happening	True
c.	for example - How do red blood cells transport oxygen?	True
d.	How physiological process are happening	True
e.	reason for something which serves as a function of its cause	True
f.	thinking about the " why " regarding different functions	False
g.	explaining " why " various functions are happening	False
h.	for example - Why do red blood cells transport oxygen?	False
i.	what needs the physiological process fills	False
j.	reason for something which serves as a function of its end	False

4	Are Specialties of Physiology	
a.	Cellular physiology	True
b.	Ergophysiology	True
c.	Cardiovascular Physiology	True
d.	Neuro-Physiology	True
e.	Pathophysiology	True
f.	Spatial Physiology	False
g.	Fusion Physiology	False
h.	Diffusion Physiology	False
i.	Caloric Physiology	False
j.	Stone Physiology	False
5	Physiological variables can be:	
a.	Gender	True
b.	Age	True
c.	Diet	True

d.	Weight	True
e.	Body temperature	True
f.	Social statute	False
g.	Economic performance	False
h.	Esthetic image	False
i.	Evaporation	False
j.	Conductivity	False

6	Functional levels of organization in physiology can be:	
a.	Chemical or molecular level	True
b.	Cellular level	True
c.	Tissue level	True
d.	Organ level	True
e.	Body system level	True
f.	Atomic level	False
g.	Organizational level	False
h.	Environmental level	False
i.	Social level	False
j.	Economic level	False

7	Homeostasis in physiology means maintaining a constant level within an organism regarding, for example	
a.	Body temperature	True
b.	Heart rate	True
c.	Blood glucose	True
d.	Electrolytes concentration in the blood	True
e.	Blood pH	True
f.	Atoms number in the organism	False
g.	Electrical charges in the organism	False
h.	Molecules in the organism	False
i.	Cells in the organism	False
j.	Subatomic particles in the organism	False

8	Equilibrium in physiology means:	
a.	A state of rest	True
b.	A state of equal balance	True
c.	biological actions for adjust	True
d.	Adjustment	True
e.	which has nothing external to derange it	True
f.	Homeostasis	False
g.	disequilibrium	False
h.	dynamic disequilibrium	False
i.	the mechanism of spatial integration	False
j.	regulation	False
9	Homeostasis and Physiological Controls involve	
a.	Internal interventions	True
b.	Sensors to detect changes	True
c.	Integrating center process	True
d.	Response of cells and organs	True
e.	External interventions	True
f.	Failure to compensate	False
g.	disequilibrium	False

h.	illness	False
i.	disease	False
j.	death	False

10	Are mechanisms for Homeostasis in physiology:	
a.	Autoregulation	True
b.	Intrinsic regulation	True
c.	Extrinsic regulation	True
d.	Thermoregulation	True
e.	Behavioral regulation	True
f.	Meta-regulation	False
g.	Optional regulation	False
h.	Extra-regulation	False
i.	Over-regulation	False
j.	Antiregulation	False

11	Homeostatic regulation includes:	
a.	A receptor	True
b.	A control center	True
c.	An effector	True
d.	Input signal	True
e.	Efferent signal	True
f.	A producer	False
g.	A codifier	False
h.	A source	False
i.	An emergent	False
j.	A variable	False

12	Negative Feedback means:	
a.	Decrease of the stimulus after response	True
b.	Decrease of the stimulus after effector action	True
c.	Decrease of the stimulus as a biological consequence	True
d.	Decrease of the stimulus as an effect	True
e.	Decrease of the stimulus as homeostatic intervention	True
f.	Increase of the stimulus after response	False
g.	Increase of the stimulus after effector action	False
h.	Increase of the stimulus as a biological consequence	False
i.	Increase of the stimulus as an effect	False
j.	Increase of the stimulus as homeostatic intervention	False

13	Positive Feedback means:	
a.	Increase of the stimulus after response	True
b.	Increase of the stimulus after effector action	True
c.	Increase of the stimulus as a biological consequence	True
d.	Increase of the stimulus as an effect	True
e.	Increase of the stimulus as homeostatic intervention	True
f.	Decrease of the stimulus after response	False
g.	Decrease of the stimulus after effector action	False
h.	Decrease of the stimulus as a biological consequence	False
i.	Decrease of the stimulus as an effect	False
j.	Decrease of the stimulus as homeostatic intervention	False

14	Harmful Positive Feedback Loop in case of Fever	

a.	metabolic rate increases	True
b.	body produces heat even faster	True
c.	Cycle continues to reinforce itself - further increasing metabolic rate	True
d.	Damage to brain occurs around 41.6°Celsius degrees	True
e.	Becomes fatal at 45 °Celsius degrees	True
f.	metabolic rate decreases	False
g.	body produces heat slower	False
h.	Cycle continues to reinforce itself - further decreasing metabolic rate	False
i.	Damage to brain occurs around 36°Celsius degrees	False
j.	Becomes fatal at 55 °Celsius degrees	False

15	Functions of the cell as a whole, in human physiology, can be:	
a.	Obtaining O2 & nutrients from the environment	True
b.	Synthesis of proteins for structure, growth	True
c.	Controlling the exchange of material	True
d.	Intracellular movement of materials	True
e.	Sensitiveness &response to the environment	True
f.	Obtaining CO2 & nutrients from the environment	False
g.	Synthesis of proteins as waste products	False
h.	Controlling waste products accumulation	False
i.	Extracellular movement of liquids	False
j.	Human physical activity	False

16	Intercellular communication can be	
a.	Paracrine communication	True
b.	Endocrine communication	True
c.	Neurocrine communication	True
d.	Exocrine communication	True
e.	Synaptic communication	True
f.	Radio-communication	False
g.	Electrical communication	False
h.	Thermal communication	False
i.	Infrared communication	False
j.	Psychological communication	False

17	Membrane Proteins role can be:	
a.	Anchoring proteins	True
b.	Enzymatic Proteins	True
c.	Receptor proteins	True
d.	Carrier proteins	True
e.	Ion channel proteins	True
f.	Thermal proteins	False
g.	Electrical Proteins	False
h.	Osmotic proteins	False
i.	Facilitated proteins	False
j.	Waste proteins	False

18	Are Cell membrane functions:	
a.	Forms physical boundary of the cell	True
b.	Selectively permeable – regulates transport across the membrane	True
c.	Motility– facilitated by the presence of cilia	True
d.	Signal Transduction – the movement of a stimulus from one form to another	True
e.	Structural support	True

f.	Protein secretion	False
g.	Lipid oxidation	False
h.	Water transport in the body	False
i.	Intracellular movement of materials	False
j.	Control electrical charges in the organism	False

19	Are methods of transport across cell membranes	
a.	Simple Diffusion	True
b.	Osmosis	True
c.	Filtration	True
d.	Facilitated diffusion	True
e.	Protein channels	True
f.	Complex Diffusion	False
g.	Oxmosis	False
h.	Separation	False
i.	Oriented diffusion	False
j.	Lipid channels	False

20	Types of active transport across cell membranes	
a.	Primary active transport	True
b.	Secondary active transport	True
c.	Uniport	True
d.	Synport	True
e.	Antiport	True
f.	Simple Diffusion	False
g.	Osmosis	False
h.	Filtration	False
i.	Facilitated diffusion	False
j.	Protein channels	False

21	Passive Transport across cell membranes invloves:	
a.	The cell doesn't use energy	True
b.	Diffusion	True
c.	Facilitated Diffusion	True
d.	Osmosis	True
e.	Protein channels	True
f.	The cell use energy	False
g.	Protein Pumps	False
h.	Endocytosis	False
i.	Exocytosis	False
j.	Transport from Low to High Concentrations	False

22	Active Transport across cell membranes invloves:	
a.	The cell does use energy	True
b.	Protein Pumps	True
c.	Endocytosis	True
d.	Exocytosis	True
e.	Transport from Low to High Concentrations	True
f.	The cell doesn't use energy	False
g.	Diffusion	False
h.	Facilitated Diffusion	False
i.	Osmosis	False
j.	Protein channels	False

23	Regarding Facilitated Diffusion is true:	
a.	Can involve protein channels	True
b.	Transport substances from High to Low Concentrations	True
c.	The cell doesn't use energy	True
d.	Is an example: Glucose transport into red blood cells	True
e.	Is a type of passive transport	True
f.	Can involve protein pumps	False
g.	Transport substances from Low to High Concentrations	False
h.	The cell use energy	False
i.	Is an example: diffusion of water	False
j.	Is a type of active transport	False

24	The Na/K-ATPase:	
a.	is an electrogenic pump	True
b.	moves three Na+ ions out of the cell	True
c.	moves two K+ ions into the cytoplasm	True
d.	Uses ATP hydrolysis to ADP and inorganic phosphate	True
e.	Is a types of active transport across cell membranes	True
f.	is an ion channel	False
g.	moves two K+ ions out of the cell	False
h.	moves three Na+ ions into the cytoplasm	False
i.	Uses ADP hydrolysis to ATP and inorganic phosphate	False
j.	Is a types of passive transport across cell membranes	False
25	Types of voltage-gated ion channels	
a.	Na+ channel	True
b.	Ca2+ channel	True
c.	K+ channel	True
d.	Cl- channel	True
e.	H+ channel	True
f.	K+ - Ca2+ activated channel	False
g.	Na+ - Glutamate activated channel	False
h.	Na+ - cyclic nucleotide activated channel	False
i.	Na+ - Acetylcholine activated channel	False
j.	Ca2+ - inositol triphosphate (IP3) activated channel	False

26	Types of ligand-gated ion channels	
a.	K+ - Ca2+ activated channel	True
b.	Na+ - Glutamate activated channel	True
c.	Na+ - cyclic nucleotide activated channel	True
d.	Na+ - Acetylcholine activated channel	True
e.	Ca2+ - inositol triphosphate (IP3) activated channel	True
f.	Na+ channel	False
g.	Ca2+ channel	False
h.	K+ channel	False
i.	Cl- channel	False
j.	H+ channel	False

27	Endocytosis: taking bulky material into a cell by:	
a.	Uses energy	True
b.	Cell membrane in-folds around food particle	True
c.	"cell eating"	True

d.	forms food vacuole & digests food	True
e.	this is how white blood cells eat bacteria	True
f.	membrane surrounding the material inside the cell and fuses with cell membrane	False
g.	hormones are released from cell in this way	False
h.	wastes released from cell	False
i.	neurotransmitters are released from cell in this way	False
j.	Forces material out of cell in bulk	False

28	Exocytosis	
a.	membrane surrounding the material inside the cell and fuses with cell membrane	True
b.	hormones are released from cell in this way	True
c.	wastes released from cell	True
d.	neurotransmitters are released from cell in this way	True
e.	Forces material out of cell in bulk	True
f.	The cell doesn't use energy	False
g.	Cell membrane in-folds around food particle	False
h.	"cell eating"	False
i.	forms food vacuole & digests food	False
j.	this is how white blood cells eat bacteria	False
29	The Membrane potential of a cell at rest involves:	
a.	High level of Na+ outside the cell (extracellular space)	True
b.	High level of Cl- outside the cell (extracellular space)	True
c.	High level of K+ inside the cell	True
d.	Na+ and K+ channels are closed	True
e.	Na+ / K+ pumps are working	True
f.	Low level of Na+ outside the cell (extracellular space)	False
g.	Low level of Cl- outside the cell (extracellular space)	False
h.	Low level of K+ inside the cell	False
i.	Na+ and K+ channels are open	False
j.	Na+ / K+ pumps are inactivated	False

30	Action Potential involves:	
a.	Stimulus open Na+ channels	True
b.	Na+ enters the cell, from high to low-level concentrations	True
c.	After reaching the threshold, voltage-gated Na+ channels are open for 1 ms	True
d.	In the repolarization phase, K+ exit the cell, from high to low-level concentrations	True
e.	Na+ / K+ pumps are working to regain the resting membrane potential	True
f.	Stimulus open K+ channels	False
g.	Na+ exit the cell, from high to low-level concentrations	False
h.	After reaching the threshold, voltage-gated K+ channels are open for 1 ms	False
i.	In the repolarization phase, K+ enters the cell, from high to low-level concentrations	False
j.	Na+ / K+ pumps are closed to regain the resting membrane potential	False

Course 2: Physiology of the Nervous System. Membrane Action and Resting Potential
Sub-topic: Primary and Secondary Messengers

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1. Membrane Resting Potential

- Definition and importance of resting potential.
- Ion distribution across the cell membrane (Na+, K+, Cl-).
- Role of ion channels in establishing and maintaining resting potential.
- Mechanism of the Na+/K+ ATPase pump.
- Electrochemical gradients and equilibrium potential (Nernst equation).
- Factors influencing resting membrane potential.

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2. Membrane Action Potential

- Initiation of action potential: threshold stimulus.
- Phases of action potential: depolarization, repolarization, hyperpolarization.
- Role of voltage-gated ion channels in action potential (Na+, K+, and Ca2+ channels).
- Absolute and relative refractory periods.
- All-or-nothing principle of action potential generation.
- Propagation of action potentials along axons (saltatory conduction in myelinated axons, continuous conduction in unmyelinated axons).

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3. Primary Messengers

- Definition and role of primary messengers in cellular signaling.
- Types of primary messengers: neurotransmitters, hormones, growth factors.
- Mechanisms of receptor-ligand binding.
- Role of G-protein coupled receptors (GPCR) and ion channels in primary messenger signaling.
- Examples of primary messengers and their functions: acetylcholine, dopamine, epinephrine.

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4. Secondary Messengers

- Definition and function of secondary messengers in signal transduction.
- Common secondary messengers: cAMP, cGMP, IP3, DAG, Ca2+.
- Role of secondary messengers in amplifying and propagating signals.
- Pathways involving secondary messengers: adenylyl cyclase-cAMP pathway, phospholipase C-IP3/DAG pathway.
- Regulation of cellular processes by secondary messengers (e.g., gene expression, metabolism, ion channel regulation).

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5. Signal Transduction Mechanisms

- Overview of signal transduction pathways involving primary and secondary messengers.
- G-protein coupled receptors (GPCR) and their role in activating secondary messengers.
- Enzyme-linked receptors and their involvement in cellular signaling.
- Ion channel-linked receptors and their regulation by primary messengers.
- Cross-talk between different signaling pathways.

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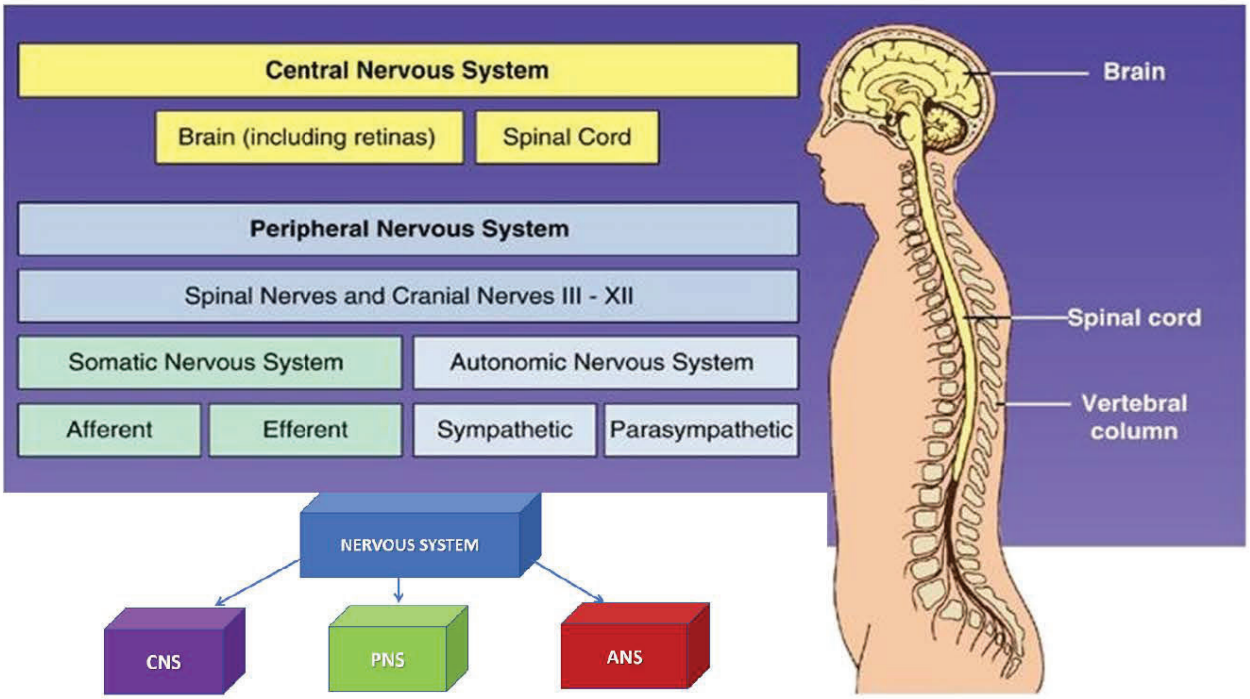
6. Practical Applications and Clinical Implications

- Role of membrane potentials in excitable tissues (neurons, muscle cells).
- Dysfunction in membrane potentials and associated diseases (e.g., epilepsy, cardiac arrhythmias).
- Signal transduction abnormalities in diseases (e.g., cancer, diabetes, neurodegenerative diseases).

Examination and Assessment

Course 2: Physiology of the Nervous System. Membrane Action and Resting Potential
Sub-topic: Primary and Secondary Messengers

- **To survive, all organisms need to be able to sense changes in their environment and to control their responses to these changes.**
- **The nervous system and the endocrine system are important communication systems that coordinate, integrate, and carry out the activity of body cells, tissues, organs, and the organism.**
- **They maintain a constant internal balance while reacting to the changes that occur in both the external and internal environment**



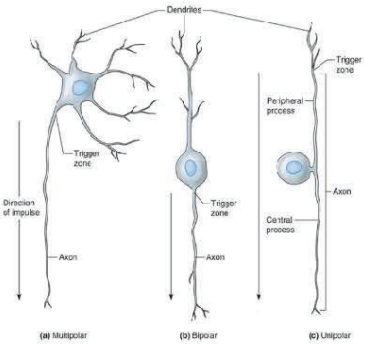
The nervous system consists of two divisions:

- the Central Nervous System containing the brain and spinal cord,
- the Peripheral Nervous System which is a network of nerves and neural tissues branching out throughout the body.

General functions of the nervous system

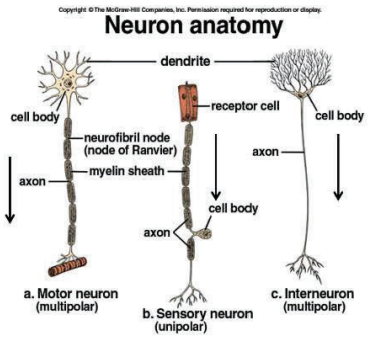
- Sensory
  - Gather information
  - Info carried to CNS
- Integrative
  - Sensory information used to create sensations, memory, thoughts, decisions
- Motor
  - Decisions acted upon
  - Information carried from CNS to PNS

Neurons can be grouped in two ways: on the basis of structural differences (bipolar, unipolar, and multipolar neurons), and by functional differences (sensory neurons, interneurons, and motor neurons).
Bipolar neurons are found in the eyes, nose, and ears, and have a single axon and a single dendrite extending from opposite sides of the cell body.
Unipolar neurons are found in ganglia outside the CNS and have an axon and a dendrite arising froma single short fiber extending from the cell body.
Multipolar neurons have many nerve fibers arising from their cell bodies and are commonly found in the brain and spinal cord.

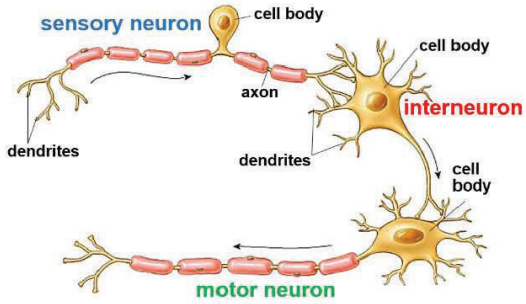


– Motor functions can be divided into the consciously controlled somatic nervous system and the unconscious autonomic system.

Sensory neurons (afferent neurons) conduct impulses from peripheral receptors to the CNS and are usually unipolar, although some are bipolar neurons.
Interneurons are multipolar neurons lying within the CNS that form links between other neurons.
Motor neurons are multipolar neurons that conduct impulses from the CNS to effectors.

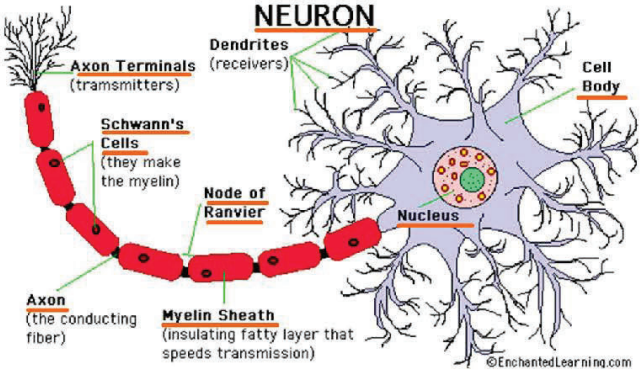


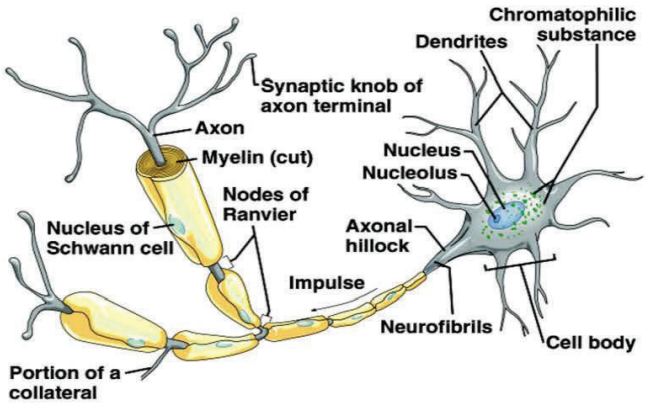
Types of neurons



The nervous system is composed of neurons and neuroglia.

1. Neurons transmit nerve impulses along nerve fibers to other neurons.
2. Nerves are made up of bundles of nerve fibers.
3. Neuroglia carry out a variety of functions to aid and protect components of the nervous system.

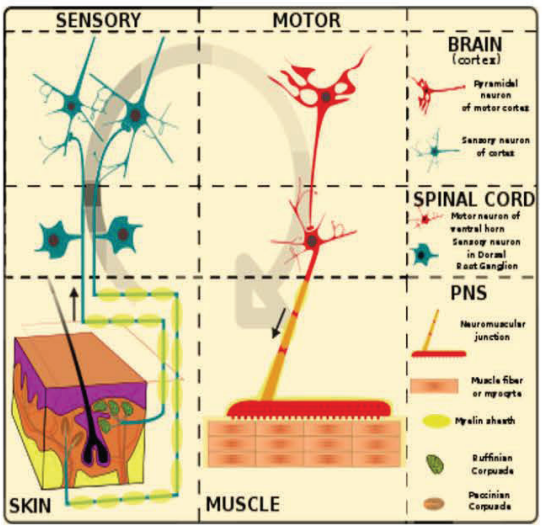




A neuron has a cell body with mitochondria, lysosomes, a Golgi apparatus, chromatophilic substance (Nissl bodies) containing rough endoplasmic reticulum, and neurofibrils.
Axons carry impulses away from the cell body.

- **Sensory neurons**
  - **afferent neurons**
  - **carry impulses to CNS**
  - **either unipolar or bipolar**
  - **sensitive to stimuli in the environment**
- **Connector/inter neurons**
  - **receive impulse from sense organs**
  - **always multipolar**
  - **integrates or analyses information**
  - **effect a response**
- **Motor neurons**
  - **efferent neurons**
  - **carry impulses away from CNS**
  - **always multipolar**
  - **effect a response**

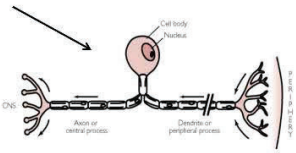
Functional neurons



Types of neurons…

Sensory neurons do not have true dendrites. They are attached to sensory receptors and transmit impulses to the central nervous system, which then stimulate the interneurons, and then motor neurons.

NERVE RECEPTORS
↓
SENSORY NEURONS
↓
INTERNEURONS
↓
MOTOR NEURONS

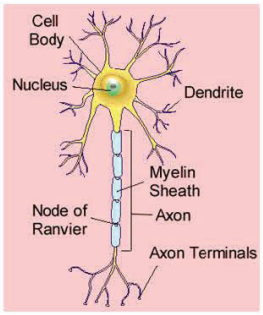


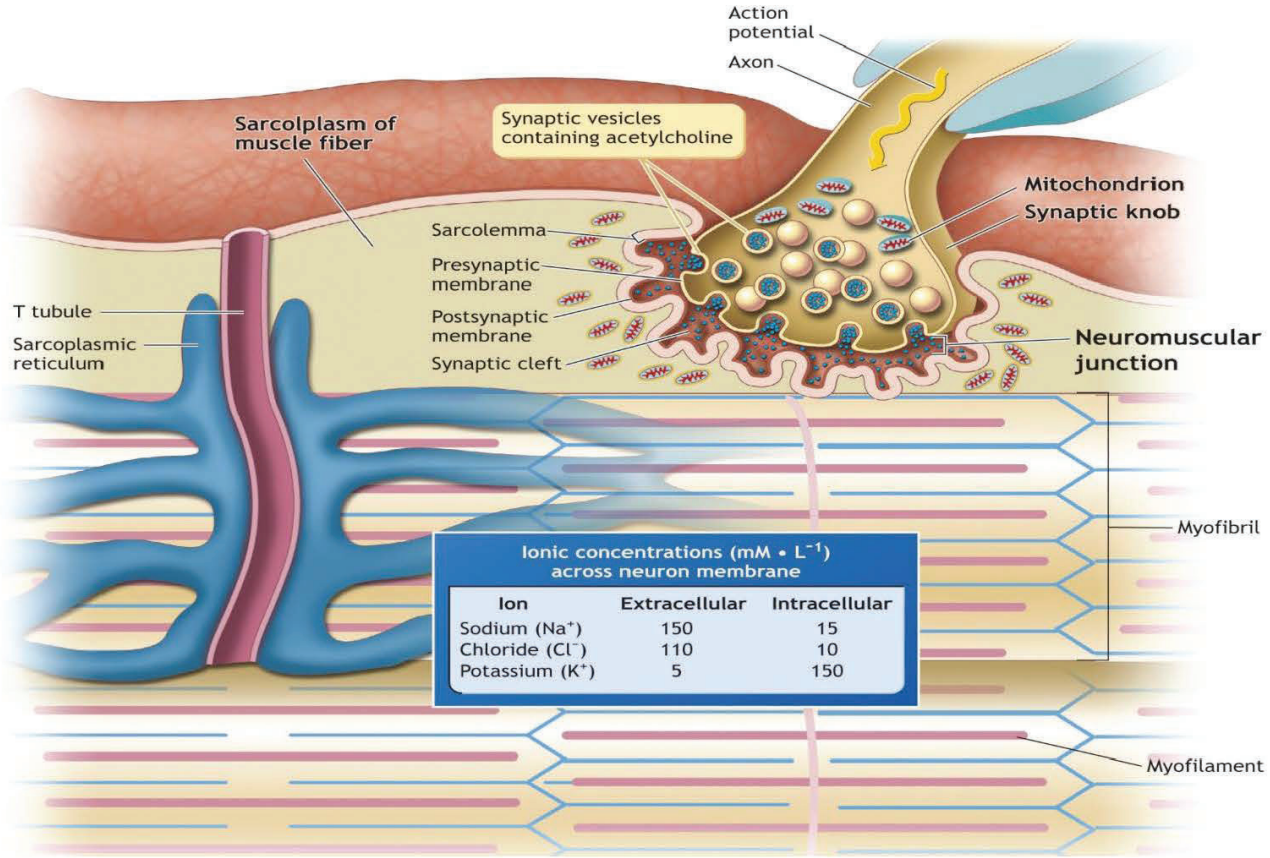
Interneurons are located entirely within the central nervous system. They intercept the impulses from the sensory neurons and transmit the signals to the motor neurons.

Types of neurons…

The motor neurons usually have one axon and several dendrites. The axon is covered with a insulating fatty layer called a myelin sheath, and transmits signals a long distance from the neuron to the area to be activated. Dendrites are short and unsheathed.

Motor neurons cause muscle contractions and control secretions from glands and organs… controlling body functions.





Ionic concentrations (mM • L^{-1}) across neuron membrane

Ion	Extracellular	Intracellular
Sodium (Na^+)	150	15
Chloride (Cl^-)	110	10
Potassium (K^+)	5	150

Neuroglial Cells

Neuroglial cells fill spaces, support neurons, provide structural frameworks, produce myelin, and carry on phagocytosis. Four are in the CNS and the last in the PNS.

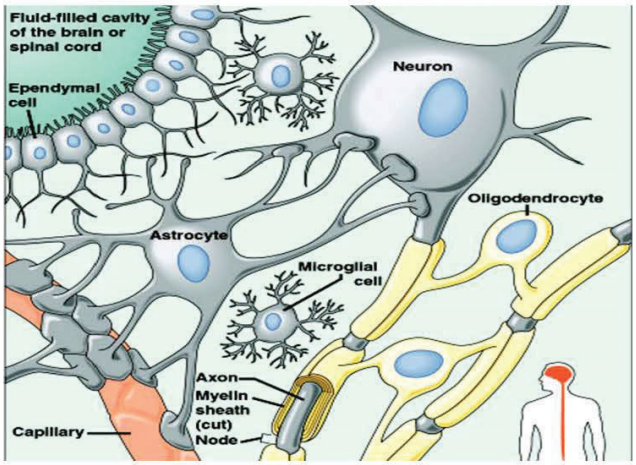
Microglial cells are small cells that phagocytize bacterial cells and cellular debris.

Oligodendrocytes form myelin in the brain and spinal cord.

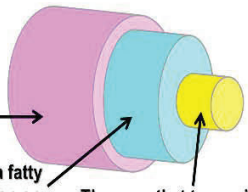
Astrocytes are near blood vessels and support structures, aid in metabolism, and respond to brain injury by filling in spaces.

Ependymal cells cover the inside of ventricles and form choroid plexuses within the ventricles.

Schwann cells are the myelin-producing neuroglia of the peripheral nervous system.



Nerve fibers…



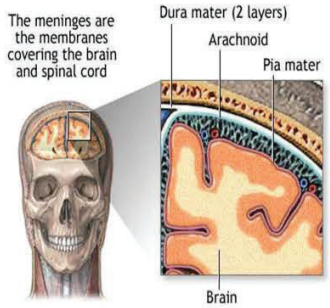
Schwann cells, only found on peripheral nerves which can regenerate

Myelin sheath, a fatty layer of insulation on some nerve fibers

The axon that transmits the message

There are no Schwann cells on nerve fibers in the central nervous system, therefore damage to those nerve fibers is not reversible. A bundle of nerve fibers is simply called 'a nerve'. AFFERENT nerves conduct impulses to the central nervous system; EFFERENT nerves conduct impulses to the muscles, organs, and glands.

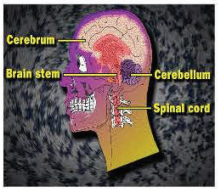
Brain and spinal cord meninges…

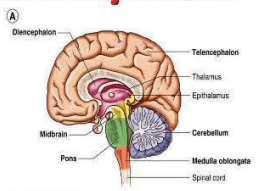


The brain and spinal cord are enclosed by 3 membranes, collectively known as the meninges

the outside membrane is the dura mater; the middle membrane is the arachnoid; and the inside membrane is the pia mater.

The Brain - 3 Major Areas

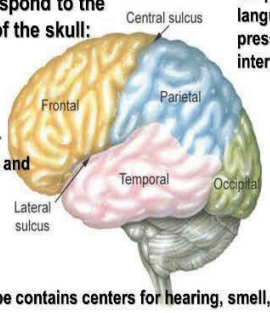




- Cerebrum composed of Telencephalon (Cerebral Cortex - gray matter because nerve fibers lack white myelin coating) and Diencephalon
- Cerebellum
- Brainstem (midbrain, pons, medulla oblongata)

Parts of the brain…the cerebrum

The cortex is also divided into 4 lobes that correspond to the overlying bones of the skull:



the parietal lobe is where language, temperature, pressure, touch are interpreted;

the frontal lobe specializes in motor activity, personality, and speech;

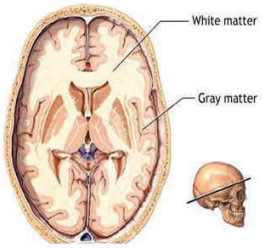
the occipital lobe specializes in vision

the temporal lobe contains centers for hearing, smell, and language input

Gray and white matter of the central nervous system…

The brain and spinal cord of the central nervous system receive impulses, process the information, and respond with the appropriate action.

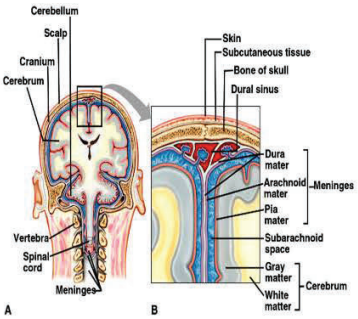
Gray matter of the brain and spinal cord consists of unsheathed nerve fibers (cannot be regenerated if damaged) in the cortex or surface layer. The white matter makes up the internal structure, and consists of myelinated nerve fibers.



The brain and spinal cord are surrounded by membranes called meninges that lie between the bone and the soft tissues.

The outermost meninx is made up of tough, white dense connective tissue, contains many blood vessels, and is called the dura mater. It forms the inner periosteum of the skull bones. In some areas, the dura mater forms partitions between lobes of the brain, and in others, it forms dural sinuses. The sheath around the spinal cord is separated from the vertebrae by an epidural space.

The middle meninx, the arachnoid mater, is thin and lacks blood vessels. It does not follow the convolutions of the brain. Between the arachnoid and pia maters is a subarachnoid space containing cerebrospinal fluid.



The innermost pia mater is thin and contains many blood vessels and nerves. It is attached to the surface of the brain and spinal cord and follows their contours.

Parts of the brain…the cerebrum

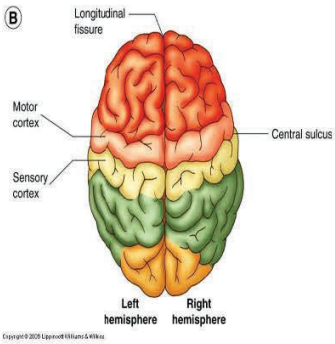
Taking up 7/8 ths of the brain's weight, the cerebrum governs all sensory and motor activity. This includes sensory perception, emotions, consciousness, memory, and voluntary movements.



It is divided into the left and right hemispheres. The surface or cortex is arranged in bulging folds, each one called a gyrus, and furrows, each one called a sulcus.

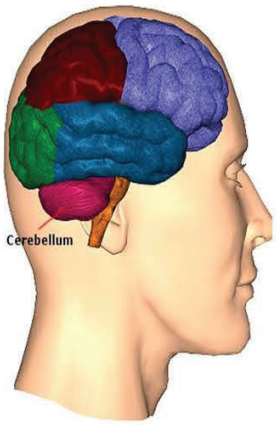
Functions of the Cerebral Cortex

- Intellectual processes: thought, intelligence.
- Processes sensory information and integrates with past experience to produce appropriate motor response.



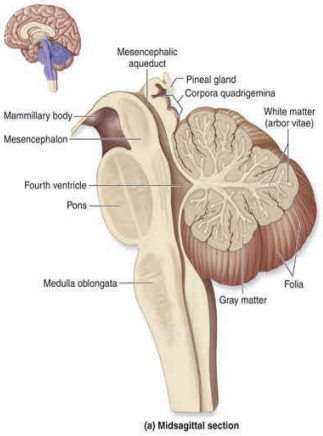
Cerebellum

The cerebellum is the second largest part of the brain. It contains nerve fibers that connect it to every part of the central nervous system. It coordinates voluntary and involuntary patterns of movements. It also adjusts muscles to automatically maintain posture.

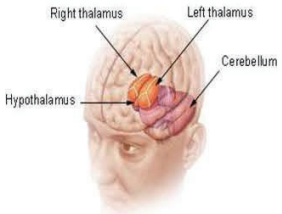


Cerebellum

- Located behind the brainstem
- Helps monitor and regulate movement
- Integrates postural adjustments, maintenance of equilibrium, perception of speed, and other reflexes related to fine tuning of movement.



Diencephalon

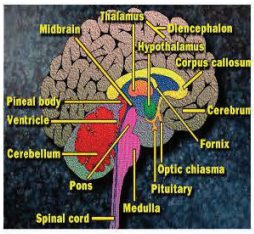


The diencephalon refers to the thalamus and hypothalamus.
The thalamus is the relay center for all sensory impulses except olfactory (sense of smell) and motor areas of the cortex.

The hypothalamus regulates behavior and emotional expression, body temperature, and many metabolic activities. Attached to the pituitary gland, it also controls hormonal secretions of this gland.

Diencephalon - 2 Major Parts

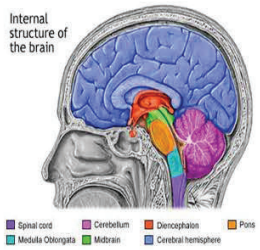
- Thalamus
  - Relays stimuli received from all sensory neurons to cortex for interpretation
  - Relays signals from the cerebral cortex to the proper area for further processing
- Hypothalamus
  - Monitors many parameters
    - temperature, blood glucose levels, various hormone levels
  - Helps maintain homeostasis
  - Signals the pituitary via releasing factors
  - Signals the lower neural centers



Parts of the brain... the brainstem

The brainstem consists of 3 structures: midbrain, pons, and medulla oblongata. The gray matter of the midbrain control visual reflexes and sense of hearing. The white matter of the pons plays a role in regulating visceral (internal organ) control.

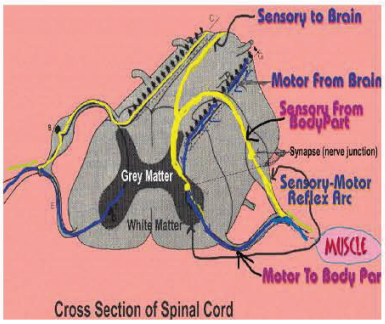
The medulla oblongata connects the rest of the brain to the spinal cord. It regulates breathing, swallowing, coughing, sneezing, vomiting, heartbeat, and blood pressure.



Contains both gray and white matter
Gray matter is H-shape in core of cord
The spinal cord has 31 segments: 8 cervical segments that correspond to the C1-C8 vertebrae; 12 thoracic segments corresponding to the T1-T12 vertebrae; 5 lumbar segments corresponding to L1-L5 vertebrae, 5 sacral segments corresponding to S1-S5 vertebrae, and 1 coccygeal segment.

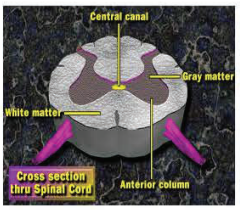
The spinal cord...

At each segment of the spinal cord, left and right pairs of sensory and motor nerves branch out and connect to the peripheral nervous system. Impulses travel back and forth to the brain and back to the muscles.



Gray Matter

- Regions of brain and spinal cord made up primarily of cell bodies and dendrites of nerve cells
- Interneurons in spinal cord
  - small nerves which do not leave the spinal cord
- Terminal portion of axons



White Matter

- Contains tracts or pathways made up of bundles of myelinated nerves
- Carry ascending and descending signals
  - Ascending nerve tract from sensory receptors through dorsal root, up cord to thalamus, to cerebral cortex
  - Pyramidal tract transmits impulses downward eventually excites motoneurons control muscles.
  - Extrapyramidal originate in brain stem descend to control posture.

Descending Nerve Tracts

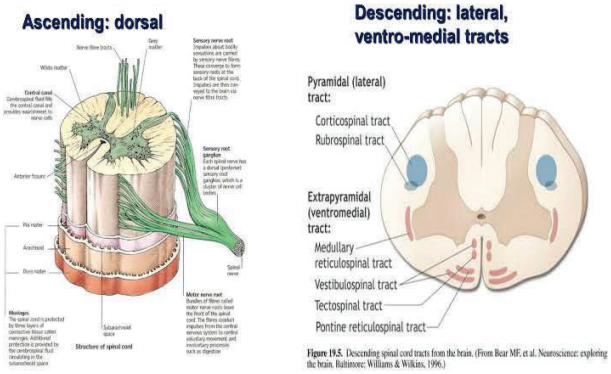
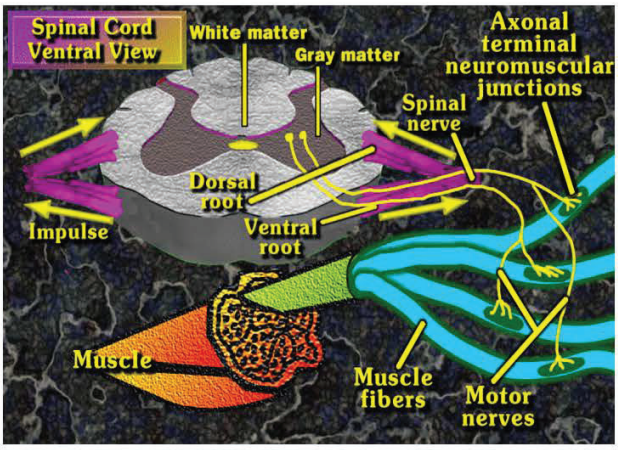
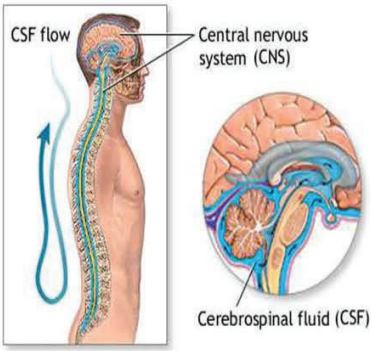


Figure 19.5. Descending spinal cord tracts from the brain. (From Bear MF, et al. Neuroscience: exploring the brain. Baltimore: Williams & Wilkins, 1996.)



Cerebrospinal fluid…

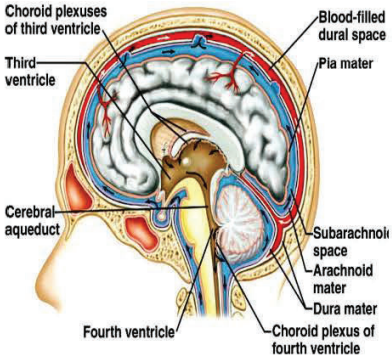
A colorless fluid is produced in the ventricles of the brain; it surrounds the brain and spinal cord. It is called cerebrospinal fluid, and it cushions the brain and cord from shocks that could cause injury. It is maintained at a level around 1/2 - 2/3 cup.



Ventricles and Cerebrospinal Fluid

The ventricles are a series of connected cavities within the cerebral hemispheres and brain stem. The ventricles are continuous with the central canal of the spinal cord, and are filled with fluid.

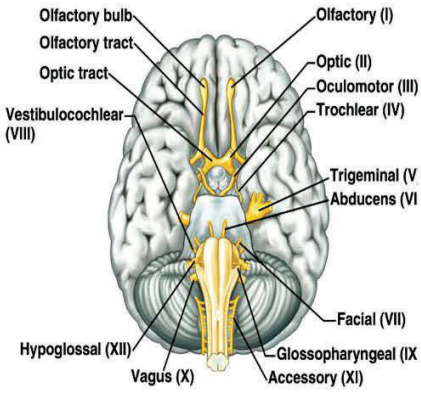
Choroid plexuses, specialized capillaries from the pia mater, secrete cerebrospinal fluid. Most cerebrospinal fluid arises in the lateral ventricles. Cerebrospinal fluid has nutritive as well as protective (cushioning) functions.



Peripheral nervous system…

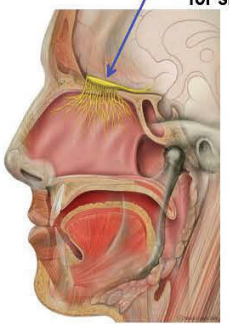
The network of nerves branching out throughout the body from the brain and spinal cord is called the peripheral nervous system. In addition to the 31 pairs of spinal nerves mentioned in the slides on the spinal cord, there are 12 pairs of cranial nerves that attach to the brain.

- Twelve pairs of cranial nerves arise from the underside of the brain, most of which are mixed nerves.
- The 12 pairs are designated by number and name and include the olfactory, optic, oculomotor, trochlear, trigeminal, abducens, facial, vestibulocochlear, glossopharyngeal, vagus, accessory, and hypoglossal nerves.



Peripheral nervous system…

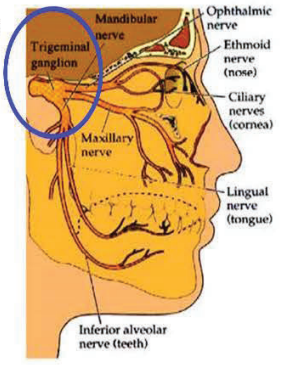
I. The olfactory nerve carries sensory input for smell



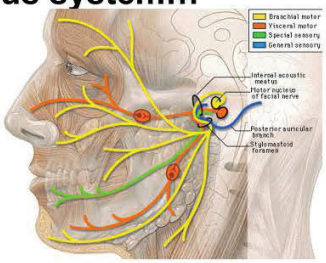
Peripheral nervous system…

II. The optic nerve carries sensory input for vision
III. The oculomotor nerve controls muscles of the eye and eyelid
IV. The trochlear nerve controls the eyeball
V. The trigeminal nerve controls the face, nose, mouth, forehead, top of head, and jaw.

VI. The abducens nerve also controls the eyeball



Peripheral nervous system…



VII. The facial nerve controls muscles of the face and scalp, and part of the tongue for sense of taste.

VIII. The auditory or cochlear nerve provides sensory input for hearing and equilibrium.

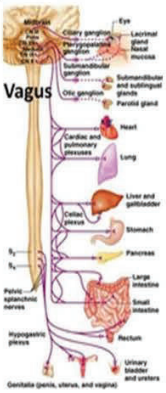
IX. The glossopharyngeal nerve controls saliva, swallowing, and taste.

Peripheral nervous system…

X. The vagus nerve is the longest cranial nerve, extending to and controlling the heart, lungs, stomach, and intestines.

XI. The accessory nerve permits movement of the head and shoulders.

XII. The hypoglassal nerve controls the muscles of the tongue.



Spinal Nerves

Thirty-one pairs of mixed nerves make up the spinal nerves.

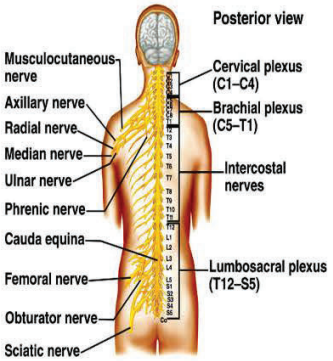
Spinal nerves are grouped according to the level from which they arise and are numbered in sequence beginning with those in the cervical region.

Each spinal nerve arises from two roots: a dorsal, or sensory, root, and a ventral, or motor, root. The main branches of some spinal nerves form plexuses.

The cervical plexuses lie on either side of the neck and supply muscles and skin of the neck.

The brachial plexuses arise from lower cervical and upper thoracic nerves and lead to the upper limbs.

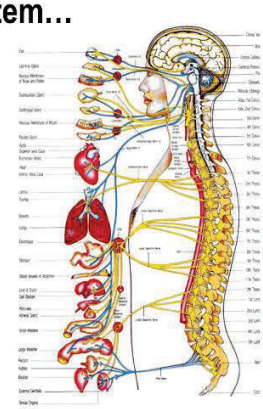
The lumbrosacral plexuses arise from the lower spinal cord and lead to the lower abdomen, external genitalia, buttocks, and legs.



Autonomic nervous system…

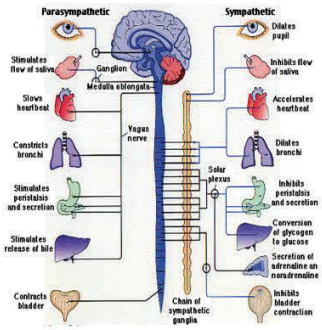
The autonomic nervous system is a part of the peripheral nervous system.. it controls the involuntary bodily functions such as sweating, gland secretions, blood pressure, and the heart. It is divided into the 'sympathetic' and 'parasympathetic' divisions.

In the autonomic motor system, motor pathways include two fibers: a preganglionic fiber that leaves the CNS, and a postganglionic fiber that innervates the effector.



Autonomic nervous system…

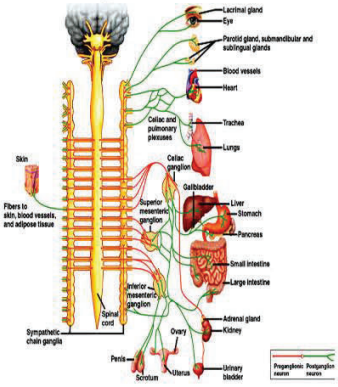
The sympathetic nervous system is responsible for the 'flight or fight' responses… increased alertness, metabolic rate, respiration, blood pressure, heart rate, and sweating AND a decrease in digestive and urinary function. The parasympathetic nervous system counteracts the responses of the sympathetic system… restoring homeostasis.



Autonomic nervous system…

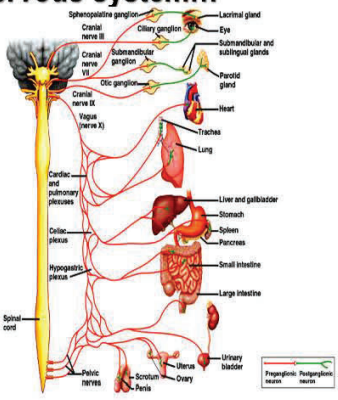
Sympathetic Division

Fibers in the sympathetic division arise from the thoracic and lumbar regions of the spinal cord, and synapse in paravertebral ganglia close to the vertebral column. Postganglionic axons lead to an effector organ.



Autonomic nervous system…

Fibers in the parasympathetic division arise from the brainstem and sacral region of the spinal cord, and synapse in ganglia close to the effector organ.



Autonomic nervous system…

The autonomic nervous system has the task of maintaining homeostasis of visceral activities without conscious effort.

The autonomic nervous system includes two divisions: the sympathetic and parasympathetic divisions, which exert opposing effects on target organs.

The parasympathetic division operates under normal conditions.

The sympathetic division operates under conditions of stress or emergency.

Preganglionic fibers of both sympathetic and parasympathetic divisions release acetylcholine.

Parasympathetic postganglionic fibers are cholinergic fibers and release acetylcholine.

Sympathetic postganglionic fibers are adrenergic and release norepinephrine.

The effects of these two divisions, based on the effects of releasing different neurotransmitters to the effector, are generally antagonistic.

The autonomic nervous system is largely controlled by reflex centers in the brain and spinal cord.

The limbic system and cerebral cortex alter the reactions of the autonomic nervous system through emotional influence.

1. Membrane Resting Potential

Definition and Importance of Resting Potential

The resting membrane potential (RMP) is the voltage difference across the plasma membrane of a cell when it is not actively transmitting signals. In neurons, this is typically around -70 mV, with the inside of the cell more negative than the outside. This voltage difference is crucial because it primes the cell for excitability, enabling neurons to fire action potentials in response to stimuli.

Without the resting membrane potential, excitable cells such as neurons, cardiac cells, and muscle fibers would not be able to propagate electrical signals essential for communication, muscle contraction, and other physiological processes. The maintenance of this potential is a finely balanced process involving selective permeability to ions and active transport mechanisms.

Ion Distribution Across the Cell Membrane

The RMP is largely determined by the unequal distribution of ions across the membrane. The key ions involved are:

- Sodium (Na^+): Concentration is high outside the cell (~145 mM) and low inside (~12 mM). Sodium tends to move into the cell due to both its concentration gradient and the negative charge inside the cell.
- Potassium (K^+): The concentration is high inside the cell (~150 mM) and low outside (~5 mM). Potassium ions are critical for maintaining the negative charge inside the cell because they move out of the cell more easily than other ions can move in.
- Chloride (Cl^-): Chloride ions are also more concentrated outside the cell, contributing to the overall negative charge inside the neuron.
- Large Anions (A^-): These include negatively charged proteins and organic molecules trapped inside the cell, which contribute to the intracellular negativity.

Role of Ion Channels in Establishing and Maintaining Resting Potential

Ion channels are pivotal in maintaining the RMP:

- K^+ leakage channels allow potassium ions to passively diffuse out of the cell, creating a negative charge inside.
- Na^+ leakage channels are less prevalent, and thus Na^+ does not significantly enter the cell to counteract the negative charge created by K^+.
- The selective permeability of the membrane to these ions is critical for establishing the RMP.

Na^+/K^+ ATPase Pump

This pump is a crucial component in maintaining ion concentration gradients. It actively transports 3 Na^+ out of the cell and 2 K^+ in for every ATP molecule hydrolyzed. This action is vital for several reasons:

1. Maintaining Ionic Gradients: By continuously pumping Na^+ out and K^+ in, the pump prevents the equalization of ion concentrations, which would eliminate the resting potential.
2. Electrogenic Effect: Although minor, the pump contributes to the membrane potential by making the inside of the cell more negative.
3. Recovery After Action Potentials: After action potentials, the Na^+/K^+ ATPase helps restore the original ion concentrations, maintaining homeostasis.

Electrochemical Gradients and the Nernst Equation

The Nernst equation is used to calculate the equilibrium potential (E_x) for any ion, where the electrochemical gradient for that ion is balanced, and there is no net movement of ions across the membrane. The equation is as follows:

$$E_{\text{ion}} = \frac{RT}{zF} \ln \left(\frac{[\text{ion outside}]}{[\text{ion inside}]} \right)$$

For potassium (K^+), the equilibrium potential is approximately -90 mV, while for sodium (Na^+), it is +60 mV. The resting potential (~-70 mV) is closer to the equilibrium potential of K^+, reflecting the membrane's higher permeability to potassium.

Factors Influencing Resting Membrane Potential

- Ion Concentration Gradients: The differences in concentration of Na^+, K^+, and Cl^- across the membrane are the primary factors.
- Membrane Permeability: The greater permeability of the membrane to K^+ than to Na^+ is responsible for the resting potential being closer to the K^+ equilibrium potential.
- Na^+/K^+ Pump Activity: The constant activity of the Na^+/K^+ ATPase maintains the ionic gradients necessary for the resting potential.
- Temperature and Ionic Strength: Changes in temperature and extracellular ion concentration can affect membrane potential by altering ion channel dynamics.

---

2. Membrane Action Potential

Initiation of Action Potential

An action potential is initiated when a stimulus causes the membrane potential to depolarize to the threshold level, typically around -55 mV. This threshold is reached when excitatory stimuli cause enough Na^+ to enter the cell through ligand-gated or mechanically-gated ion channels, triggering the opening of voltage-gated Na^+ channels.

Phases of Action Potential

1. Depolarization:
    - Voltage-gated Na^+ channels open, allowing a rapid influx of Na^+ into the cell.
    - The membrane potential moves from -70 mV toward +30 mV due to the large concentration gradient for Na^+ and the negative interior of the cell, which attracts Na^+ ions.
2. Repolarization:
    - Na^+ channels inactivate and voltage-gated K^+ channels open, allowing K^+ to exit the cell, bringing the membrane potential back down toward the resting level.
3. Hyperpolarization:
    - K^+ channels remain open longer than necessary, causing the membrane potential to briefly become more negative than the resting potential (e.g., -80 mV).
    - This phase ensures the neuron cannot be re-excited immediately, contributing to the refractory period.

Role of Voltage-Gated Ion Channels

- Voltage-gated Na^+ Channels: Open during depolarization and close during repolarization, playing a critical role in initiating and propagating the action potential.
- Voltage-gated K^+ Channels: Open more slowly than Na^+ channels and are responsible for repolarization and hyperpolarization.
- Voltage-gated Ca^{2+} Channels: Important in specific cells like cardiac muscle cells, where Ca^{2+} influx prolongs depolarization (the plateau phase), contributing to excitation-contraction coupling.

Refractory Periods

- Absolute Refractory Period: During this time, no new action potential can be generated regardless of stimulus strength, as the Na^+ channels are inactivated.
- Relative Refractory Period: A stronger-than-normal stimulus can initiate an action potential because some Na^+ channels have reset, but the membrane is still hyperpolarized.

All-or-Nothing Principle

Action potentials are all-or-nothing events, meaning once the threshold is reached, the action potential will proceed with a fixed amplitude and duration. Increasing the stimulus intensity does not change the size of the action potential but can increase the frequency of action potentials.

Propagation of Action Potentials

- Saltatory Conduction (in Myelinated Axons): The action potential jumps from one Node of Ranvier (gaps in the myelin sheath) to the next, increasing the speed of conduction. Myelin acts as an insulator, preventing ion leakage and allowing rapid transmission.
- Continuous Conduction (in Unmyelinated Axons): The action potential propagates more slowly because every segment of the membrane must depolarize and repolarize sequentially.

---

3. Primary Messengers

Definition and Role in Cellular Signaling

Primary messengers are extracellular signaling molecules that initiate cellular responses by binding to specific receptors on the target cell membrane. These signals can act locally (as in neurotransmission) or over long distances (as in hormonal signaling).

Types of Primary Messengers

- Neurotransmitters: Released by neurons to transmit signals across synapses (e.g., acetylcholine, glutamate, gamma-aminobutyric acid (GABA)).
- Hormones: Secreted by endocrine glands and travel through the bloodstream to target distant cells (e.g., insulin, epinephrine).
- Growth Factors: Stimulate cell growth, proliferation, and differentiation (e.g., nerve growth factor, epidermal growth factor).

Mechanisms of Receptor-Ligand Binding

- Ligand-Gated Ion Channels: When a primary messenger (ligand) binds to these receptors, ion channels open, allowing ions such as Na^+, K^+, or Ca^{2+} to flow into or out of the cell, altering membrane potential.
- G-Protein Coupled Receptors (GPCRs): These receptors activate intracellular G-proteins when a primary messenger binds, triggering downstream signaling pathways involving secondary messengers.

Examples of Primary Messengers

- Acetylcholine: Binds to nicotinic receptors on muscle cells, causing muscle contraction, and to muscarinic receptors in the autonomic nervous system to regulate organ function.
- Dopamine: Plays roles in reward, motivation, and motor control through its action on dopaminergic receptors.
- Epinephrine (Adrenaline): Increases heart rate and mobilizes energy stores by binding to adrenergic receptors during stress (fight-or-flight response).

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4. Secondary Messengers

Definition and Function

Secondary messengers are intracellular signaling molecules that propagate and amplify the signal initiated by a primary messenger. After the primary messenger binds to its receptor, the production or activation of secondary messengers amplifies the signal, ensuring a robust cellular response.

Common Secondary Messengers

- cAMP (Cyclic Adenosine Monophosphate): Synthesized by adenylate cyclase in response to GPCR activation, cAMP activates protein kinase A (PKA), which phosphorylates target proteins to alter cellular processes.
- cGMP (Cyclic Guanosine Monophosphate): Similar to cAMP, cGMP is involved in processes like vasodilation and phototransduction.
- IP_3 (Inositol Triphosphate) and DAG (Diacylglycerol): Produced by the cleavage of phospholipids by phospholipase C, IP_3 releases Ca^{2+} from intracellular stores, while DAG activates protein kinase C (PKC).
- Ca^{2+} Ions: Serve as universal secondary messengers in muscle contraction, neurotransmitter release, and other processes.

Role of Secondary Messengers in Amplifying and Propagating Signals
A single receptor-ligand binding event can result in the generation of thousands of secondary messenger molecules, amplifying the signal and ensuring a large physiological response. This amplification is critical in many systems, such as hormone signaling and neurotransmission.
Pathways Involving Secondary Messengers

- Adenylyl Cyclase-cAMP Pathway: GPCR activation increases cAMP production, which activates PKA. PKA phosphorylates various target proteins, leading to changes in gene expression, metabolism, and other cellular activities.
- Phospholipase C-IP_3/DAG Pathway: Activation of phospholipase C by GPCRs generates IP_3 and DAG, leading to the release of Ca^{2+} from the endoplasmic reticulum and activation of PKC, respectively.

Regulation of Cellular Processes by Secondary Messengers
Secondary messengers regulate a wide range of cellular activities, including:

- Gene expression: By activating transcription factors.
- Metabolism: Through the regulation of enzymes involved in metabolic pathways.
- Ion Channel Activity: Modulation of ion channels to alter membrane potential and cellular excitability.

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5. Signal Transduction Mechanisms
Overview of Signal Transduction Pathways
Signal transduction involves a series of molecular events that translate an extracellular signal (primary messenger) into an intracellular response. This process typically involves the activation of secondary messengers and a cascade of enzyme activations that lead to changes in cellular behavior.
GPCR and Secondary Messenger Activation
GPCRs are a major class of receptors involved in signal transduction. Upon binding a ligand, GPCRs activate G-proteins, which in turn activate enzymes like adenylate cyclase or phospholipase C, leading to the production of secondary messengers such as cAMP, IP_3, or DAG. These messengers propagate the signal within the cell.
Enzyme-Linked Receptors
Enzyme-linked receptors, such as tyrosine kinase receptors, become activated when ligands bind. This activation results in the phosphorylation of intracellular proteins, leading to various cellular responses. Insulin receptors are a prime example of this, initiating glucose uptake and metabolism.
Ion Channel-Linked Receptors
These receptors directly regulate the flow of ions across the membrane in response to ligand binding. Examples include nicotinic acetylcholine receptors, which open to allow Na^+ influx, depolarizing the membrane and initiating muscle contraction.
Cross-Talk Between Signaling Pathways
Cells integrate signals from multiple pathways through cross-talk, ensuring that cellular responses are coordinated. For instance, signaling via GPCR pathways can intersect with tyrosine kinase receptor pathways to regulate gene expression or cell survival.

---

6. Practical Applications and Clinical Implications
Role of Membrane Potentials in Excitable Tissues
The generation and maintenance of membrane potentials are essential in excitable tissues like neurons, cardiac muscle, and skeletal muscle. Proper function of these potentials allows for coordinated contraction of the heart, voluntary movement, and sensory processing.
Membrane Potential Dysfunction in Disease

- Epilepsy: Abnormal ion channel function can lead to hyperexcitability in neurons, resulting in seizures.
- Cardiac Arrhythmias: Defects in ion channels that govern action potential propagation can disrupt normal heart rhythms, leading to arrhythmias such as long QT syndrome or Brugada syndrome.

Practical Session 2: Physiology of the Nervous System

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1. Introduction to the Nervous System

Function of the Nervous System

The nervous system coordinates and regulates body activities through electrical and chemical signals. It processes sensory input from the environment, integrates the information, and generates appropriate motor responses. The nervous system also plays a key role in maintaining homeostasis, cognition, and behavior.

Key Components

The nervous system is divided into:

- Central Nervous System (CNS): Comprising the brain and spinal cord, the CNS is the control center, processing information and issuing commands.
- Peripheral Nervous System (PNS): Consisting of sensory and motor neurons, the PNS transmits signals between the CNS and the rest of the body.

---

2. Types of Neurons

Neurons are specialized cells responsible for transmitting signals in the nervous system. There are three main types of neurons based on their functions:

2.1. Sensory Neurons (Afferent Neurons)

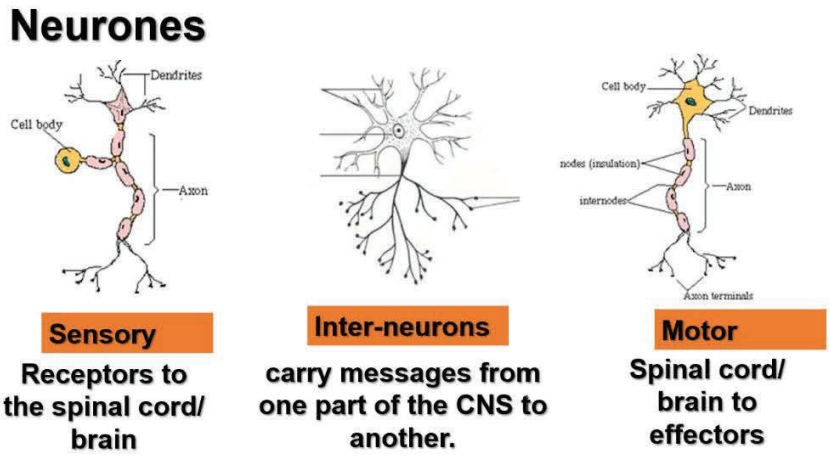
These neurons transmit signals from sensory receptors (such as skin, muscles, and organs) toward the CNS. They allow the body to perceive stimuli like heat, pain, and pressure.

2.2. Interneurons

Interneurons are located within the CNS and connect sensory and motor neurons. They process and integrate sensory input, playing a crucial role in reflexes and higher functions like learning and memory.

2.3. Motor Neurons (Efferent Neurons)

Motor neurons carry signals from the CNS to muscles and glands, eliciting a response such as muscle contraction or hormone release.



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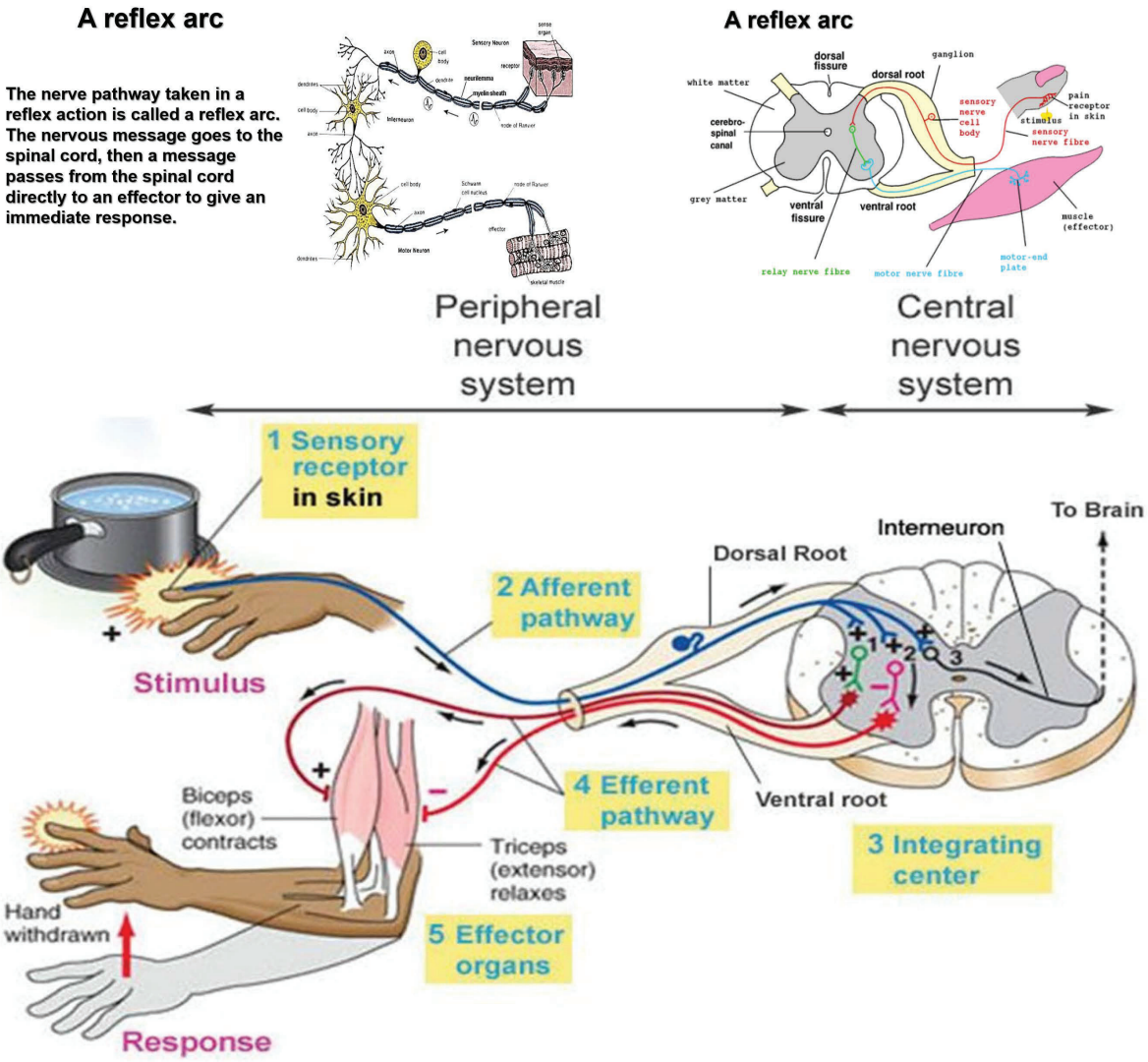
3. Structure of Neurons

Neurons have a unique structure that allows them to transmit electrical impulses efficiently.

- Axon:
  A long projection that transmits signals away from the neuron's cell body to other neurons or muscles. The axon is often covered by the myelin sheath, a fatty layer that insulates the axon and increases the speed of signal conduction through saltatory conduction.
- Dendrites:
  Branch-like structures that extend from the neuron's cell body and receive incoming signals from other neurons.
- Myelin Sheath:
  The myelin sheath is produced by Schwann cells in the peripheral nervous system and oligodendrocytes in the central nervous system. It allows rapid signal transmission along axons by insulating them from the surrounding extracellular fluid.



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4. Reflex Arc

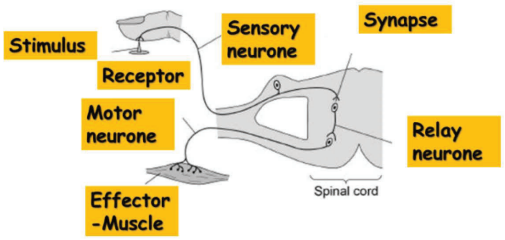
A reflex arc is a neural pathway that controls reflex actions, allowing the body to respond quickly to stimuli without conscious thought.

Components of a Reflex Arc:

1. Receptor: Detects the stimulus (e.g., muscle stretch).
2. Sensory Neuron: Carries the signal to the CNS.
3. Interneuron: Processes the signal (in spinal cord).
4. Motor Neuron: Sends the signal to the effector muscle.
5. Effector: Muscle or gland that performs the reflex action (e.g., muscle contraction).

Reflex Arc

- **A reflex arc is the nerve pathway which makes such a fast, automatic response as possible.**
- **They do not involve the conscious part of the brain**



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5. Motor Control and Coordination

Components of Proper Motor Control

- **Volition**
  transformation of abstract goals into activation of specific set of muscles
- **Coordination of signals to many muscle groups**
- **Proprioception**
  constant updates about muscle length, force, joint position
- **Postural adjustments**
- **Sensory feedback**
- **Compensation for body and muscles**
- **Unconscious processing**
  Walking, postural adjustments, etc.
- **Adaptability**
  acquisition of motor skills

Voluntary Motor Control

Voluntary movement is initiated in the motor cortex of the brain and coordinated by the cerebellum and basal ganglia, which ensure smooth and precise actions.

Proprioception

Proprioception is the body's ability to sense its position and movement in space. It relies on sensory feedback from muscle spindles and Golgi tendon organs to adjust posture and movement without conscious effort.

Postural Adjustments

Postural adjustments are automatic corrections the body makes to maintain balance and posture, often involving reflexive control.

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6. Motor Units and Muscle Force Control

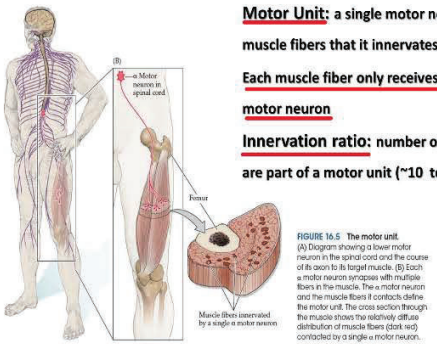


FIGURE 16.5 The motor unit. (A) Diagram showing a lower motor neuron in the spinal cord and the course of its axon to its target muscle. (B) Each α motor neuron synapses with multiple fibers in the muscle. The α motor neuron and the muscle fibers it contacts define the motor unit. The cross section through the muscle shows the relatively diffuse distribution of muscle fibers (dark red) contacted by a single α motor neuron.

Motor Unit: a single motor neuron and all of the muscle fibers that it innervates.

Each muscle fiber only receives input from one motor neuron

Innervation ratio: number of muscle fibers which are part of a motor unit (~10 to more than 1000)

6.1. Motor Units

A motor unit consists of a single motor neuron and all the muscle fibers it innervates. The size of the motor unit varies depending on the precision of muscle control required; muscles that require fine control (e.g., eye muscles) have smaller motor units, while those involved in gross movements (e.g., leg muscles) have larger motor units.

6.2. Recruitment of Motor Units

The recruitment of motor units follows the size principle: smaller motor units (with fewer muscle fibers) are recruited first for fine control and low-force actions, while larger motor units are recruited for stronger, more forceful contractions.

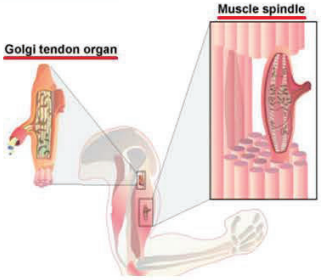
---

7. Proprioception and Sensory Feedback

Proprioception depends on sensory receptors within muscles and tendons that monitor changes in muscle length and tension.

Proprioception

Receptors
- muscle spindles
  - in parallel with muscle
  - signal length and velocity
- golgi tendon organs
  - in series with muscle
  - signal tension (force)



- Muscle Spindles:
  Specialized muscle fibers that detect changes in muscle length and provide information about muscle stretch to the CNS. They help adjust muscle contraction to maintain posture and coordinate movement.
- Golgi Tendon Organs:
  Located at the junction of muscles and tendons, Golgi tendon organs detect changes in muscle tension. They play a role in preventing excessive force that could damage muscles or tendons by inhibiting further contraction.

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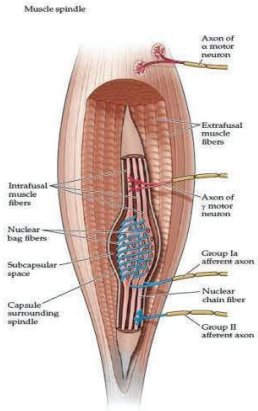
8. Practical Demonstrations and Experiments

8.1. Reflex Testing

- Stretch Reflex:
  The simplest reflex arc, exemplified by the knee-jerk reflex. Tapping the patellar tendon stretches the quadriceps muscle, triggering a reflexive contraction.
- Hyporeflexia and Hyperreflexia:
  Testing for decreased (hyporeflexia) or exaggerated (hyperreflexia) reflexes can indicate damage to the nervous system, such as in peripheral neuropathy or upper motor neuron lesions.

8.2. Muscle Contraction and Motor Unit Recruitment
Using electromyography (EMG), students can record electrical activity in muscles during contraction. By varying the intensity of contraction, students can observe the recruitment of different motor units.
8.3. EEG and Brain Activity
Electroencephalography (EEG) measures the electrical activity of the brain, typically used to study brain wave patterns during different states of consciousness and in diagnosing conditions like epilepsy.



Gamma motor neurons – control sensitivity of muscle spindles

- **innervate intrafusal fibers only**
- **ensure that muscle spindle stays taut and responsive during changes in muscle length**
- ***alpha-gamma coactivation* (coordinated contraction of extra- and intrafusal fibers**

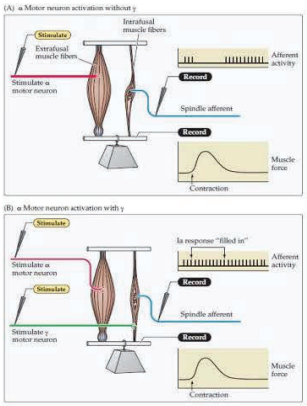


FIGURE 16.11 The role of γ motor neurons in regulating muscle spindle responses. (A) When α motor neurons are stimulated without activation of γ motor neurons, the response of the Ia fiber decreases as the muscle contracts. (B) When both α and γ motor neurons are activated, there is no decrease in Ia firing during muscle shortening. Thus, the γ motor neurons can regulate the gain of muscle spindles so they can operate efficiently at any length of the parent muscle. (After Hunt and Kuffler, 1951.)

9. Clinical Relevance and Applications

Motor Disorders
Neurological disorders affecting motor control demonstrate the critical role of motor neurons and sensory feedback systems. Examples include:

- Amyotrophic Lateral Sclerosis (ALS): A progressive neurodegenerative disorder that affects motor neurons, leading to muscle weakness and paralysis.
- Multiple Sclerosis (MS): An autoimmune disease that damages the myelin sheath, impairing the conduction of nerve impulses.
- Parkinson's Disease: A disorder of the basal ganglia that affects movement control, leading to tremors, rigidity, and bradykinesia (slowness of movement).

Reflex Abnormalities
Abnormal reflexes can indicate neurological problems. For instance:

- Absent reflexes may suggest peripheral nerve damage.
- Exaggerated reflexes might indicate damage to the central nervous system, such as in stroke or spinal cord injury.

EEG Rhythms:

can characteristically be broken down into different frequency bands

Attenuated during movement
Seen during alertness, active concentration

Relaxation, closing of the eyes
Control of inhibition

Drowsiness, meditation, action inhibition

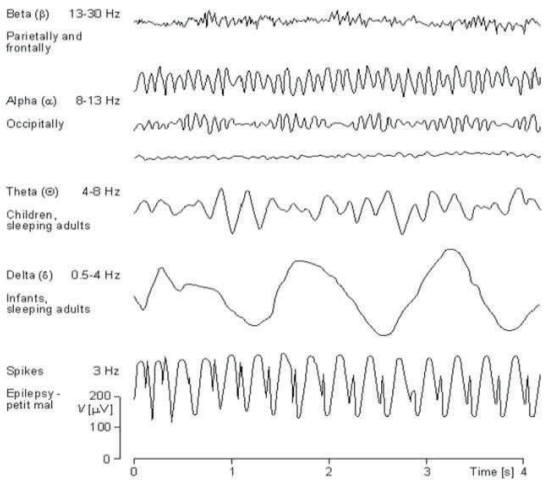
Continuous attention, slow wave sleep

• Mu (8 – 13 Hz):

Rest state motor neurons

• Gamma (30 – 100+ Hz):

Cross-modal sensory processing, short-term perceptual memory



Examination and Assessment

1	The Human Nervous System include:	
a.	Millions of interconnected neurons	True
b.	Central nervous system	True
c.	Peripheral nervous system	True
d.	Somatic nervous system	True
e.	Autonomic nervous system	True
f.	Neuroendocrine nervous system	False
g.	Paracrine nervous system	False
h.	Endocrine nervous system	False
i.	Exocrine nervous system	False
j.	Autocrine nervous system	False

2	General functions of the nervous system:	
a.	Gather information through the sensory elements	True
b.	Sensory information used to create sensations, memory, thoughts, decisions	True
c.	Integrative function	True
d.	Motor function	True
e.	unconscious autonomic effector activities	True
f.	Gather information through the motor elements	False
g.	Motor information used to create sensations, memory, thoughts, decisions	False
h.	Exocrine function	False
i.	Excretory function	False
j.	Conscious autonomic effector activities	False

3	Are neuron components:	
a.	Axon terminals	True
b.	Axons	True
c.	Dendrites	True
d.	Cell body	True
e.	Neurofibrils	True
f.	Myelin sheath	False
g.	Schwann cells	False
h.	Neuroglia	False
i.	Nerves	False
j.	Neurilemma	False

4	Are types of neurons:	
a.	Bipolar neurons	True
b.	Multipolar neurons	True
c.	Sensory neurons	True
d.	Interneurons	True
e.	Motor neurons	True
f.	Spatial neurons	False
g.	Fusion neurons	False
h.	Schwann neurons	False
i.	Glial neurons	False
j.	Gray neurons	False

5	A neuron has a cell body with:	
a.	mitochondria	True
b.	lysosomes	True
c.	Golgi apparatus	True
d.	chromatophilic substance (Nissl bodies) containing rough endoplasmic reticulum	True
e.	neurofibrils	True
f.	Axon terminals	False
g.	Axons	False
h.	Dendrites	False
i.	Synaptic knobs	False
j.	Myelin sheath	False

6	Larger axons are enclosed by sheaths of myelin provided by:	
a.	Schwann cells	True
b.	Specific glial cells	True
c.	A type of glial cells	True
d.	Myelin producing cells	True
e.	Myelin producing glial cells	True
f.	Ranvier nodes	False
g.	Axon terminals	False
h.	Dendrites	False
i.	Golgi apparatus	False
j.	Neurofibrils	False

7	Sensory neurons characteristics:	
a.	afferent neurons	True
b.	conduct impulses from peripheral receptors to the CNS	True
c.	are usually unipolar	True
d.	some are bipolar neurons	True
e.	Gather information	True
f.	are only multipolar neurons	False
g.	conduct impulses from the CNS to effectors	False
h.	form links between other neurons	False
i.	efferent neurons	False
j.	integrates or analyses information	False

8	Motor neurons characteristics:	
a.	efferent neurons	True
b.	carry impulses away from CNS	True
c.	always multipolar	True
d.	effect a response	True
e.	are multipolar neurons that conduct impulses from the CNS to effectors	True
f.	afferent neurons	False
g.	conduct impulses from peripheral receptors to the CNS	False
h.	are usually unipolar	False
i.	some are bipolar neurons	False
j.	Gather information	False

9	Interneurons characteristics:	
a.	intercept the impulses from the sensory neurons and transmit the signals to the motor neurons	True
b.	are located entirely within the central nervous system	True
c.	always multipolar	True
d.	integrates or analyses information	True
e.	effect a response – action potential	True
f.	conduct impulses from peripheral receptors to the CNS	False
g.	are usually unipolar neurons	False
h.	some are bipolar neurons	False
i.	Gather information	False
j.	are usually bipolar neurons	False

10	Types of Neuroglial Cells	
a.	Microglial cells	True
b.	Oligodendrocytes	True
c.	Astrocytes	True
d.	Ependymal cells	True
e.	Schwann cells	True
f.	Bipolar glial cells	False
g.	Multipolar glial cells	False
h.	Sensory glial cells	False
i.	Inter-glial cells	False
j.	Motor glial cells	False

11	Gray matter of the central nervous system...	
a.	receive impulses	True
b.	process the information	True
c.	respond with the appropriate action	True
d.	consists of unsheathed nerve fibers (cannot be regenerated if damaged) in the cortex or surface	True
e.	H-shape in core of spinal cord	True
f.	makes up the internal structure	False
g.	consists of myelinated nerve fibers	False
h.	Composed of Microglial cells	False
i.	Composed of Astroglial cells	False
j.	Composed of oligodendrocytes	False

12	Brain and spinal cord meninges...	
a.	The brain and spinal cord are enclosed by 3 membranes, collectively known as the meninges	True
b.	the outside membrane is the dura mater	True
c.	the middle membrane is the arachnoid	True
d.	the inside membrane is the pia mater	True
e.	lie between the bone and the soft tissues	True
f.	The brain and spinal cord are enclosed by 4 membranes, collectively known as the meninges	False
g.	the outside membrane is the pia dura mater	False
h.	the middle membrane is a soft tissue	False
i.	the inside membrane is the dura mater	False
j.	lie between the bone and the blood vessels	False

13	Cerebrum include	
a.	Telencephalon	True
b.	Diencephalon	True
c.	Cerebral Cortex	True
d.	Thalamus	True
e.	Hypothalamus	True
f.	Cerebellum	False
g.	Midbrain	False
h.	Pons	False
i.	Medulla oblongata	False
j.	Brainstem	False

14	The cerebrum	
a.	up 7/8 ths of the brain's weight	True
b.	governs all sensory and motor activity	True
c.	place for sensory perception	True
d.	governs emotions	True
e.	governs consciousness, memory, and voluntary movements	True
f.	up 1/8 ths of the brain's weight	False
g.	governs all vegetative activity	False
h.	adjusts muscles to automatically maintain posture	False
i.	governs emotions	False
j.	governs consciousness, memory, and voluntary movements	False

15	Functions of the Cerebral Cortex:	
a.	Intellectual processes	True
b.	Thought	True
c.	Processes sensory information	True
d.	Integrates sensory information with past experience	True
e.	Produces appropriate motor responses	True
f.	coordinates voluntary and involuntary patterns of movements	False
g.	adjusts muscles to automatically maintain posture	False
h.	Integrates postural adjustments	False
i.	maintenance of equilibrium	False
j.	perception of speed, and other reflexes related to fine tuning of movement	False

16	Functions of the Cerebellum:	
a.	coordinates voluntary and involuntary patterns of movements	True
b.	adjusts muscles to automatically maintain posture	True
c.	Integrates postural adjustments	True
d.	maintenance of equilibrium	True
e.	perception of speed, and other reflexes related to fine tuning of movement	True
f.	Intellectual processes	False
g.	Thought	False
h.	Processes sensory information	False
i.	Integrates sensory information with past experience	False
j.	Produces appropriate motor responses	False

17	Hypothalamus regulates:	
a.	behavior	True
b.	emotional expression	True
c.	body temperature	True
d.	maintain homeostasis in many metabolic activities	True
e.	controls hormonal secretions of the pituitary gland	True
f.	maintenance of equilibrium	False
g.	perception of speed, and other reflexes related to fine tuning of movement	False
h.	Intellectual processes	False
i.	Thought	False
j.	Processes sensory information	False

18	Thalamus functions:	
a.	Relays stimuli received from all sensory neurons to cortex for interpretation	True
b.	Relays signals from the cerebral cortex to the proper area for further processing	True
c.	is the relay center for all sensory impulses except olfactory and motor areas of the cortex	True
d.	thalamus helps decide what to focus on among the vast amount of information that it receives	True
e.	thalamus plays an important role in regulating states of sleep and wakefulness	True
f.	behavior	False
g.	emotional expression	False
h.	body temperature	False
i.	maintain homeostasis in many metabolic activities	False
j.	controls hormonal secretions of the pituitary gland	False

19	The brainstem	
a.	consists of 3 structures: midbrain, pons, and medulla oblongata	True
b.	The gray matter of the midbrain control visual reflexes and sense of hearing	True
c.	The white matter of the pons plays a role in regulating visceral (internal organ) control	True
d.	The medulla oblongata connects the rest of the brain to the spinal cord	True
e.	regulates breathing, swallowing, coughing, sneezing, vomiting, heartbeat, and blood pressure	True
f.	controls hormonal secretions of the pituitary gland	False
g.	maintenance of equilibrium	False
h.	perception of speed, and other reflexes related to fine tuning of movement	False
i.	Intellectual processes	False
j.	maintain homeostasis in many metabolic activities	False

20	The spinal cord...	
a.	Contains both gray and white matter	True
b.	Gray matter is H-shape in core of cord	True
c.	The spinal cord has 31 segments	True
d.	At each segment of the spinal cord, left and right pairs of sensory and motor nerves branch out	True
e.	Impulses travel back and forth to the brain and back to the muscles	True
f.	regulates breathing, swallowing, coughing, sneezing, vomiting, heartbeat, and blood pressure	False
g.	controls hormonal secretions of the pituitary gland	False
h.	maintenance of equilibrium	False
i.	perception of speed, and other reflexes related to fine tuning of movement	False
j.	Intellectual processes	False

21	Descending Nerve Tracts in the spinal cord are:	
a.	Pyramidal tracts	True
b.	Rubrospinal tract	True
c.	Vestibulospinal tract	True
d.	Reticulospinal tract	True
e.	Tectospinal tract	True
f.	Lateral Spinothalamic tract	False
g.	Dorsal Spinocerebellar tract	False
h.	Ventral Spinocerebellar tract	False
i.	Spinotectal tract	False
j.	Spinovestibular tract	False

22	Cerebrospinal fluid...	
a.	A colorless fluid, has nutritive as well as protective (cushioning) functions	True
b.	produced in the ventricles of the brain;	True
c.	cushions the brain and cord from shocks that could cause injury	True
d.	serves a vital function in the cerebral autoregulation of cerebral blood flow	True
e.	maintained at a level around 1/2 - 2/3 cup	True
f.	body fluid in the circulatory system	False
g.	Regulation of core body temperature	False
h.	contain red blood cells	False
i.	controls hormonal secretions	False
j.	accounts for 7% of the human body weight	False

23	Peripheral nervous system includes:	
a.	31 pairs of spinal nerves and 12 pairs of cranial nerves designated by number and name	True
b.	Twelve pairs of cranial nerves arise from the underside of the brain, most of which are mixed nerves	True
c.	olfactory, optic, oculomotor, trochlear	True
d.	trigeminal, abducens, facial, vestibulocochlear	True
e.	glossopharyngeal, vagus, accessory, hypoglossal	True
f.	32 pairs of spinal nerves and 12 pairs of cranial nerves	False
g.	Cranial nerves are all mixed nerves	False
h.	spinal nerves are all sensitive nerves	False
i.	Cranial nerves are all sensitive nerves	False
j.	Cranial nerves are all motor nerves	False

24	Spinal Nerves:	
a.	Thirty-one pairs of mixed nerves.	True
b.	are grouped according to the level from which they arise and are numbered beginning from the cervical region	True
c.	Each spinal nerve arises from two roots: a dorsal, or sensory, root, and a ventral, or motor, root.	True
d.	The cervical plexuses lie on either side of the neck and supply muscles and skin of the neck.	True
e.	The brachial plexuses arise from lower cervical and upper thoracic nerves and lead to the upper limbs.	True
f.	32 pairs of spinal nerves	False
g.	Spinal nerves are all sensitive nerves	False

h.	Spinal nerves are all motor nerves	False
i.	Spinal nerves are designated by number and name	False
j.	Spinal nerves arise from the underside of the brain	False

25	Autonomic nervous system…	
a.	is a part of the peripheral nervous system	True
b.	controls the involuntary bodily functions	True
c.	controls sweating, gland secretions,	True
d.	controls blood pressure	True
e.	It is divided into the 'sympathetic' and 'parasympathetic' divisions	True
f.	maintenance of equilibrium	False
g.	perception of speed, and other reflexes related to fine tuning of movement	False
h.	Intellectual processes	False
i.	Thought	False
j.	Processes sensory information	False

26	The sympathetic nervous system is responsible for:	
a.	the 'flight or fight' responses…	True
b.	increased alertness, metabolic rate, respiration, blood pressure, heart rate, and sweating	True
c.	decrease digestive function	True
d.	decrease urinary function	True
e.	operates under conditions of stress or emergency	True
f.	arise from the brainstem and sacral region of the spinal cord	False
g.	synapse in ganglia close to the effector organ	False
h.	operates under normal conditions	False
i.	The parasympathetic nervous system counteracts the responses of the sympathetic system	False
j.	restores homeostasis	False

27	Parasympathetic nervous system:	
a.	arise from the brainstem and sacral region of the spinal cord	True
b.	synapse in ganglia close to the effector organ	True
c.	operates under normal conditions	True
d.	The parasympathetic nervous system counteracts the responses of the sympathetic system	True
e.	restores homeostasis	True
f.	the 'flight or fight' responses…	False
g.	increased alertness, metabolic rate, respiration, blood pressure, heart rate, and sweating	False
h.	decrease digestive function	False
i.	decrease urinary function	False
j.	operates under conditions of stress or emergency	False

28	Neurotransmitters released by the Autonomic nervous system	
a.	Preganglionic fibers of both sympathetic and parasympathetic divisions release acetylcholine	True
b.	Parasympathetic postganglionic fibers are cholinergic fibers and release acetylcholine.	True
c.	Sympathetic postganglionic fibers are adrenergic and release norepinephrine	True
d.	The effects of releasing different neurotransmitters to the effector are generally antagonistic	True
e.	The limbic system and cerebral cortex alter the reactions of the vegetative system through emotional influence.	True
f.	Dopamine is the main neurotransmitter released by the parasympathetic nervous system	False

g.	Serotonin is a monoamine neurotransmitter released by the sympathetic nervous system	False
h.	GABA neurotransmitter released by the sympathetic nervous system	False
i.	Glutamate neurotransmitter released by the parasympathetic nervous system	False
j.	Glycine neurotransmitter released by the parasympathetic nervous system	False

29	A reflex arc include	
a.	Sensory receptor	True
b.	Afferent pathway	True
c.	Integrating center	True
d.	Efferent pathway	True
e.	Effector organs	True
f.	Axon terminals	False
g.	Axons	False
h.	Dendrites	False
i.	Synaptic knobs	False
j.	Myelin sheath	False

30	A reflex arc	
a.	Stimulus initiate a reflex arc	True
b.	The nerve pathway taken in a reflex action is called a reflex arc.	True
c.	The nervous message goes to the spinal cord	True
d.	Message passes from the spinal cord directly to an effector	True
e.	An effector to give an immediate response to a stimulus	True
f.	regulates breathing, swallowing, coughing, sneezing, vomiting, heartbeat, and blood pressure	False
g.	controls hormonal secretions of the pituitary gland	False
h.	maintenance of equilibrium	False
i.	perception of speed, and other reflexes related to fine tuning of movement	False
j.	Intellectual processes	False

Course 3: Sense Organs

Sub-topic: Overview, Types of Senses, Receptors, and Sensory Systems

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1. The Senses
   - General Senses:
   - Special Senses:

---

2. Sensory Systems and Integration

---

3. Stimulus and Receptor Classification

---

4. General Properties of Sensory Systems

---

5. Types of Sensory Receptors (Based on Stimuli)

---

6. Sensory Receptor Functions

---

7. Sensory Adaptation

---

8. Four Steps to Sensation

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9. Sensory Modality

---

10. Somatic Pathways

---

11. Touch and Pressure

---

12. Temperature and Pain Sensation

---

13. Proprioception

---

14. Pain and Itch

---

15. Chemical Senses: Taste and Smell

---

16. Hearing and Equilibrium

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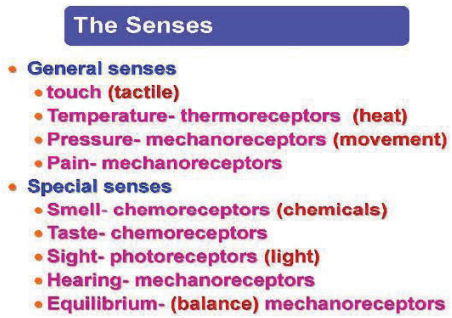
17. Vision

Examination and Assessment

Course 3: Sense Organs
Sub-topic: Overview, Types of Senses, Receptors, and Sensory Systems

1. The Senses



The human body has a complex system for detecting and interpreting stimuli from both internal and external environments, allowing for appropriate physiological and behavioral responses. The senses can be broadly classified into two categories: general senses and special senses.

- General Senses: These are distributed throughout the body and are primarily associated with detecting tactile sensations, temperature, pain, and proprioception. General senses include:
    - Touch (Tactile): Detected by mechanoreceptors that respond to pressure, vibration, and texture. Receptors in the skin include Meissner's corpuscles, which respond to light touch, and Pacinian corpuscles, which detect deep pressure and vibration.
    - Temperature (Thermoreception): Thermoreceptors detect changes in temperature and are classified into cold receptors and warm receptors. These are free nerve endings that detect thermal stimuli, with different receptor types for detecting heat and cold.
    - Pain (Nociception): Nociceptors are specialized sensory neurons that respond to damaging or potentially damaging stimuli, leading to the perception of pain. These receptors are essential for protecting the body from injury by triggering reflexes and conscious awareness of harmful stimuli.
    - Proprioception: This sense provides awareness of body position and movement. Proprioceptors are located in muscles, tendons, and joints, with important receptors such as muscle spindles that detect changes in muscle length and Golgi tendon organs that monitor tension in tendons.
- Special Senses: These are associated with specialized organs and are responsible for the detection of stimuli related to vision, hearing, balance, taste, and smell. Special senses include:
    - Vision (Photoreception): Detected by photoreceptors in the retina of the eye. These photoreceptors—rods and cones—convert light energy into electrical signals that the brain processes into images.
    - Hearing (Audition): Mechanoreceptors in the cochlea of the inner ear detect sound waves, which are transduced into nerve impulses. The auditory system distinguishes between different frequencies and intensities of sound.
    - Balance (Equilibrium): The vestibular apparatus in the inner ear, consisting of the semicircular canals and the otolithic organs (utricle and saccule), detects changes in head position and movement, maintaining balance and spatial orientation.
    - Taste (Gustation): Taste receptors located in taste buds on the tongue detect chemicals dissolved in saliva. Five primary taste modalities are recognized: sweet, salty, sour, bitter, and umami.
    - Smell (Olfaction): Olfactory receptors located in the nasal cavity detect airborne chemicals, allowing for the perception of odors. Olfaction is highly sensitive and capable of detecting a vast range of chemical compounds.

2. Sensory Systems and Integration

Sensory systems function as complex networks that convert environmental stimuli into electrical signals, which are then processed and interpreted by the central nervous system (CNS). The sensory pathway typically follows these steps:

1. Detection of the stimulus by specialized sensory receptors.

2. Transduction of the stimulus into an electrical signal, usually in the form of a graded potential.
3. Transmission of the signal via afferent neurons to the CNS.
4. Processing and integration in the CNS, which leads to perception and appropriate responses.

The sensory integration occurs in various parts of the brain, including the somatosensory cortex, visual cortex, and auditory cortex, depending on the modality. Higher-order processing involves the integration of multiple sensory inputs to create a coherent perception of the environment. The thalamus acts as a relay center, directing incoming sensory signals to the appropriate cortical areas for further processing.

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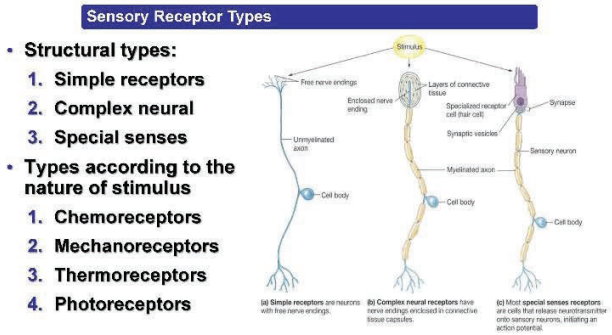
3. Stimulus and Receptor Classification

Stimuli can be classified based on their origin and type:



- Exteroceptors: Detect stimuli from outside the body, such as light, sound, temperature, and chemicals (e.g., in taste and smell).
- Interoceptors: Detect internal stimuli, such as changes in blood pressure, blood pH, and the composition of body fluids.
- Proprioceptors: Provide information about body position and movement, monitoring the stretch and tension in muscles, tendons, and joints.

Sensory receptors are further classified based on the type of stimulus they respond to:

- Mechanoreceptors: Respond to mechanical pressure or distortion. Examples include tactile receptors in the skin, baroreceptors in blood vessels (which monitor blood pressure), and proprioceptors in muscles and joints.
- Chemoreceptors: Detect chemical changes, including taste, smell, and the chemical composition of blood (e.g., CO_2 and pH levels).
- Thermoreceptors: Detect changes in temperature and are sensitive to either heat or cold.
- Photoreceptors: Located in the retina, these receptors detect light intensity and color, contributing to vision.
- Nociceptors: Sensitive to tissue-damaging stimuli, leading to the perception of pain.

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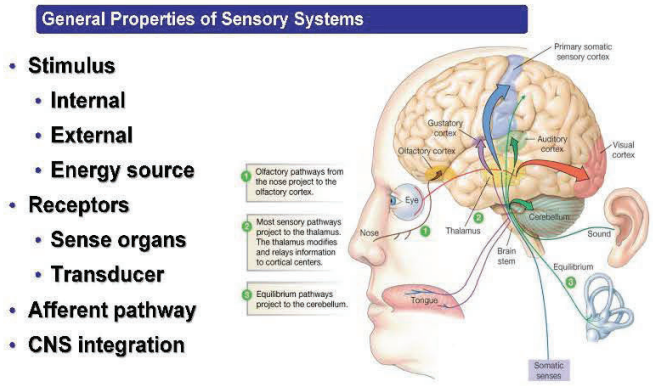
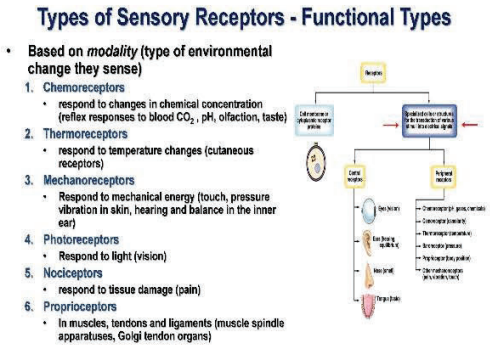
4. General Properties of Sensory Systems

The general properties of sensory systems include:



- Receptive Fields: The area monitored by a single sensory receptor. Smaller receptive fields allow for more precise localization of stimuli, which is why the fingertips have a higher tactile resolution compared to the back.
- Sensory Transduction: The process by which a stimulus is converted into an electrical signal. This occurs when a receptor is activated, leading to a change in ion permeability and the generation of a receptor potential.
- Adaptation: Sensory receptors may adapt to sustained stimuli, resulting in a decreased response over time. This allows the nervous system to ignore constant, unchanging stimuli and focus on novel or changing stimuli.
- Modality Specificity: Each sensory receptor is specialized to detect a specific type of stimulus (e.g., photoreceptors for light, mechanoreceptors for pressure).

5. Types of Sensory Receptors (Based on Stimuli)



Sensory receptors are specialized to detect different types of stimuli:

- Mechanoreceptors: Respond to physical deformation caused by touch, pressure, stretch, or vibration. Mechanoreceptors include:
  - Tactile receptors in the skin (e.g., Meissner's and Pacinian corpuscles).
  - Baroreceptors in blood vessels that monitor blood pressure.
  - Proprioceptors in muscles and joints that detect changes in body position.
- Chemoreceptors: Sensitive to chemical substances. Examples include:
  - Olfactory receptors in the nasal cavity, which detect airborne chemicals.
  - Taste receptors in taste buds, which detect chemicals dissolved in saliva.
  - Chemoreceptors in the carotid body, which detect changes in blood pH, CO_2, and O_2 levels.
- Thermoreceptors: Detect changes in temperature and are categorized into cold receptors and warm receptors. These are found in the skin and hypothalamus, helping regulate body temperature.
- Photoreceptors: Detect light in the retina. There are two types:
  - Rods, which detect light intensity and are responsible for vision in dim light.
  - Cones, which detect color and are responsible for sharp, detailed vision.
- Nociceptors: Specialized to detect noxious stimuli that may cause damage to tissues. These receptors are involved in the sensation of pain and are present in the skin, muscles, joints, and certain internal organs.

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6. Sensory Receptor Functions

Sensory receptors have specialized functions depending on their type:

- Detection: Each receptor is tuned to a specific type of stimulus. For example, photoreceptors in the eye detect light, while mechanoreceptors in the skin detect pressure.
- Transduction: The receptor converts the stimulus into an electrical signal, initiating a receptor potential. This is typically achieved through changes in ion channel activity, leading to the generation of an action potential if the stimulus is strong enough.
- Amplification: In some systems, the initial stimulus is amplified before it is transmitted. For instance, in vision, the light signal is amplified by multiple enzymatic reactions in photoreceptors.
- Adaptation: Receptors can either rapidly or slowly adapt to a continuous stimulus. Rapidly adapting (phasic) receptors detect changes in stimuli, while slowly adapting (tonic) receptors continue to respond to sustained stimuli.
- Transmission: The electrical signal travels along afferent neurons to the CNS, where it is processed and integrated for perception.

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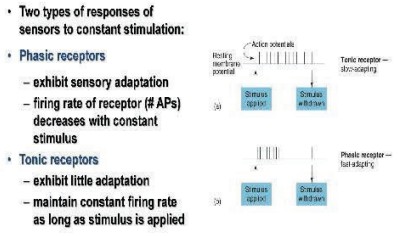
7. Sensory Adaptation



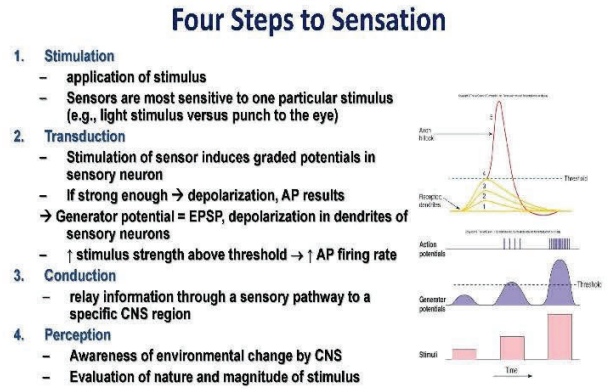
Sensory adaptation is the process by which sensory receptors reduce their sensitivity to a constant stimulus over time. Adaptation allows the nervous system to focus on new or changing stimuli rather than background noise. There are two types of adaptation:

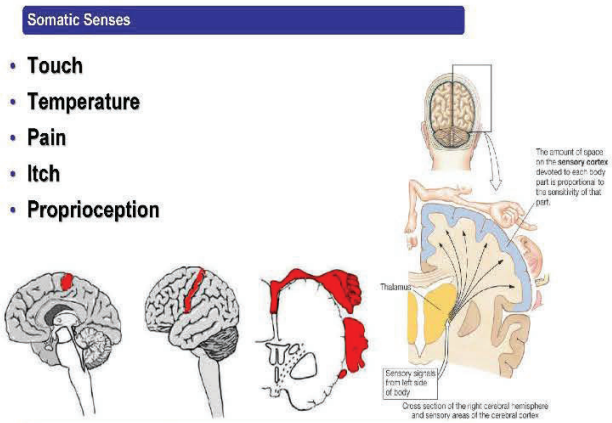
- Phasic Receptors: These receptors are rapidly adapting and respond primarily to changes in stimuli. Examples include receptors involved in detecting vibration or pressure.
- Tonic Receptors: These are slowly adapting receptors that maintain a consistent response over time. Examples include pain receptors and proprioceptors.

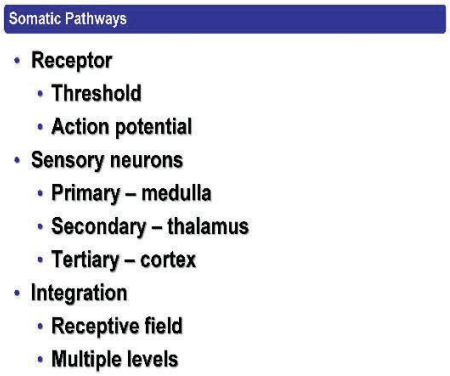
8. Four Steps to Sensation

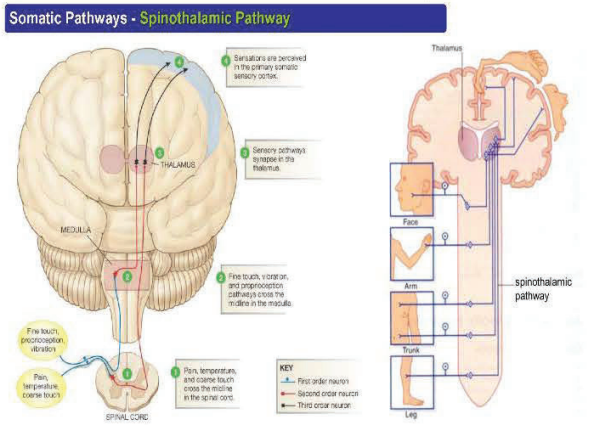
The process of sensation involves four key steps:

1. Stimulation: A stimulus activates a sensory receptor.
2. Transduction: The receptor converts the stimulus into a graded potential by altering ion permeability.
3. Conduction: If the graded potential is strong enough to reach the threshold, it generates an action potential transmitted via afferent sensory neurons to the CNS.
4. Perception: The brain interprets the incoming signal, resulting in conscious stimulus awareness.









9. Sensory Modality

Sensory modality refers to the specific type of sensation detected by a receptor. Each sensory system is designed to detect one or more specific modalities, such as:

- Vision (light)
- Hearing (sound waves)
- Taste (chemical substances)
- Smell (airborne chemicals)
- Touch (pressure or vibration)
- Proprioception (body position)

Each modality is processed by specialized receptors and neural pathways that deliver the signal to the appropriate sensory cortex in the brain.

Sensory Modality

- Location
  - Lateral inhibition
  - Receptive field
- Intensity
- Duration
- Tonic receptors
- Phasic receptors
- Adaptation

Classification of Sensory Input

- Somatesthetic senses
  - sensors located over wide areas of the body (i.e., cutaneous receptors and proprioceptors)
  - Information is usually conducted to the spinal cord first (then possibly the brain)
- Special Senses
  - Changes detected only by specialized sensory organs in the head
  - Information conducted directly to the brain

10. Somatic Pathways

Somatic sensory pathways carry information from the body's surface and muscles to the CNS. These pathways typically involve three neurons:

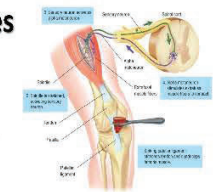
1. First-order neuron: Carries the signal from the receptor to the spinal cord or brainstem.
2. Second-order neuron: Transmits the signal to the thalamus, where sensory information is relayed.
3. Third-order neuron: Carries the signal from the thalamus to the somatosensory cortex, where perception occurs.

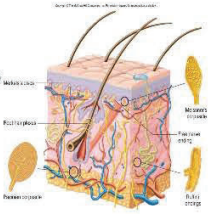
General Senses

- Skin receptors – touch, pressure, heat, cold, pain
- Proprioceptors – Stretch receptors in joints, ligaments, and tendons
- Pain receptors – skin, skeletal muscle and visceral

Somatesthetic Senses

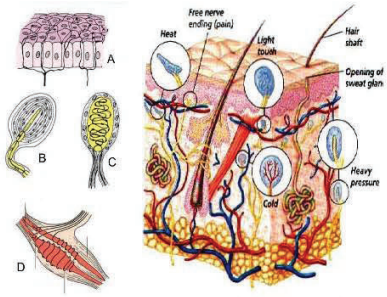
- Proprioceptors
  - Sensory receptors in muscles, tendons and joints
  - Detect stretch of muscles, limb movements, position of body parts, etc.
  - Examples: spindle fibers, Golgi tendon organs
- Cutaneous receptors
  - Sensory receptors present in the skin
  - Touch and Pressure
  - Heat and Cold
  - Pain



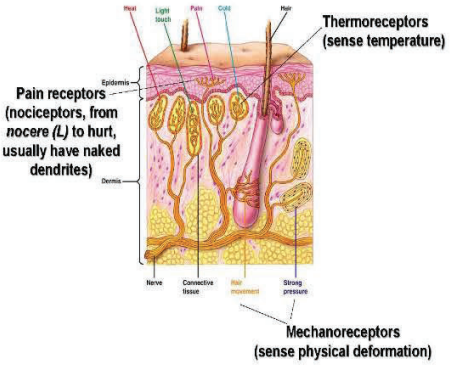


Senses in Skin

- Heat
- Cold
- Light pressure
- Heavy Pressure
- Pain



A: Free nerve endings (pain, temperature)
B: Pacinian corpuscle (pressure)
C: Meissner's corpuscle (touch)
D: Muscle spindle (stretch)

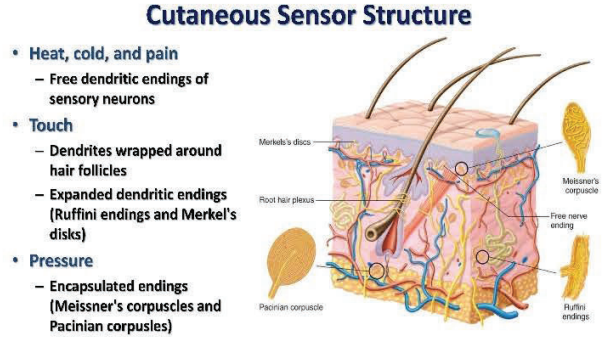


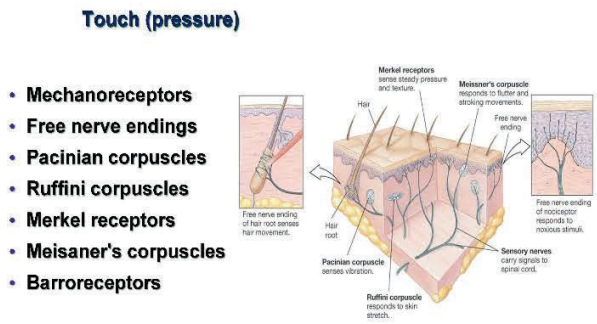
There are many types of sensory receptors:

11. Touch and Pressure

Mechanoreceptors in the skin detect touch and pressure. These include:

- Meissner's corpuscles: Sensitive to light touch and located just beneath the epidermis in glabrous (hairless) skin.
- Pacinian corpuscles: Detect deep pressure and vibration.
- Ruffini endings: Sensitive to skin stretch and sustained pressure, aiding in detecting object manipulation.
- Merkel discs: Respond to steady pressure and texture.





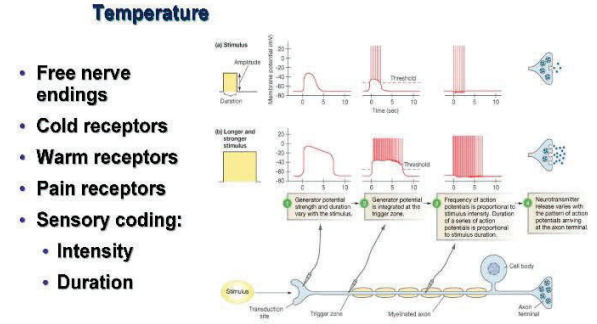
12. Temperature and Pain Sensation

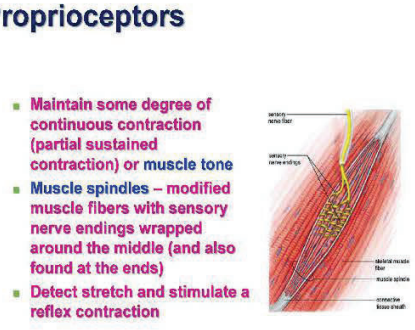
- Thermoreceptors: Detect temperature changes. Cold receptors are activated by temperatures below 35°C, while warm receptors respond to temperatures between 30°C and 45°C. Beyond these thresholds, nociceptors (pain receptors) are activated, signaling potential tissue damage.
- Nociceptors: Detect noxious stimuli, including extreme temperature, mechanical damage, and chemical irritation. Pain perception can be fast (sharp pain mediated by A-delta fibers) or slow (dull, aching pain mediated by C fibers).

13. Proprioception

Proprioception is the sense of body position and movement. Proprioceptors include:

- Muscle Spindles: Detect changes in muscle length and trigger reflexes that adjust muscle contraction.
- Golgi Tendon Organs: Monitor tension in tendons and inhibit excessive muscle contraction to prevent injury.
- Joint Receptors: Provide information about joint angle, position, and movement.





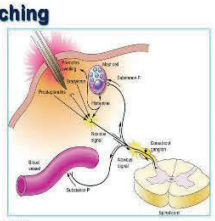
14. Pain and Itch

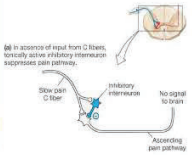
- Nociceptors detect pain and serves as a warning system to prevent tissue damage. Pain pathways involve both fast and slow transmission mechanisms. Fast pain is sharp and localized, while slow pain is dull and diffuse.
- Itch: Often triggered by chemical mediators like histamine, itch is closely related to pain but involves different neural pathways and mediators.

Pain Receptors

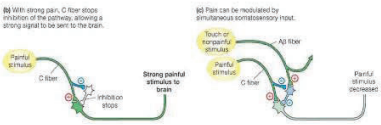
- Somatic nociceptors - from skin and skeletal muscle
- Visceral nociceptors - receptors that help maintain internal homeostasis
  - Respond to stretch, lack of O_2, chemicals released from damaged cells and inflammatory cells.
  - *Referred pain* – visceral pain afferents travel along the same pathways as somatic pain afferents, so sometimes the brain interprets the visceral pain as the more common somatic pain. Example – Often pain from the heart felt during a heart attack is perceived as a pain that originates in the left arm.

Pain and Itching





- Nociceptors
- Reflexive path
- Itch
- Fast pain
- Slow pain



15. Chemical Senses: Taste and Smell

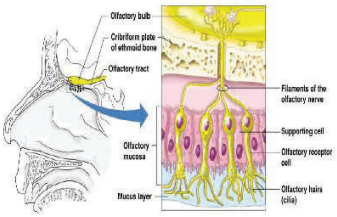
- Taste (Gustation): Taste buds contain gustatory cells that detect dissolved substances in saliva. These cells respond to five primary taste modalities: sweet, salty, sour, bitter, and umami (savory). Each taste modality corresponds to different chemicals (e.g., sugars, acids, salts).
- Smell (Olfaction): Olfactory receptors in the nasal epithelium detect volatile chemicals in the air. These receptors send signals to the olfactory bulb, where the information is processed and relayed to the brain.

Chemical Senses – Taste and Smell

- Both senses use chemoreceptors
  - Stimulated by chemicals in solution
  - Taste has four types of receptors
  - Smell can differentiate a large range of chemicals
- Both senses complement each other and respond to many of the same stimuli

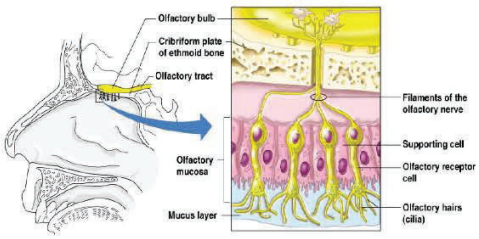
Olfaction – The Sense of Smell

- Olfactory receptors are in the roof of the nasal cavity
  - Neurons with long cilia
  - Chemicals must be dissolved in mucus for detection



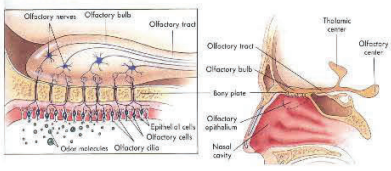
Olfaction – The Sense of Smell

- Impulses are transmitted via the olfactory nerve
- Interpretation of smells is made in the cortex (olfactory area of temporal lobe)



Olfactory Receptors

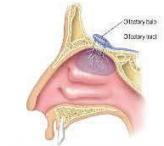
- Chemical Receptors
- Top of nasal cavity
- Extremely sensitive
- Easily fatigued
- Much of "taste" involves smell

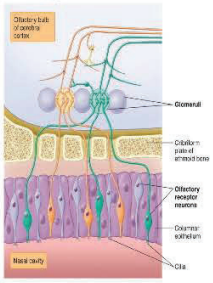


Taste and Smell Depend on Chemoreceptors

Smell (Olfaction):

- Receptors for olfaction are bipolar sensory neurons partly embedded in the olfactory epithelium
- Bipolar neurons:
  - 1 dendrite/cell projecting into nasal cavity
  - Dendritic end = knob of cilia
  - Cilia contain receptor proteins for smell
  - olfactory protein receptors associated with G-proteins

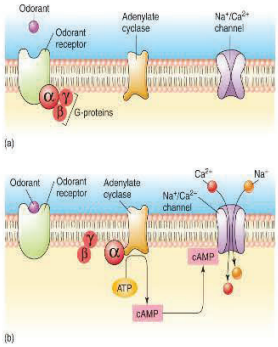




Taste and Smell Depend on Chemoreceptors

Smell (Olfaction):

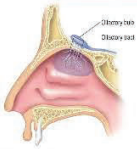
- Olfactory protein receptors on bipolar neurons associated with G-proteins
- G-proteins dissociate when odorant binds to receptor
- G-protein subunit activates the enzyme *adenylate cyclase*
- *Adenylate cyclase* produces cyclic AMP necessary to open Na+ and Ca++ transmembranous channels → depolarization
- As many as 50 G-proteins associated with each receptor
  → high sensitivity to odors

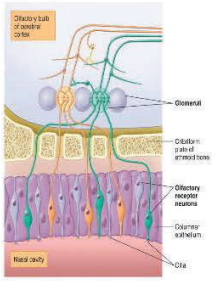


Taste and Smell Depend on Chemoreceptors

Smell (Olfaction):

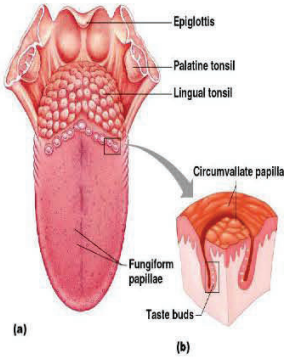
- Action potential travels via axon of bipolar neuron through cribriform plate to olfactory bulb
- In olfactory bulb, axon synapses with other neurons grouped in *glomeruli*
- Each *glomerulus* receives input from 1 particular type of olfactory receptor
- Olfactory information is then sent to other brain regions (e.g., limbic system)





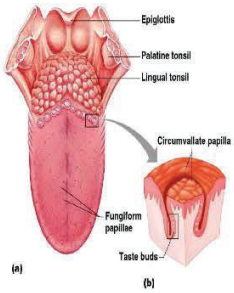
The Sense of Taste

- Taste buds house the receptor organs
- Location of taste buds
  - Most are on the tongue
  - Soft palate
  - Cheeks



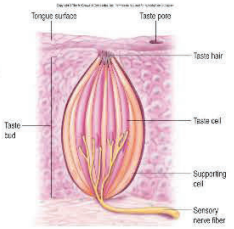
The Tongue and Taste

- The tongue is covered with projections called papillae
  - Filiform papillae – sharp with no taste buds
  - Fungifiorm papillae – rounded with taste buds
  - Circumvallate papillae – large papillae with taste buds
- Taste buds are found on the sides of papillae



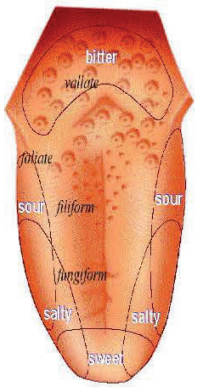
Taste and Smell Depend on Chemoreceptors

- Taste
- *Taste cells :*
  - specialized epithelial cells within barrel-shaped buds on tongue
  - have microvilli extending into external environment
  - not neurons but respond to stimuli by depolarization
  - release chemical transmitters to stimulate sensory neurons (yellow fibers on diagram)



Taste Sensations

- Sweet receptors
  - Sugars
  - Saccharine
  - Some amino acids
- Sour receptors
  - Acids
- Bitter receptors
  - Alkaloids
- Salty receptors
  - Metal ions
- Umami
  - Glutamate, aspartate (meats)

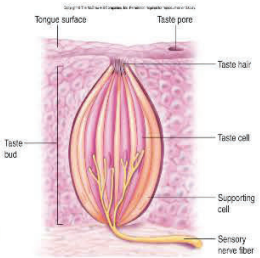


Taste and Smell Depend on Chemoreceptors

- Taste

How is a particular taste detected?

1. Salty and sour tastes:
   - activate taste sensitive cells by passing through ion channels on the membranes of these cells:
     - presence of Na+ in food: salty
     - presence of H+ in food: sour
2. Sweet, bitter and umami:
   - produced through binding of molecules to protein receptors embedded in plasma membrane



16. Hearing and Equilibrium

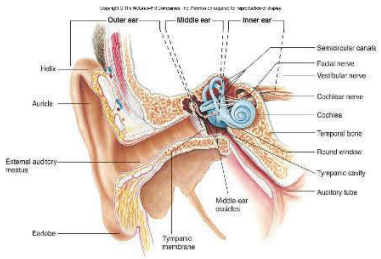
- Hearing: Sound waves enter the ear canal, causing vibrations of the tympanic membrane (eardrum). These vibrations are transferred via the ossicles (malleus, incus, stapes) to the cochlea in the inner ear. Inside the cochlea, hair cells convert mechanical vibrations into electrical signals that are transmitted to the auditory cortex.
- Equilibrium: The vestibular system, consisting of the semicircular canals and otolithic organs, detects changes in head position and motion. The semicircular canals detect rotational movements, while the utricle and saccule detect linear accelerations and head tilts.

The Ear

- **Houses two senses**
  - **Hearing (interpreted in the auditory cortex of the temporal lobe)**
  - **Equilibrium (balance) (interpreted in the cerebellum)**
- **Receptors are mechanoreceptors**
- **Different organs house receptors for each sense**

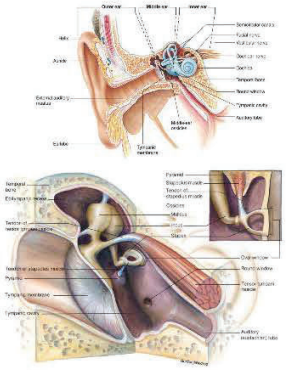
Anatomy of the Ear: Outer (External) Ear

- **Pinna (Auricle)**
  - collects and channels sound waves
- **External Auditory Meatus**
  - Conduction of sound waves
- **Tympanic Membrane**
  - vibrates when struck by sound waves



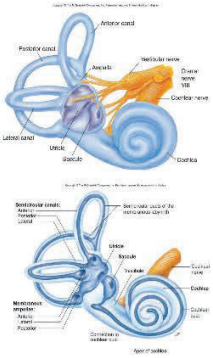
Anatomy of the Ear: Middle Ear

- **Air-filled chamber**
- **Eustachian(auditory) tube**
  - connects middle ear to pharynx
- **Three auditory ossicles act as sound amplifiers**
  1. **Malleus against tympanic membrane**
  2. **Incus**
  3. **Stapes linked to *oval window***



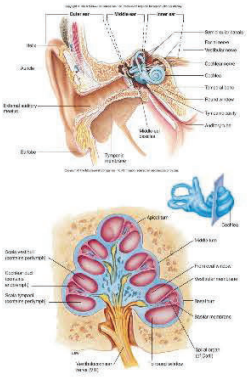
Inner Ear

- **Houses structures for the senses of equilibrium and hearing.**
- **Bony labyrinth**
  - Series of curved passages within the skull bones
  - Two distinct regions
    - Cochlea (anterior) – hearing
    - Vestibular apparatus (posterior) – equilibrium
      - Semicircular canals, utricle and saccule
- **Membranous labyrinth**
  - Membranous network that parallels the bony network
  - Perilymph - fluid between membranous and bony labyrinths
  - Endolymph – fluid contained within the membranous labyrinth



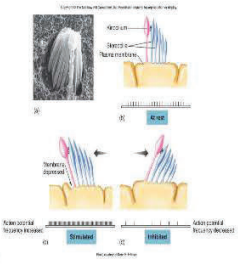
Anatomy of the Ear: Cochlea

- **Anterior portion of the inner ear, contains hair cells that change sound into action potentials;**
- **Three snail-shaped tubes filled with fluid**
  - Outer canals
    1. Scala vestibuli – upper
       - Leads from oval window to apex of the spiral, contains perilymph
    2. Scala tympani – lower
       - Leads from apex of the spiral to the round window
    - Located between bony and membranous labyrinths
    - filled with perilymph
    - Continuous with one another
    3. Cochlear duct
    - Inner canal contained within the membranous labyrinth
    - Contains endolymph



Hair Cells

- **Mechanoreceptor cells responsible for the senses of hearing AND equilibrium**
  - Housed within the membranous labyrinth
  - Possess hair-like extensions known as stereocilia on surface (in blue), and a longer, single large kinocilium (in pink)
- **Bending of stereocilia alters membrane potential**
  - Bending toward kinocilium depolarizes membrane
  - Bending away from kinocilium hyperpolarizes membrane
- **Depolarization induces more neurotransmitter to be released to associated sensory neurons**
  - Greater AP frequency in sensory neurons

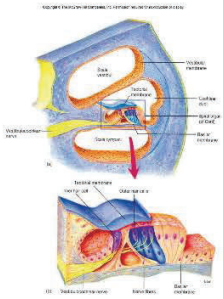


Organ of Corti (Spiral Organ)

- Forms the floor of the cochlear duct

Architecture of Organ of Corti:

- Hair cells embedded in supporting cells
- Hair cells positioned atop the basilar membrane
  - Forms border between cochlear duct and scala tympani
  - Flexible, vibratory
- Tectorial membrane
  - Lies top of hair cells
  - Stereocilia imbedded in this gelatinous membrane
  - The bending of stereocilia stimulates the associated sensory neurons (of CN VIII) to produce APs)

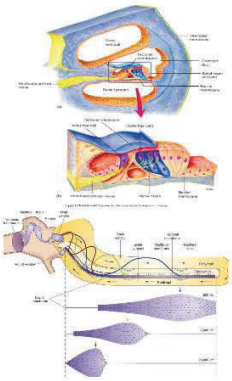


Neural Conduction and Perception of Auditory Information

- Fluid pressure waves in perilymph cause basilar membrane to vibrate
  - Louder sounds causes bigger vibrations, causing high frequency of APs.
  - Sounds of different frequency (pitch):
  - a. low pitches vibrate membrane closer to the apex most
  - b. higher pitches vibrate membrane closer to the base of the cochlea most

Next:

- Hair cells move against tectorial membrane, bending stereocilia
- Stimulates neurotransmitter release to sensory neurons of the vestibulocochlear nerve (VIII)
- Signals conducted to auditory cortex (temporal lobe)

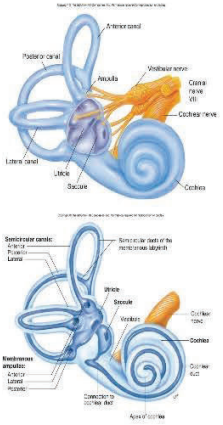


Vestibular Apparatus

Function: equilibrium

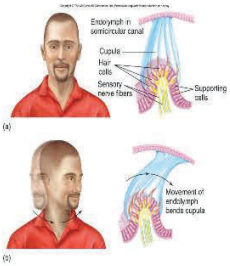
records changes in the position and motion of the head, responsible for balance and coordination of body movement

- Fluid-filled compartments in the inner ear
- 3 Semi-circular canals (anterior, lateral and posterior)
  - Record rotation of the head.
  - Anterior – vertical movement
  - Lateral – lateral movement
  - Posterior – rotational movement
- Otolith organs
  - Record the linear movement of head and orientation relative to gravity
- Sensory information relayed via the *vestibulocochlear nerve* (VIII) to the *cerebellum* and *medulla*



Semicircular Canals

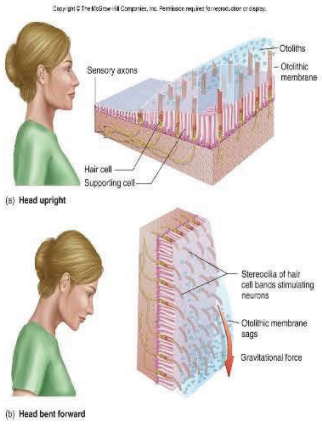
- 3 Fluid-filled circular tubes oriented in three planes
- Bell-shaped ampulla at the base of each canal
  - Contains hair cells whose stereocils are embedded in gel-like cupula surrounded by endolymph
- Rotation of head in one direction generates inertial pressure in endolymph
  - It pushes and bends cupula the way the wind pushes a sail;
  - Pushes hair cells in one direction;
  - Stimulates vestibular neurons;



Example: If you turn your head to the right, endolymph in the lateral semicircular canal causes the cupula to bend to the left

Otolith Organs

- Found within two fluid-filled chambers
  - Utricle (horizontal acceleration) and saccule (vertical acceleration)
- Mound of hair cells covered with otolithic membrane
  - jelly like membrane, containing otoliths ($CaCO_3$ crystals)
- Linear movement or tilting of head causes otolithic membrane to sag
  - bends hair cells
  - stimulates vestibular neurons



Vision

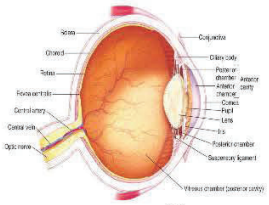
- Perception of electromagnetic (EM) radiation
  - narrow portion of the EM spectrum
- Photoreceptors
  - stimulated by photons of light
  - contain photopigments
    - undergo chemical changes in response to light
    - induces metabolic changes in photoreceptors leading to receptor potential generation

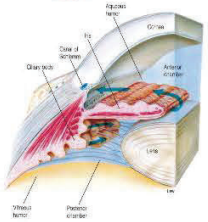
17. Vision

- Photoreceptors in the retina (rods and cones) detect light and convert it into electrical signals. Rods are sensitive to low-light conditions and provide black-and-white vision, while cones detect color and are responsible for high-acuity vision.
- The optic nerve transmits visual information from the retina to the brain, where it is processed in the visual cortex. The brain integrates signals from both eyes to create depth perception and a three-dimensional image of the environment.

Anatomy of the Eye

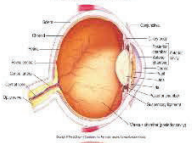
- **Sclera**
  - "White" of the eye
  - Tough connective tissue
    - Protects inner structures
    - Maintains eye shape
- **Cornea**
  - Transparent – lets light pass into the eye
  - Fixed convex lens
    - bends light inward
  - Covers the *anterior chamber*
    - Space between cornea and iris
    - filled with *aqueous humor*

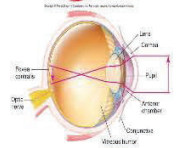


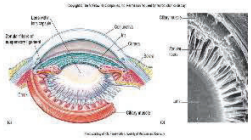


Anatomy of the Eye

- **Lens**
  - Solid but pliable transparent body
  - Used to focus light on the retina
- **Ciliary Body**
  - Ring-shaped smooth muscle encircling lens
  - Linked to lens by *suspensory ligaments*
  - Adjusts shape of lens to focus light
- **Posterior chamber**
  - Space between the iris and lens/ciliary body

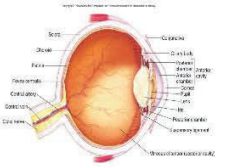


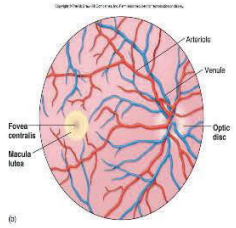




Anatomy of the Eye

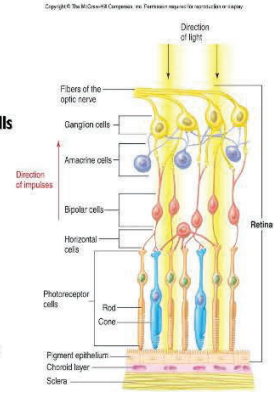
- **Vitreous chamber**
  - Large chamber posterior to the lens and ciliary body
  - Filled with gelatinous *vitreous body*
- **Retina**
  - Lining of the vitreous chamber
  - Contains photoreceptors
  - Fovea centralis
    - point where light from the center of the visual field is focused
    - high density of cone cells
  - Optic disc
    - where optic nerve joins the eye
    - no photoreceptors - "blind spot"





Photoreceptors

- **Rods**
  - More numerous than cones
  - Cannot distinguish different colors
  - Many rods converge onto single ganglion cells
    - Highly sensitive to light (low light levels detected)
    - Low visual acuity (image not as sharp)
- **Cones**
  - Found mainly in fovea centralis
  - Can distinguish among colors
  - Few cone cells converge on single ganglion cell
    - Low light sensitivity (need more light to see with cones)
    - High acuity (image is sharper)



Anatomy of the Eye

- **Iris**
  - Thin ring of pigmented muscle in front of lens
- **Pupil**
  - opening at center of the iris
  - Muscles alter pupil size, thus amount of light passing into the eye
  - Radial muscles
    - open pupil to let in more light (sympathetic)
  - Circular muscles
    - close pupil in bright light (parasympathetic)

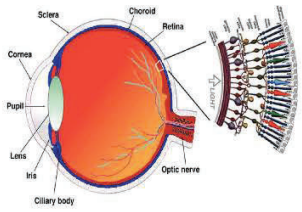
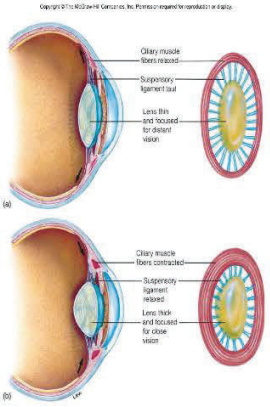


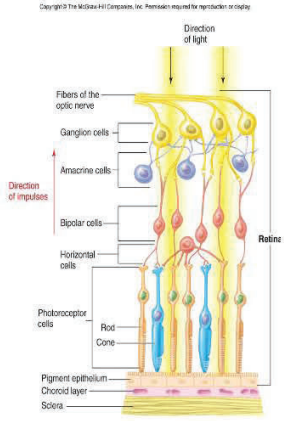
Fig. 1.1. A drawing of a section through the human eye with a schematic enlargement of the retina.

- Changing lens shape to focus light from objects at different distances on the retina
- Achieved by contracting ciliary body to different degrees
- **Far objects**
  - light from object enters eye from narrow range of angles
  - ciliary body relaxes, lens stretched
  - less convex, less bending of light
- **Near objects**
  - light from object enters eye from wide range of angles
  - ciliary body contracts, lens recoils
  - more convex, more bending of light



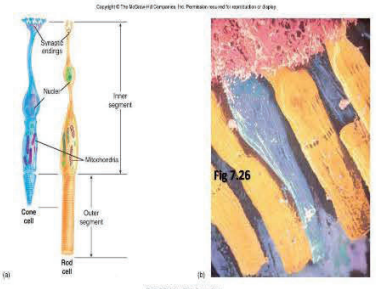
Retina Cells

- **Photoreceptors**
  - rods and cones
- **Bipolar cells**
  - Neurons that receive neurotransmitter from the photoreceptors
  - Synapse with ganglion cells
- **Ganglion cells**
  - Neurons that receive neurotransmitter from the bipolar cells
  - Conduct action potentials to CNS (visual cortex of occipital lobe) via the optic nerve (II)



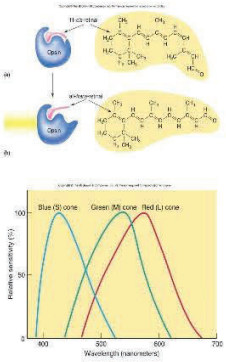
Photoreceptor Structure

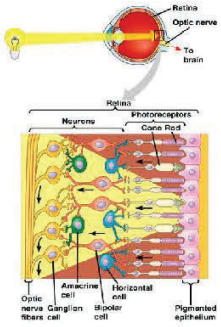
- Each photoreceptor has two segments
  - Inner segment
    - metabolic machinery
    - synaptic endings
  - Outer segment
    - contains layers of internal membranes containing photopigments



Photopigments

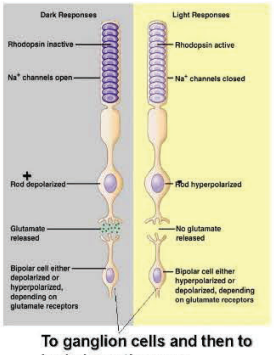
- Rhodopsin (rod cell photopigment)
  - Consists of retinal (vitamin A derivative) and opsin (protein)
  - Retinal undergoes a photchemical change when struck by light
    - 11-*cis*-retinal converted to *trans*-retinal
    - Induces change in membrane potential of rod
    - Ultimately leads to generation of action potentials in ganglion cells
- Cone cell photopigment
  - Each cone has one of three different opsins
  - Respond to different wavelengths of light
    - Blue (S), Green (M), or Red (L)
  - Enables color discrimination





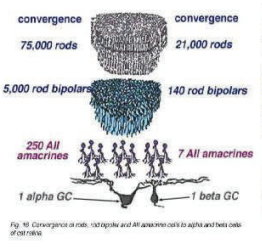
The retina contains photoreceptors (rods and cones), cells that integrate information across the retina (horizontal cells and amacrine cells), and cells that receive information from several rods and cones (bipolar cells) and relay it to ganglion cells which transmit action potentials to the brain by the optic nerve.

The stimulus by which rods and cone stimulate or inhibit bipolar cells is the release of the neurotransmitter glutamate.



To ganglion cells and then to brain by optic nerve.

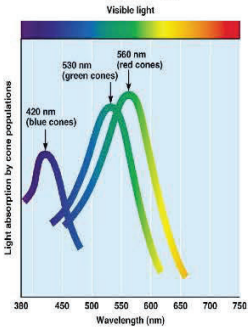
ROD CELLS



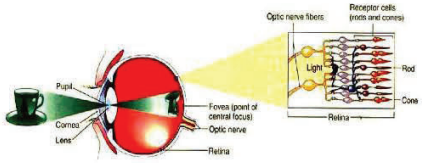


Cone Sensitivity

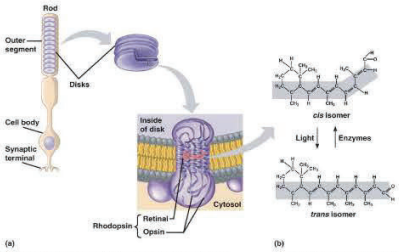
- There are three types of cones
- Different cones are sensitive to different wavelengths
  - red - long
  - green - medium
  - blue - short
- Color blindness is the result of lack of one or more cone type



Images



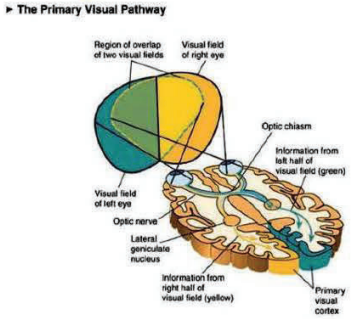
Cornea and the lens help to produce the image
Images are upside down and backwards when they reach the retina



Rods contain the visual pigment rhodopsin, which is embedded in a stack of membrane disks. Rhodopsin consists of the protein (pigment) opsin and the light absorbing molecule retinal (there are many opsins!).

Retinal exists in two forms. Light converts the cis form to a trans form and enzymes return it to its original form.

Visual Pathway



Neurons of the Retina and Vision

- Cones
  - Allow for detailed color vision
  - Densest in the center of the retina
  - Fovea centralis – area of the retina with only cones
  - Respond best in bright light
- No photoreceptor cells are at the optic disk, or blind spot

How do we see colors?

- To see any color, the brain must compare the input from different kinds of cone cells—and then make many other comparisons as well.
- The lightning-fast work of judging a color begins in the retina, which has three layers of cells. Signals from the red and green cones in the first layer are compared by specialized red-green "opponent" cells in the second layer. These opponent cells compute the balance between red and green light coming from a particular part of the visual field. Other opponent cells then compare signals from blue cones with the combined signals from red and green cones.

Practical Session 3: Metabolism and Thermoregulation

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1. Introduction to Metabolism

Definition of Metabolism

Metabolism refers to the sum of all biochemical reactions occurring within an organism to sustain life. It involves the conversion of food into energy, the building blocks necessary for growth and repair, and the elimination of waste products.

Types of Metabolism

- Anabolism: The building up of complex molecules from simpler ones, which requires energy (e.g., protein synthesis, DNA replication).
- Catabolism: The breakdown of complex molecules into simpler ones, releasing energy (e.g., glycolysis, fatty acid oxidation).

---

2. Energy Balance and Metabolic Rate

2.1. Energy Balance

Energy balance occurs when the energy intake from food equals the energy expended by the body for its various functions. It can be categorized into:

- Positive energy balance: More energy intake than expenditure, leading to weight gain.
- Negative energy balance: Less energy intake than expenditure, leading to weight loss.

2.2. Metabolic Rate

Metabolic rate refers to the rate at which the body expends energy. It varies depending on activity level, age, body composition, and hormonal status. The metabolic rate is typically divided into:

- Basal Metabolic Rate (BMR): The energy expenditure required to maintain basic physiological functions at rest.
- Active Metabolic Rate: The energy used during physical activities and exercise.

---

3. Basal Metabolic Rate (BMR)

Definition

Basal Metabolic Rate (BMR) is the number of calories the body needs to perform essential life-sustaining functions such as breathing, circulation, and cellular metabolism while at rest. BMR accounts for approximately 60-70% of total daily energy expenditure.

Clinical Relevance

BMR is used to assess metabolic health and can be a diagnostic tool in conditions such as hyperthyroidism (increased BMR) and hypothyroidism (decreased BMR). Factors that affect BMR include age, gender, body size, muscle mass, and hormonal status.

Conditions for Measuring BMR

To obtain accurate BMR measurements, certain conditions must be met:

- The subject should be in a fasting state (no food for at least 12 hours).
- The individual should be physically and mentally at rest in a thermoneutral environment.
- BMR is measured after a full night of sleep.

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4. Thermoregulation

Thermoregulation is the body's ability to maintain its internal temperature within a narrow, safe range, typically around 37°C (98.6°F). The balance between heat production and heat loss is critical for proper physiological functioning.

4.1. Heat Production

Heat is produced as a byproduct of metabolic reactions, with muscle activity (e.g., shivering) and hormonal regulation (e.g., thyroid hormones, catecholamines) playing key roles in heat generation.

4.2. Heat Loss Mechanisms

The body loses heat through several mechanisms, including:

- Radiation: The transfer of heat from the body to the surrounding environment.
- Conduction: The direct transfer of heat to a cooler object in contact with the body.
- Convection: The transfer of heat through the movement of air or water over the skin.
- Evaporation: The loss of heat through the evaporation of sweat from the skin surface.

4.3. Body Temperature Regulation

The body's temperature is regulated by the hypothalamus, which acts as the body's thermostat. It receives inputs from:

- Heat-sensitive neurons: Detect increases in body temperature and activate heat loss mechanisms.
- Cold-sensitive neurons: Detect drops in temperature and activate heat production mechanisms.
- Peripheral receptors: Located in the skin and other tissues, they provide feedback to the hypothalamus about external temperature conditions.

4.4. Role of the Hypothalamus in Thermoregulation

The hypothalamus integrates signals from central and peripheral receptors to maintain temperature balance:

- Heat-sensitive neurons: Trigger responses to dissipate heat, such as sweating and vasodilation.
- Cold-sensitive neurons: Trigger heat-generating mechanisms like shivering and vasoconstriction.

4.5. Temperature Control Mechanisms

- Decreasing Temperature Mechanisms:
  - Vasodilation: Blood vessels in the skin widen, increasing blood flow to the skin and promoting heat loss.
  - Sweating: The evaporation of sweat from the skin surface cools the body.
- Increasing Temperature Mechanisms:
  - Vasoconstriction: Blood vessels in the skin constrict, reducing heat loss and conserving body heat.
  - Shivering: Involuntary muscle contractions generate heat through increased metabolic activity.
  - Thermogenesis: Hormonal responses (e.g., thyroid hormones, catecholamines) enhance metabolic heat production, especially in cold environments.

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5. Practical Experiments and Demonstrations

5.1. Measurement of Metabolic Rate

- Direct Calorimetry: Measures the amount of heat produced by the body in a controlled environment, directly assessing energy expenditure.
- Indirect Calorimetry: Estimates metabolic rate by measuring oxygen consumption and carbon dioxide production, which reflect energy usage.

5.2. Temperature Regulation

Students will observe how the body responds to changes in environmental temperature by measuring skin and core temperature under various conditions (e.g., exercise, rest, cold exposure).

5.3. Metabolic Rate Testing

Students will use indirect calorimetry to measure their resting metabolic rate (RMR) and analyze how factors like body composition and activity level influence energy expenditure.

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6. Clinical Relevance

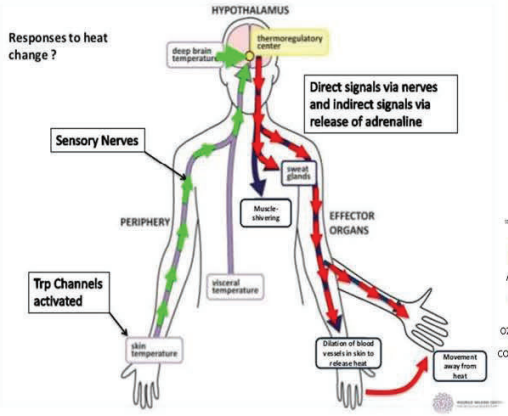
6.1. Disorders of Thermoregulation

- Hyperthermia:
  Hyperthermia occurs when heat production exceeds the body's ability to dissipate heat, leading to elevated body temperatures. Heat exhaustion and heatstroke are extreme forms of hyperthermia that require urgent medical intervention to prevent organ damage.
- Hypothermia:
  Hypothermia occurs when prolonged exposure to cold environments causes the core body

temperature to drop below 35°C (95°F). Symptoms include shivering, confusion, and reduced heart rate, and if untreated, hypothermia can lead to coma or death.

6.2. Metabolic Disorders

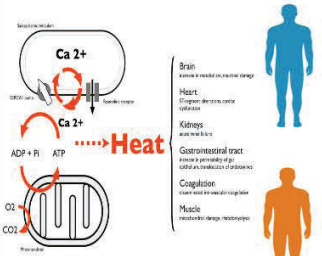
- Thyroid Dysfunction:
  - Hyperthyroidism leads to an elevated metabolic rate, increased heat production, and weight loss.
  - Hypothyroidism results in a decreased metabolic rate, reduced heat production, and weight gain.



Normal Body Temperature

- **Skin temperature → rise and falls ≈ surroundings**
- **Core temperature → constant (36°C – 37.5°C)**

Body Temperature = Heat Production >< Heat Loss



Normal Body Temperature range

Rectal	97.9°F (36.11°C) ~ 100°F (37.94°C)
Ear	96.4°F (35.78°C) ~ 100.4°F (38°C)
Mouth	95.9°F (35.5°C) ~ 99.5°F (37.5°C)
Armpit	94.5°F (34.72°C) ~ 99.1°F (37.27°C)

Symptoms of a fever

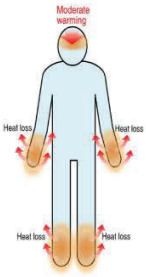
Rectal / Ear	100.4°F (38° C) or higher
Mouth	100°F (37.8° C) or higher
Armpit	99° F (37.2° C) or higher

Heat Loss

Heat is mostly produced in the liver, brain, heart, exercised skeletal muscle

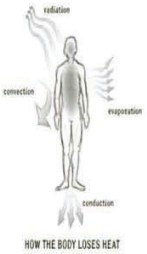
The rate of heat lost:

- **Conduction from the body core to the skin**
  - **The degree of vasoconstriction (sympathetic nerves)**
- **Transfer from the skin to the surroundings**
  - **Insulator system (skin, subcutaneous tissue, fat)**
  - **Fat → transfer 1/3 heat**
  - **Women = better insulation**
  - **Clothing; wet clothing**



Heat Loss

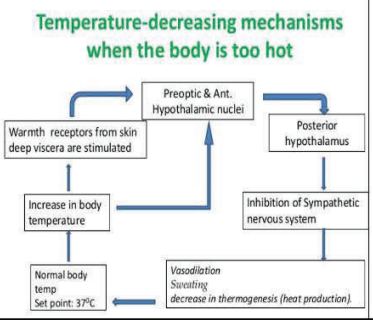
- **Radiation → infrared heat rays (60% total heat loss)**
- **Conduction → to solid objects (3%)**
  → to air (15%) → to water 30x of air
- **Convection → conduction to the air first → convection (air currents) → heat loss ≈ wind speed**
  → heat conductivity in water >> than in air
- **Evaporation → insensible evaporation (lungs + skin) = 600 – 700 ml/ day → cannot be controlled**
  → sweating evaporation can be controlled
  → the only means to get rid of heat in high temperature environment



- **Respiration ≈ evaporation (water droplets evaporated)**
  → contribute to hypothermia in cool, windy, and dry environments

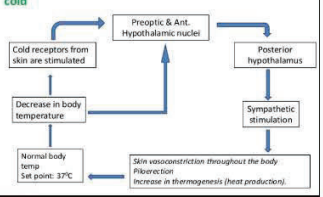
Temperature – Decreasing Mechanisms:

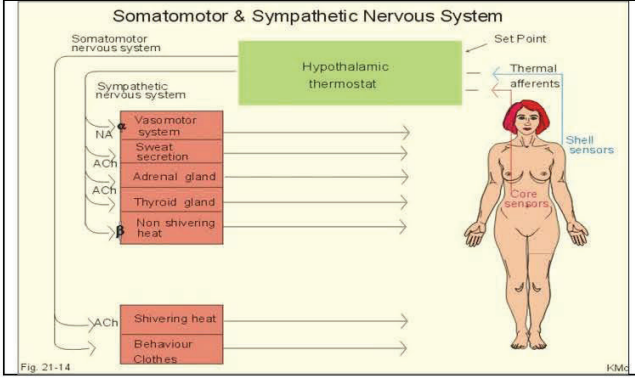
1. Vasodilation of skin blood vessels
   - Inhibition of the sympathetic center (posterior hypothalamus)
2. Sweating
3. Decrease in heat production

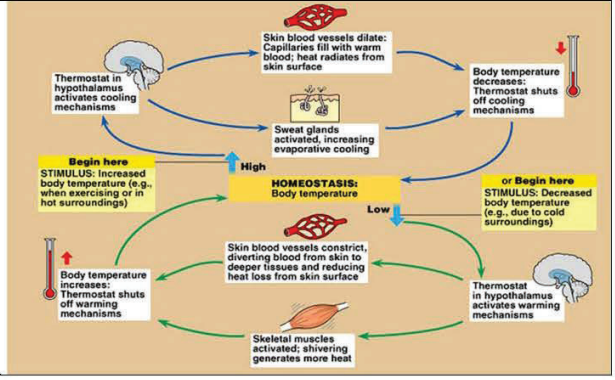


Temperature – Increasing Mechanisms:

1. Skin vasoconstriction
   - Stimulation of sympathetic centers (posterior hypothalamus)
2. Piloerection
   - Entrapping "insulator air"
3. Increase in thermAogenesis
   - Shivering
   - Sympathetic excitation
   - Thyroxine







Examination and Assessment

1	Special senses	
a.	Smell- chemoreceptors (chemicals)	True
b.	Taste- chemoreceptors	True
c.	Sight- photoreceptors (light)	True
d.	Hearing- mechanoreceptors	True
e.	Equilibrium- (balance) mechanoreceptors	True
f.	touch (tactile)	False
g.	Temperature- thermoreceptors (heat)	False
h.	Pressure- mechanoreceptors (movement)	False
i.	Pain- mechanoreceptors	False
j.	General senses	False

2	Types of Sensory Receptors - Functional Types	
a.	Chemoreceptors	True
b.	Thermoreceptors	True
c.	Mechanoreceptors	True
d.	Photoreceptors	True
e.	Nociceptors	True
f.	Immunoreceptors	False
g.	Phasic receptors	False
h.	Tonic receptors	False
i.	Alpha receptors	False
j.	Beta receptors	False

3	Sensations are:	
a.	action potentials in response to specific stimuli	True
b.	Data reach specific areas of the brain	True
c.	Brain interprets it, giving the perception (color, taste, sound, taste) of a stimulus	True
d.	information from the environment	True
e.	Neuronal impulses in response to specific stimuli	True
f.	Receptive field	False
g.	application of stimulus	False
h.	graded potentials	False
i.	depolarization in dendrites	False
j.	environmental changes	False

4	Sensory Modality:	
a.	Intensity	True
b.	Duration	True
c.	Tonic receptors	True
d.	Phasic receptors	True
e.	Adaptation	True
f.	Primary	False
g.	Fusion	False
h.	Diffusion	False
i.	Caloric	False
j.	Stone	False

5	Somatic Senses:	
a.	Touch	True
b.	Temperature	True
c.	Pain	True
d.	Itch	True
e.	Proprioception	True
f.	Smell- chemoreceptors (chemicals)	False
g.	Taste- chemoreceptors	False
h.	Sight- photoreceptors (light)	False
i.	Hearing- mechanoreceptors	False
j.	Equilibrium- (balance) mechanoreceptors	False

6	Skin receptors are for:	
a.	touch	True
b.	pressure	True
c.	heat	True
d.	cold	True
e.	pain	True
f.	Smell	False
g.	Taste	False
h.	Sight	False
i.	Hearing	False
j.	Equilibrium	False

7	Touch (pressure) receptors are:	
a.	Free nerve endings	True
b.	Pacinian corpuscles	True
c.	Ruffini corpuscles	True
d.	Merkel receptors	True
e.	Meisaner's corpuscles	True
f.	Muscle spindles	False
g.	Nociceptors	False
h.	Photoreceptors	False
i.	Photopigments	False
j.	Thermoreceptors	False

8	Olfaction – The Sense of Smell:	
a.	Olfactory receptors are in the roof of the nasal cavity	True
b.	Neurons with long cilia	True
c.	Chemicals must be dissolved in mucus for detection	True
d.	Impulses are transmitted via the olfactory nerve	True
e.	Interpretation of smells is made in the cortex (olfactory area of temporal lobe)	True
f.	Receptors are mechanoreceptors	False
g.	Interpretation of smells is made in the auditory cortex	False
h.	Records changes in the position and motion	False
i.	Sensory information relayed via the vestibulocochlear nerve	False
j.	Olfactory receptors undergo chemical changes in response to light	False

9	Olfactory Receptors properties:	
a.	Chemical Receptors	True
b.	Top of nasal cavity	True
c.	Extremely sensitive	True
d.	Easily fatigued	True
e.	Much of “taste” involves smell	True
f.	Receptors are mechanoreceptors	False
g.	Interpretation of smells is made in the auditory cortex	False
h.	Records changes in the position and motion	False
i.	Sensory information relayed via the vestibulocochlear nerve	False
j.	Olfactory receptors undergo chemical changes in response to light	False

10	(Smell) Olfactory Receptors:	
a.	Receptors for olfaction are bipolar sensory neurons partly embedded in the olfactory epithelium	True
b.	1 dendrite/cell projecting into nasal cavity	True
c.	Dendritic end = knob of cilia	True
d.	Cilia contain receptor proteins for smell	True
e.	Olfactory protein receptors associated with G-proteins	True
f.	Receptors are mechanoreceptors	False
g.	Interpretation of smells is made in the auditory cortex	False
h.	Records changes in the position and motion	False
i.	Sensory information relayed via the vestibulocochlear nerve	False
j.	Olfactory receptors undergo chemical changes in response to light	False

11	Smell (Olfaction):	
a.	Olfactory protein receptors on bipolar neurons associated with G-proteins	True
b.	G-proteins dissociate when odorant binds to receptor	True
c.	G-protein subunit activates the enzyme adenylate cyclase	True
d.	Adenylate cyclase produces cyclic AMP necessary to open Na+ and Ca2+ transmembranous channels	True
e.	As many as 50 G-proteins associated with each receptor	True
f.	Olfactory protein receptors are protein pumps	False
g.	G-proteins bind together when odorant binds to receptor	False
h.	G-protein subunit inactivates the enzyme adenylate cyclase	False
i.	Adenylate cyclase degrades cyclic AMP	False
j.	Only one G-protein is associated with each receptor	False

12	Olfaction information:	
a.	Action potential travels via axon of bipolar neuron through cribriform plate to olfactory bulb	True
b.	In olfactory bulb, axon synapses with other neurons grouped in glomeruli	True
c.	Each glomerulus receives input from 1 particular type of olfactory receptor	True
d.	Olfactory information is then sent to other brain regions	True
e.	Olfactory protein receptors on bipolar neurons associated with G-proteins	True
f.	Olfactory protein receptors are protein pumps	False
g.	G-proteins bind together when odorant binds to receptor	False
h.	G-protein subunit inactivates the enzyme adenylate cyclase	False

i.	Adenylate cyclase degrades cyclic AMP	False
j.	Only one G-protein is associated with each receptor	False

13	The Sense of Taste:	
a.	Taste buds house the receptor organs	True
b.	Receptors for taste are chemoreceptors	True
c.	Most of taste buds are on the tongue	True
d.	Taste buds are located on soft palate	True
e.	Taste buds are located on cheeks	True
f.	Receptors are mechanoreceptors	False
g.	Interpretation of taste is made in the auditory cortex	False
h.	Records changes in the position and motion	False
i.	Sensory information relayed via the vestibulocochlear nerve	False
j.	Taste receptors undergo chemical changes in response to light	False

14	The Tongue and Taste:	
a.	The tongue is covered with projections called papillae	True
b.	Filiform papillae – sharp with no taste buds	True
c.	Fungifiorm papillae – rounded with taste buds	True
d.	Circumvallate papillae – large papillae with taste buds	True
e.	Taste buds are found on the sides of papillae	True
f.	Receptors are mechanoreceptors	False
g.	Interpretation of taste is made in the auditory cortex	False
h.	Records changes in the position and motion	False
i.	Sensory information relayed via the vestibulocochlear nerve	False
j.	Taste receptors undergo chemical changes in response to light	False

15	Taste receptors:	
a.	Receptors for taste are chemoreceptors	True
b.	specialized epithelial cells within barrel-shaped buds on tongue	True
c.	have microvilli extending into external environment	True
d.	not neurons but respond to stimuli by depolarization	True
e.	release chemical transmitters to stimulate sensory neurons (yellow fibers on diagram)	True
f.	Receptors are mechanoreceptors	False
g.	Interpretation of taste is made in the auditory cortex	False
h.	Records changes in the position and motion	False
i.	Sensory information relayed via the vestibulocochlear nerve	False
j.	Taste receptors undergo chemical changes in response to light	False

16	Taste Sensations:	
a.	Sweet receptors: sugars, saccharine, some amino acids	True
b.	Sour receptors: acids	True
c.	Bitter receptors: alkaloids	True
d.	Salty receptors: metal ions	True
e.	Umami: Glutamate, aspartate (meats)	True
f.	Sweet receptors: acids	False
g.	Sour receptors: alkaloids	False
h.	Bitter receptors: sugars, saccharine, some amino acids	False

i.	Salty receptors: Glutamate, aspartate (meats)	False
j.	Umami: metal ions	False

17	Salty and sour tastes:	
a.	activate taste sensitive cells by passing through ion channels on the membranes of these cells	True
b.	presence of Na+ in food: salty	True
c.	presence of H+ in food: sour	True
d.	Sour receptors: acids	True
e.	Salty receptors: metal ions	True
f.	produced through binding of molecules to protein receptors embedded in plasma membrane	False
g.	presence of H+ in food: salty	False
h.	presence of Na+ in food: sour	False
i.	Sour receptors: metal ions	False
j.	Salty receptors: acids	False

18	Hearing:	
a.	Data interpreted in the auditory cortex of the temporal lobe	True
b.	Receptors are mechanoreceptors	True
c.	Inner Ear houses structures for the senses of equilibrium and hearing	True
d.	Anterior portion of the inner ear, contains hair cells that change sound into action potentials	True
e.	Mechanoreceptor cells responsible for the senses of hearing	True
f.	Receptors for hearing are chemoreceptors	False
g.	specialized epithelial cells within barrel-shaped buds on tongue	False
h.	produced through binding of molecules to protein receptors embedded in plasma membrane	False
i.	Records changes in the position and motion	False
j.	Action potential travels via axon of bipolar neuron through cribriform plate	False

19	Equilibrium (balance):	
a.	Data interpreted in the cerebellum	True
b.	Receptors are mechanoreceptors	True
c.	Receptors housed within the membranous labyrinth	True
d.	Possess hair-like extensions known as stereocilia on surface, and a longer, single large kinocilium	True
e.	Bending of stereocilia alters membrane potential	True
f.	Receptors for equilibrium are chemoreceptors	False
g.	specialized epithelial cells within barrel-shaped buds on tongue	False
h.	produced through binding of molecules to protein receptors embedded in plasma membrane	False
i.	Records changes in the chemical structure	False
j.	Action potential travels via axon of bipolar neuron through cribriform plate	False

20	Vestibular Apparatus:	
a.	records changes in the position and motion of the head	True
b.	responsible for balance and coordination of body movement	True
c.	Fluid-filled compartments in the inner ear	True
d.	Otolith organs -record the linear movement of head and orientation relative to gravity	True

e.	Sensory information relayed via the vestibulocochlear nerve (VIII) to the cerebellum and medulla	True
f.	Receptors for equilibrium are chemoreceptors	False
g.	specialized epithelial cells within barrel-shaped buds on tongue	False
h.	produced through binding of molecules to protein receptors embedded in plasma membrane	False
i.	Records changes in the chemical structure	False
j.	Action potential travels via axon of bipolar neuron through cribriform plate	False

21	Semicircular Canals:	
a.	3 Fluid-filled circular tubes oriented in three planes	True
b.	Bell-shaped ampulla at the base of each canal	True
c.	Contains hair cells whose stereocils are embedded in gel-like cupula surrounded by endolymph	True
d.	Rotation of head in one direction generates inertial pressure in endolymph	True
e.	Rotation of head in one direction stimulates vestibular neurons	True
f.	Receptors for equilibrium are chemoreceptors	False
g.	specialized epithelial cells within barrel-shaped buds on tongue	False
h.	produced through binding of molecules to protein receptors embedded in plasma membrane	False
i.	Records changes in the chemical structure	False
j.	Action potential travels via axon of bipolar neuron through cribriform plate	False

22	Otolith Organs:	
a.	Found within two fluid-filled chambers	True
b.	Utricle (horizontal acceleration) and saccule (vertical acceleration)	True
c.	Mound of hair cells covered with otolithic membrane	True
d.	jelly like membrane, containing otoliths ($CaCO_3$ crystals)	True
e.	Linear movement or tilting of head causes otolithic membrane to sag	True
f.	Receptors for equilibrium are chemoreceptors	False
g.	specialized epithelial cells within barrel-shaped buds on tongue	False
h.	produced through binding of molecules to protein receptors embedded in plasma membrane	False
i.	Records changes in the chemical structure	False
j.	Action potential travels via axon of bipolar neuron through cribriform plate	False

23	Perception of electromagnetic (EM) radiation	
a.	Photoreceptors stimulated by photons of light	True
b.	Photoreceptors contain photopigments	True
c.	Photoreceptors undergo chemical changes in response to light	True
d.	(EM) radiation induces metabolic changes in photoreceptors leading to receptor potential generation	True
e.	Vision is perception of electromagnetic (EM) radiation - narrow portion of the EM spectrum	True
f.	Receptors for vision are thermoreceptors	False
g.	specialized epithelial cells within barrel-shaped buds	False
h.	produced through binding of molecules to protein receptors embedded in plasma membrane	False
i.	Data interpreted in the cerebellum	False
j.	Action potential travels via axon of bipolar neuron through cribriform plate	False

24	Retina Cells:	
a.	Photoreceptors - rods and cones	True
b.	Bipolar cells - neurons that receive neurotransmitter from the photoreceptors	True
c.	Bipolar cells - synapse with ganglion cells	True
d.	Ganglion cells - neurons that receive neurotransmitter from the bipolar cells	True
e.	Ganglion cells - conduct action potentials to CNS (visual cortex of occipital lobe) via the optic nerve (II)	True
f.	Photoreceptors are fibroblast cells	False
g.	Bipolar cells - neurons that receive neurotransmitter from the ganglion cells	False
h.	Bipolar cells - synapse only with cones photoreceptors	False
i.	Ganglion cells - neurons that receive neurotransmitter from the photoreceptors	False
j.	Ganglion cells - synapse only with cones photoreceptors	False

25	Rod cells Photoreceptors:	
a.	Rods - more numerous than cones	True
b.	Cannot distinguish different colors	True
c.	Many rods converge onto single ganglion cells	True
d.	Highly sensitive to light (low light levels detected)	True
e.	Low visual acuity (image not as sharp)	True
f.	Found mainly in fovea centralis	False
g.	Can distinguish among colors	False
h.	Few cone cells converge o n single ganglion cell	False
i.	Low light sensitivity (need more light to see with cones)	False
j.	High acuity (image is sharper)	False

26	Cones cells Photoreceptors:	
a.	Found mainly in fovea centralis	True
b.	Can distinguish among colors	True
c.	Few cone cells converge on single ganglion cell	True
d.	Low light sensitivity (need more light to see with cones)	True
e.	High acuity (image is sharper)	True
f.	More numerous than rod cells	False
g.	Cannot distinguish different colors	False
h.	Many cones converge onto single ganglion cells	False
i.	Highly sensitive to light (low light levels detected)	False
j.	Low visual acuity (image not as sharp)	False

27	Photoreceptor Structure	
a.	Each photoreceptor has two segments	True
b.	Inner segment has a metabolic machinery	True
c.	Inner segment has synaptic endings	True
d.	Outer segment - contains layers of internal membranes	True
e.	Outer segment - contains photopigments	True
f.	Each photoreceptor has three segments	False
g.	Inner segment contains layers of internal membranes	False
h.	Inner segment contains photopigments	False
i.	Outer segment has a metabolic machinery	False
j.	Outer segment has synaptic endings	False

28	Photopigment - rhodopsin	
a.	Rhodopsin is the rod cell photopigment	True
b.	Consists of retinal (vitamin A derivative) and opsin (protein)	True
c.	Retinal undergoes a photchemical change when struck by light	True
d.	11-cis-retinal converted to trans-retinal	True
e.	Induces change in membrane potential of rod - leads to generation of action potentials in ganglion cells	True
f.	has one of three different opsins	False
g.	Rhodopsin is the cone cell photopigment	False
h.	Respond to different wavelengths of light	False
i.	Blue (S), Green (M), or Red (L)	False
j.	Enables color discrimination	False

29	Cone cell photopigment	
a.	Each cone has one of three different opsins	True
b.	Respond to different wavelengths of light	True
c.	Induces change in membrane potential of rod - leads to generation of action potentials in ganglion cells	True
d.	Blue (S), Green (M), or Red (L)	True
e.	Enables color discrimination	True
f.	Rhodopsin is the rod cell photopigment	False
g.	Consists of retinal (vitamin A derivative) and opsin (protein)	False
h.	Retinal undergoes a photchemical change when struck by light	False
i.	11-cis-retinal converted to trans-retinal	False
j.	Cannot distinguish different colors	False

30	Cone Sensitivity:	
a.	There are three types of cones	True
b.	Blue – short wavelengths	True
c.	Red – long wavelengths	True
d.	Green – medium wavelengths	True
e.	Color blindness is the result of lack of one or more cone type	True
f.	There are two types of cones	False
g.	Blue – long wavelengths	False
h.	Red – medium wavelengths	False
i.	Green – short wavelengths	False
j.	Color blindness is the result of lack of rod cells	False

Course 4: Physiology of the Heart
Sub-topic: Mechanical and Electrical Activity, Cardiac Output, and Regulation of Heart Activity

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1. Overview of the Heart
   - Anatomy of the Heart
   - Histology of Cardiac Muscle

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2. Electrical Activity of the Heart
2.1. Cardiac Action Potential
   - Resting Membrane Potential (RMP)
   - Phases of the Cardiac Action Potential

2.2. Cardiac Conduction System
   - Sinoatrial (SA) Node
   - Atrioventricular (AV) Node
   - Bundle of His and Purkinje Fibers

2.3. Electrocardiogram (ECG)
   - P Wave: Atrial depolarization.
   - QRS Complex: Ventricular depolarization.
   - T Wave: Ventricular repolarization.
   - ECG is a critical tool for diagnosing arrhythmias and heart function abnormalities.

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3. Mechanical Activity of the Heart
3.1. The Cardiac Cycle
   - Systole
   - Diastole
   - Heart Sounds

3.2. Stroke Volume and Ejection Fraction

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4. Cardiac Output (Cardiac Debit)
4.1. Determinants of Cardiac Output
   - Cardiac Output (CO)
   - Factors Affecting CO

4.2. Variations in Cardiac Output
   - Exercise: Increases both HR and SV, leading to a higher CO.
   - Resting Conditions: Lower metabolic demand results in a decreased CO.
   - Age and Fitness: Influence CO due to changes in stroke volume, heart rate, and cardiac reserve.

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5. Regulation of Heart Activity
5.1. Intrinsic Regulation (Starling's Law of the Heart)
5.2. Extrinsic Regulation
   - Autonomic Nervous System (ANS):
   - Hormonal Regulation:

5.3. Effects of Ions and Body Temperature
   - Potassium (K+): Imbalances can lead to arrhythmias.
   - Calcium (Ca2+): Necessary for contraction; imbalances can cause weak or prolonged contractions.
   - Temperature: Heart rate increases with higher body temperature and decreases with lower temperature.

Course 4: Physiology of the Heart
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1. Overview of the Heart

The heart is a highly specialized muscular organ responsible for maintaining the circulation of blood throughout the body. It is situated in the mediastinum of the thoracic cavity, enclosed by the pericardium, a double-layered membrane that reduces friction during heart contractions. The heart operates as a dual pump with two circuits: the pulmonary circuit, which transports deoxygenated blood to the lungs for gas exchange, and the systemic circuit, which delivers oxygenated blood to tissues throughout the body. The structure and histology of the heart allow for its unique function and continuous activity without fatigue.

Anatomy of the Heart

The heart is divided into four chambers:

- Two atria (right and left) that receive blood returning to the heart.
- Two ventricles (right and left) that pump blood out of the heart.
- Right Atrium: Receives deoxygenated blood from the systemic circulation through the superior and inferior vena cava and pumps it into the right ventricle.
- Right Ventricle: Pumps deoxygenated blood to the lungs via the pulmonary artery.
- Left Atrium: Receives oxygenated blood from the lungs via the pulmonary veins and pumps it into the left ventricle.
- Left Ventricle: Pumps oxygenated blood into the systemic circulation through the aorta. The left ventricle has the thickest myocardium because it must generate sufficient pressure to overcome systemic vascular resistance and propel blood throughout the body.

Histology of Cardiac Muscle

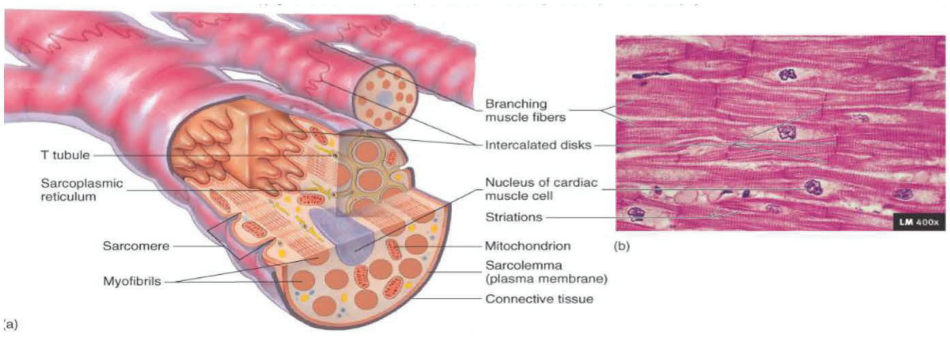
Cardiac muscle is composed of cardiomyocytes, which are specialized, striated muscle cells unique to the heart. These cells are branched and interconnected through intercalated discs, structures that contain desmosomes and gap junctions. Desmosomes provide mechanical strength by binding cells together, while gap junctions allow for the direct transfer of ions between cells, enabling synchronized contraction (functional syncytium). Cardiomyocytes have a high density of mitochondria, constituting about 25-35% of the cell volume, which allows them to sustain continuous energy production via oxidative phosphorylation, thus avoiding fatigue even during prolonged periods of activity.

Cardiac Muscle Cells

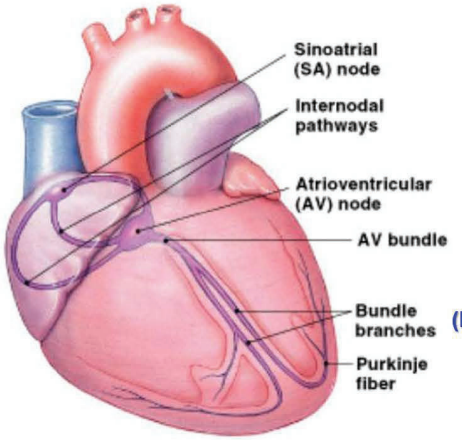
- Are branched, elongated cells with a centrally located nucleus
- Actin and myosin are organized to form sarcomeres (striated)
- T tubules and sarcoplasmic reticulum are not as organized as in skeletal muscle
- Normal contraction depends on extracellular Ca^{2+}
- Rely on aerobic respiration for ATP production
    - They have many mitochondria and are well supplied with

blood vessels

- Joined by intercalated disks
    - Specialized gap junctions that allow action potentials to move from one cell to the next, thus cardiac muscle cells function as a unit



Conduction System



(a) The conducting system

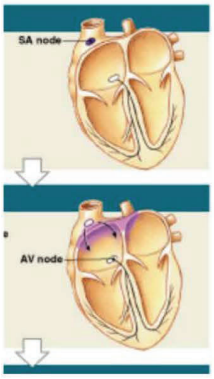
- SA node is located in the right atria, medial to the opening of SVC and has the highest rate of depolarization
- It starts each heart beat and sets the pace for the whole heart.
- It is called the pacemaker.
- From SA node, the impulse spreads through the atria to AV node, and then the atria contract.

- AV node is located at the lower portion of the right atrium.
- The impulse is delayed briefly at the AV node to give the atria time to finish contracting.
- Then impulse stimulate the ventricle to contract.

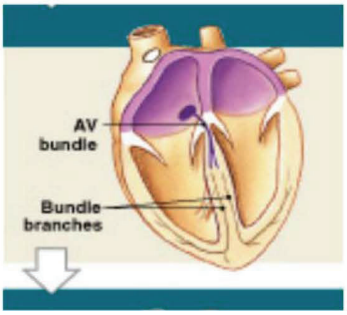
Impulse Conduction

Step 1
SA node activity and atrial activation begins
Time= 0

Step 2
Stimulus spreads across the atrial surfaces and reaches the AV node Time= 50 msec

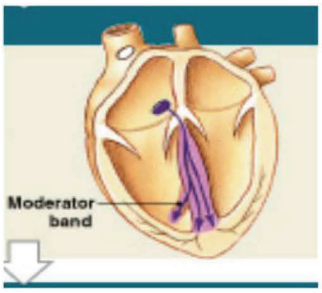


Step 3
There is a 100-msec delay at the AV node. Atrial contraction begins
Time= 150 msec



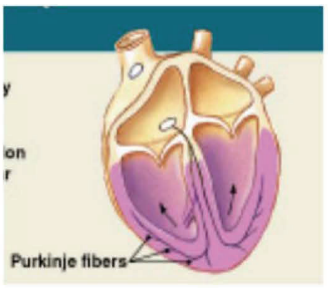
Step 4
The impulse travels along the interventricular septum within the AV bundle (Bundle of His) and the bundle branches to the Purkinje fibers to the papillary muscles of the right ventricle

Time= 175 msec

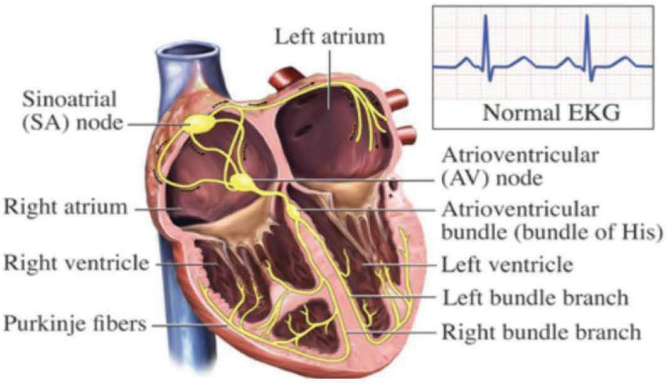


Step 5
The impulse is distributed by Purkinje fibers and relayed throughout the ventricular myocardium. Atrial contraction is completed, and ventricular contraction begins

Time= 225 msec



Electrical (Conductive) System



2. Electrical Activity of the Heart

The electrical activity is essential for coordinating the contraction of atria and ventricles, ensuring that blood is pumped efficiently through the circulatory system. The electrical impulses originate in pacemaker cells and propagate through a highly organized conduction system.

2.1. Cardiac Action Potential

The cardiac action potential is the basis for electrical activity in the heart and differs between pacemaker cells (like those in the SA node) and non-pacemaker cells (like ventricular myocytes).

- Resting Membrane Potential (RMP): In pacemaker cells (e.g., SA node), the RMP is unstable, starting around -60 mV and drifting toward threshold due to the activity of funny channels (If), which allow a slow influx of Na+ ions. In non-pacemaker cells, the RMP is stable, usually around -90 mV.
- Phases of the Cardiac Action Potential:
    1. Phase 4 (Resting Phase): Pacemaker cells undergo spontaneous depolarization due to the slow influx of Na+ ions, eventually reaching the threshold for action potential generation.
    2. Phase 0 (Depolarization): Once threshold is reached, voltage-gated Ca2+ channels open, causing a rapid influx of Ca2+ ions. In non-pacemaker cells, Na+ channels open, causing a rapid depolarization.
    3. Phase 1 (Initial Repolarization): Na+ channels close, and K+ channels open, allowing a small outward K+ current.
    4. Phase 2 (Plateau Phase): In non-pacemaker cells, this phase is characterized by the opening of slow Ca2+ channels, which prolong the depolarization and balance the K+ efflux, maintaining a plateau that ensures sustained contraction. The plateau phase is crucial for preventing tetany in cardiac muscle.
    5. Phase 3 (Repolarization): Ca2+ channels close, and K+ efflux continues, returning the cell to its resting membrane potential.
    6. Phase 4 (Resting State): The cell remains at its RMP until the next action potential is initiated.

This action potential governs the electrical activity and mechanical contraction of the heart and varies in duration depending on the region of the heart (atrial cells have shorter action potentials than ventricular cells).

2.2. Cardiac Conduction System

The cardiac conduction system consists of specialized cells that generate and conduct electrical impulses, allowing for coordinated contraction of the heart chambers.

- Sinoatrial (SA) Node: Located in the right atrium, the SA node is the primary pacemaker of the heart, generating impulses at 60-100 beats per minute. It initiates depolarization and sets the pace of the heart (sinus rhythm).
- Atrioventricular (AV) Node: Located between the atria and ventricles, the AV node delays the electrical impulse for approximately 0.1 seconds, allowing the atria to fully contract before the ventricles contract. This delay ensures efficient ventricular filling.
- Bundle of His and Purkinje Fibers: The electrical impulse is transmitted from the AV node through the Bundle of His, which divides into the right and left bundle branches, and eventually into the Purkinje fibers, which spread throughout the ventricular myocardium. This network allows rapid and synchronized depolarization of the ventricles, resulting in efficient ejection of blood.

2.3. Electrocardiogram (ECG)

An ECG records the heart's electrical activity and is a key diagnostic tool for assessing cardiac function and identifying arrhythmias.

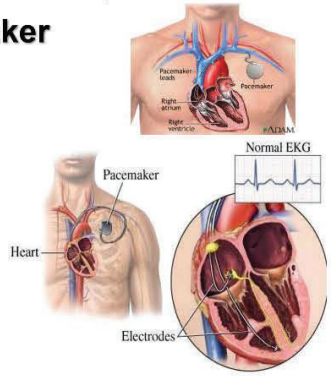
- P Wave: Represents atrial depolarization. The duration of the P wave reflects the time it takes for the electrical impulse to spread across the atria.

- QRS Complex: Represents ventricular depolarization. It is a sharp, high-voltage deflection due to the rapid spread of depolarization through the ventricles. The QRS duration indicates the time required for the impulse to pass through the ventricles.
- T Wave: Represents ventricular repolarization, where the ventricles return to their resting state. The repolarization process is slower and less synchronized, leading to a broader T wave.

Any deviation from the normal ECG pattern can indicate underlying conditions such as ischemia, infarction, electrolyte imbalances, or conduction system abnormalities (e.g., atrial fibrillation, bundle branch blocks).

Pacemaker

- **A pacemaker is a small, battery-operated electronic device which is inserted under the skin to help the heart beat regularly and at an appropriate rate. The pacemaker has leads that travel through a large vein to the heart, where the wires are anchored. The leads send the electrical impulses to the heart to tell it to beat.**

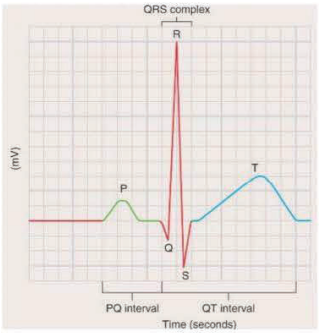


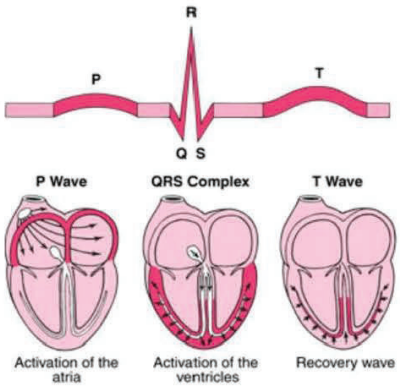
Autorhythmicity of Cardiac Muscle

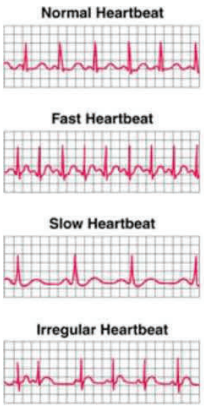
- Some cardiac muscle cells are autorhythmic because of the spontaneous development of a prepotential
  - Prepotential: slowly developing local action potential
- The sinoatrial (SA) node is the pacemaker of the heart
  - Collection of cardiac muscle cells capable of spontaneously generating action potentials
- The prepotential results from the movement of Na^+ and Ca^{2+} into the SA node cells
- The duration of the prepotential determines heart rate

EKG or ECG

- **P wave- shows how atria contract**
- **QRS complex- shows how ventricles contract**
- **T wave- shows how ventricle relax**







3. Mechanical Activity of the Heart

The heart's mechanical activity is tightly coupled with its electrical activity, resulting in cyclic contraction and relaxation that enables blood ejection and chamber refilling.

3.1. The Cardiac Cycle

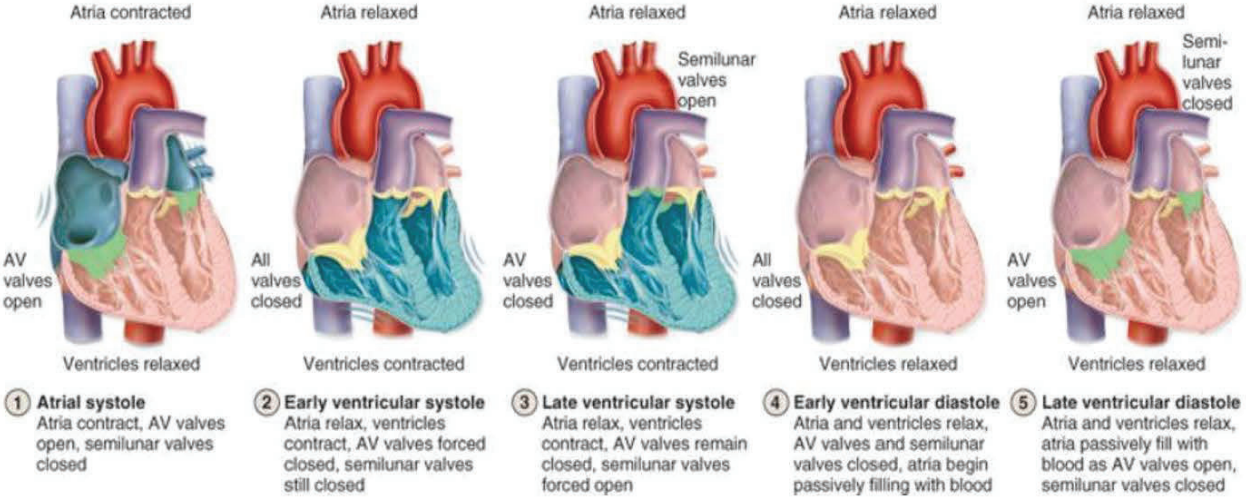
The cardiac cycle consists of two main phases: systole (contraction) and diastole (relaxation). A complete cardiac cycle occurs with each heartbeat.

- Systole: During ventricular systole, the ventricles contract, increasing pressure and closing the atrioventricular valves (mitral and tricuspid valves). As ventricular pressure exceeds the pressure in the aorta and pulmonary artery, the semilunar valves (aortic and pulmonary) open, allowing blood to be ejected into the circulation. The left ventricle generates significantly higher pressure than the right ventricle due to the higher resistance in the systemic circulation.
- Diastole: Following systole, the ventricles relax, and pressure within them drops. As ventricular pressure falls below that of the atria, the atrioventricular valves reopen, and the ventricles fill with blood from the atria. Approximately 70% of ventricular filling occurs passively during early diastole, while the remaining 30% is due to atrial contraction.
- Heart Sounds: The cardiac cycle produces characteristic heart sounds:
  - First Heart Sound (S1): Results from the closure of the atrioventricular valves at the beginning of ventricular systole.
  - Second Heart Sound (S2): Occurs with the closure of the semilunar valves at the onset of diastole.

3.2. Stroke Volume and Ejection Fraction

- Stroke Volume (SV): The amount of blood ejected by each ventricle per contraction. A normal stroke volume ranges between 60-100 mL per beat. Stroke volume is influenced by preload, afterload, and contractility.
- Ejection Fraction (EF): A percentage of the end-diastolic volume (EDV) that is ejected with each contraction. EF is a key indicator of cardiac performance, with normal values ranging between 55-70%. A low EF indicates impaired systolic function, often seen in heart failure.

Phase / Structure	Atrial systole	Early ventricular systole ⟷ Late ventricular systole	Early ventricular diastole ⟷ Late ventricular diastole
Atria	Contract	Relax	Relax
Ventricles	Relax	Contract	Relax
AV valves	Open	Closed	Open
Semilunar valves	Closed	Open	Closed



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4. Cardiac Output (CO)

4.1. Determinants of Cardiac Output

Cardiac output is the volume of blood the heart pumps per minute. It is determined by the product of heart rate (HR) and stroke volume (SV):

$$CO = HR \times SV$$

- Heart Rate (HR): The number of beats per minute, which is modulated by both intrinsic pacemaker activity and extrinsic factors such as the autonomic nervous system.
- Stroke Volume (SV): As described earlier, stroke volume depends on preload, afterload, and contractility.

4.2. Variations in Cardiac Output

- Exercise: During exercise, cardiac output increases significantly due to both increased HR and SV. The increase in heart rate is primarily due to enhanced sympathetic stimulation and reduced vagal tone.
- Resting Conditions: Under resting conditions, the metabolic demand is lower, and CO decreases accordingly. In a healthy adult, CO at rest is typically 4-6 L/min.

- Age and Fitness: As people age, the heart's ability to increase stroke volume and heart rate in response to stress or exercise diminishes, leading to a lower maximum cardiac output. Fitness also plays a significant role in CO, as trained individuals tend to have a higher stroke volume at rest, leading to a lower resting heart rate (athlete's bradycardia).

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5. Regulation of Heart Activity

Heart activity is finely regulated by intrinsic mechanisms and extrinsic factors that adjust heart rate, contractility, and overall cardiac output in response to changing physiological conditions.

5.1. Intrinsic Regulation (Starling's Law of the Heart)

Starling's Law, or the Frank-Starling mechanism, states that the force of contraction is directly proportional to the initial length of the cardiac muscle fibers. This means that an increase in ventricular filling (preload) leads to more forceful contractions, thus increasing stroke volume. This intrinsic regulation allows the heart to adapt to varying volumes of venous return without external input.

5.2. Extrinsic Regulation

- Autonomic Nervous System (ANS):
    - Sympathetic Nervous System: Activation of sympathetic nerves increases heart rate (positive chronotropy), enhances contractility (positive inotropy), and speeds up conduction through the AV node (positive dromotropy). These effects are mediated by beta-1 adrenergic receptors in response to norepinephrine and epinephrine.
    - Parasympathetic Nervous System (Vagal Tone): The vagus nerve (cranial nerve X) decreases heart rate by reducing SA node firing. Parasympathetic effects are primarily mediated by acetylcholine acting on muscarinic receptors.
- Hormonal Regulation:
    - Epinephrine and Norepinephrine: Released by the adrenal medulla during stress or exercise, these hormones increase heart rate and contractility.
    - Thyroid Hormones: Increase heart rate and enhance the response of the heart to catecholamines.
    - Renin-Angiotensin-Aldosterone System (RAAS): Regulates blood volume and pressure, indirectly affecting cardiac output by altering preload.

5.3. Effects of Ions and Body Temperature

- Potassium (K+): Potassium plays a critical role in maintaining the resting membrane potential. Hypokalemia (low K+) can cause hyperexcitability of the heart, leading to arrhythmias, while hyperkalemia (high K+) can cause decreased excitability and lead to life-threatening conduction block.
- Calcium (Ca2+): Calcium is essential for excitation-contraction coupling. Hypocalcemia reduces contractility, while hypercalcemia can cause excessive contraction and arrhythmias.
- Body Temperature: Heart rate increases with elevated body temperature (as seen during fever) due to the increased rate of metabolic reactions, while lower body temperatures slow the heart rate (bradycardia) due to reduced metabolic demand.

Practical Session 5: Composition and Properties of the Blood

1. Introduction to Blood

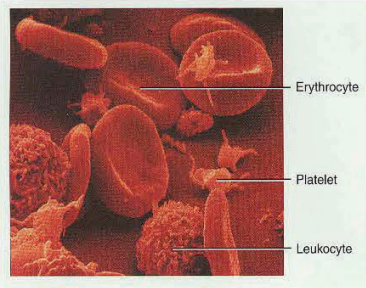
Definition and Composition

Blood is a specialized connective tissue composed of plasma (the liquid component) and formed elements (cells and cell fragments). It plays a vital role in transporting oxygen, nutrients, hormones, and waste products, while also regulating body temperature, pH balance, and defending against infections. Blood accounts for approximately 7-8% of total body weight, with an average volume of 5-6 liters in adults.

- Plasma: Makes up about 55% of blood volume and contains water, electrolytes, proteins, and other dissolved substances.
- Formed Elements: Comprise 45% of blood and include red blood cells (RBCs or erythrocytes), white blood cells (WBCs or leukocytes), and platelets (thrombocytes).

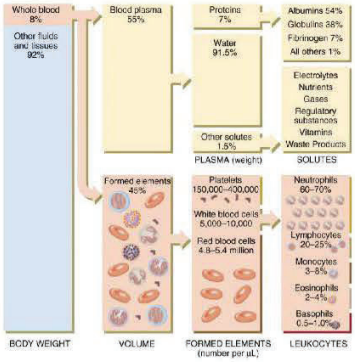
Blood

- **a suspension solution of blood cells in plasma**
- **circulating through the cardiovascular system.**



Composition

- **cellular portion (formed elements)**
- **fluid portion (plasma).**



2. Plasma Composition and Functions

Plasma

Plasma is the straw-colored liquid portion of blood and is about 90% water. It acts as a transport medium for nutrients, gases, hormones, and waste products.

Plasma Proteins

Plasma contains several proteins that are crucial for various functions:

- Albumin: Maintains osmotic pressure, preventing excessive fluid loss from blood vessels into tissues.
- Globulins: Play roles in immune function (as antibodies) and transport.
- Fibrinogen: Involved in blood clotting.

Plasma pH. The normal plasma pH range is 7.35 to 7.45, slightly alkaline. Maintaining this pH is critical for proper enzyme activity and physiological function. Buffers such as bicarbonates and proteins help regulate blood pH.

Plasma Proteins - constitute 7-9% of the plasma

- Albumins (60% - 80%)
  - Produced by the liver
  - Provide the osmotic pressure and necessary to maintain blood volume and pressure.
  - Effective Filtration Pressure = (capillary pressure + interstitial osmotic pressure) - (plasma colloid osmotic pressure + interstitial hydrostatic pressure)
- Globulins, divided into three types:
  - Alpha and beta globulin, produced by the liver and function to transport lipids and fat soluble vitamins in the blood.
  - Gamma globulins are antibodies produced by lymphocytes and function in immunity.

Plasma pH: 7.35 - 7.45

- **Maintained in a very narrow range through numerous mechanisms.**
- **Acids in the blood are buffered by bicarbonate in the plasma, and blood pH is maintained by the actions of the lungs and kidneys.**
  - **The lungs aid acid -base balance through elimination of carbon dioxide, which regulates the amount of carbonic acid in the blood.**
  - **The kidneys participate in acid - base balance by excreting H+ and retaining plasma bicarbonate.**

3. Red Blood Cells (Erythrocytes)

3.1. Structure and Function

Erythrocytes are biconcave in shape, which increases their surface area for oxygen exchange and enables flexibility to move through capillaries. They lack a nucleus and organelles, and their primary function is to carry oxygen from the lungs to tissues via hemoglobin, a protein that binds oxygen.

3.2. Hematocrit

Hematocrit measures the percentage of RBCs in a blood sample. The normal hematocrit range is:

- Men: 42-52%
- Women: 37-47%

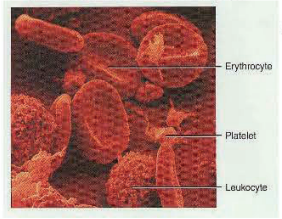
Hematocrit is a key indicator of oxygen-carrying capacity, and abnormal values can signal anemia or polycythemia.

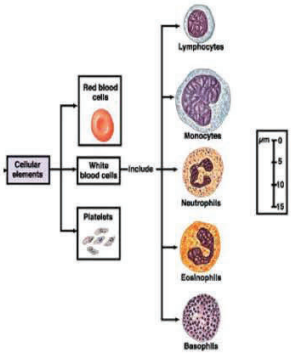
3.3. Erythropoiesis

Erythropoiesis is the process of RBC production, occurring in the bone marrow. It is stimulated by the hormone erythropoietin, primarily released by the kidneys in response to hypoxia (low oxygen levels). Adequate iron, vitamin B12, and folate are necessary for healthy erythropoiesis.

II. Blood Cells

- red blood cells (erythrocytes)
- white blood cells (leucocytes)
- platelets (thrombocytes).

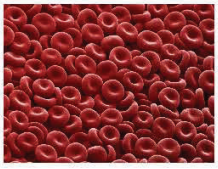




Red cells (Erythrocytes)

- Number: 5.1 to 5.8 million in males and 4.3 to 5.2 million in females per milliliter blood.
- Shape: flat, biconcave discs, about 7 um in diameter and 2.2 um thick.
- Importance of the unique shape: provides an increased surface area through which gas can diffuse.





Life Span of Red Cells

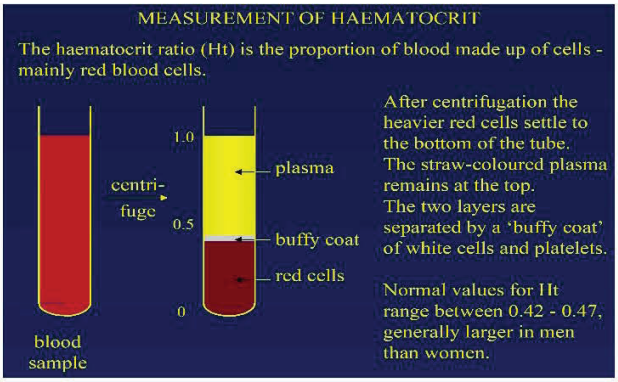
- Erythrocytes lack a nucleus and mitochondria
  - (they get energy from anaerobic (but not aerobic) respiration).
- Life span: about 120 days
  - destroyed by phagocytic cells in the liver, spleen and bone marrow.

Physical and Chemical Properties of the Red Cells

- Hematocrit
- Function
- Material for the production
- Erythropoiesis

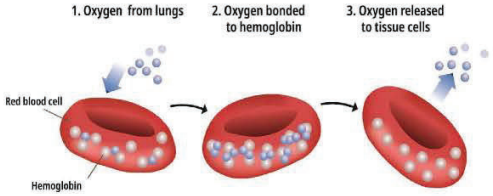
Hematocrit

- Concept: The percentage of blood volume occupied by the packed red blood cell volume
- Normal range: man, 40% - 50%, Women 37% - 48%



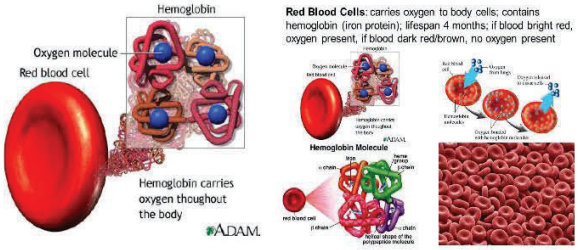
Function:

- To transport oxygen from the lungs to the tissue (function of hemoglobin)
- To transport carbon dioxide in blood.



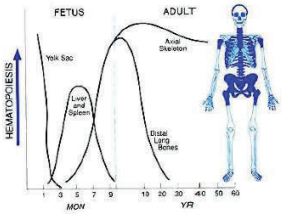
Material for the production.

- The protein and iron are used for hemoglobin synthesis.
- Both vitamin B12 and folic acid are necessary co-factors for DNA synthesis, which is essential for maturation of the red cells



Erythropoiesis

- The production of new red blood cells to replace the old and died ones
- In the adult, all the red cells are produced in bone marrow

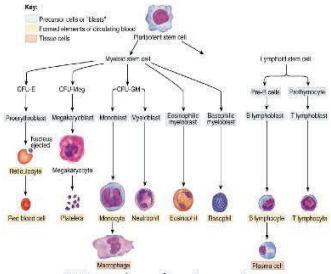


Importance of the Erythropoiesis

- Maintain the number of the red cells remarkable constant
- Anemia
  - Decrease rate of erythropoiesis or increased rate of red cells destruction
  - decreased number of red cells and weight of hemoglobin

Erythropoiesis- Pluripotent stem cells

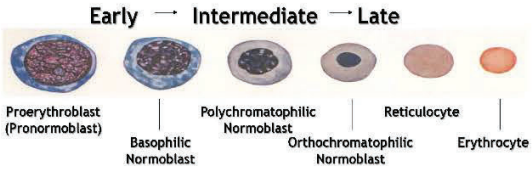
- in the bone marrow
- can produce any type of blood cells.
- is capable of both self-replication and differentiation to committed precursors-cells that can produce only a specific cell line.



CFU : colony-forming unit

Erythropoiesis-CFU-E

- the committed red cell precursor undergoes several divisions.
- The daughter cells becomes progressively smaller,
- the cytoplasm changes color from blue to pink as hemoglobin is synthesized,
- the nucleus becomes small and dense and then extrude
- The resulting non-nucleated cells is termed a reticulocyte since it still contains RNA
- Within a few days of entering the circulation, the reticulocytes lose their RNA and becomes mature red cells



Regulation of Erythropoiesis

- A. Erythropoietin,
  - a glycoprotein released predominantly from the kidneys in response to tissue hypoxia.
  - also produced by reticuloendothelial system of the liver and spleen.
  - Effect:
    - a, Stimulates the proliferation and differentiation of the committed red cell precursor
    - b, Accelerates hemoglobin synthesis
    - c, Shortens the period of red development in the bone marrow.
- B. Other hormones stimulate erythropoiesis
  - Adrenal cortical steroids,
  - Pituitary growth hormone,
  - Parathyroid hormone
  - Androgen
- C. Estrogen - inhibit erythropoiesis

4. White Blood Cells (Leukocytes)

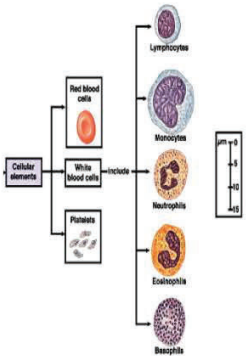
WBCs are involved in the immune response and are classified into two major groups:

4.1. Types of Leukocytes

- Granulocytes:
  - Neutrophils: The most abundant WBCs, involved in the first response to bacterial infections.
  - Eosinophils: Play a role in allergic reactions and parasitic infections.
  - Basophils: Release histamine during allergic reactions and contribute to inflammation.
- Agranulocytes:
  - Lymphocytes: Include T cells (cell-mediated immunity) and B cells (antibody production).
  - Monocytes: Differentiate into macrophages, which engulf and digest pathogens and dead cells.

White blood cells (leucocytes)

- Leukocytes contain nuclei and mitochondria and can move in an amoeboid fashion,
  - so they can squeeze through pores in capillary and get to a site of infection.
- Number, 5000 to 10000/µl
- Classification:
  - Granular leukocytes, having granules in the cytoplasm;
  - Agranular (or nongranular) leukocytes: without granules in the cytoplasm.



Granular Leukocytes - Eosinophils

- 0.5-5%.
- Function:
  - Limit the action of basophils in the rapid allergic reactions (through release of prostaglandin E and histamine oxidase)
  - Participate in the immune response to parasites



Granular Leukocytes - Basophils

- less than 1%,
- release heparin and histamine that are responsible for the allergic reaction.



Granular Leukocytes - Neutrophils

- 50 % - 70%.
- nonspecific cellular immunity :
  - After attracted by chemical substances released by bacteria,
  - They engulf and digest the bacteria or other foreign substances by means of phagocytosis



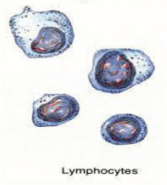
Agranular Leukocytes- Monocytes

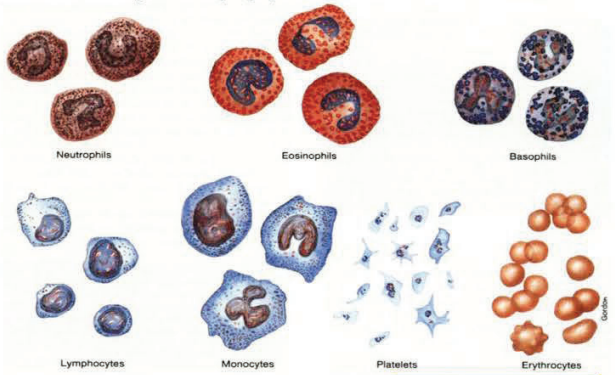
- 3% - 8%.
- Wander into the tissue and become fixed in the tissue and swell to become fixed tissue macrophages.
  - During the inflammation, they can divide in situ and form more macrophages
  - "wall process" for preventing spread of infection



Agranular Leukocytes- Lymphocytes

- 20% - 40%
- T (thymus dependent) lymphocytes, responsible for the cellular immunity
- B lymphocytes, responsible for the humoral immunity.

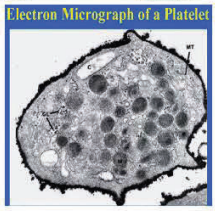


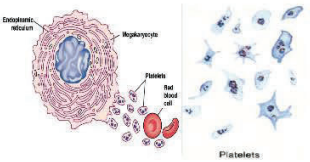


5. Platelets (Thrombocytes). Platelets are small, disk-shaped cell fragments derived from megakaryocytes in the bone marrow. They are crucial for hemostasis by forming platelet plugs at sites of vascular injury and releasing factors that promote blood clotting. The normal platelet count ranges from 150,000 to 450,000 per microliter of blood.

Platelets (thrombocyte)

- 0.13 to 0.36 million / µl; 2-4 µm in diameter
- Non-nucleated, irregularly shaped, minute round cells
- Produced in the bone marrow and
- Budded off from the cytoplasm of the megakaryocytes
- Play a key role in hemostasis
- Assist in maintaining the integrity of vascular endothelium
  - by quickly repairing the minor breaks in the endothelium.
  - When too few platelets are circulating in the blood, red cells leak more easily through blood vessel walls. (spontaneous bleeding)





6. Physical and Chemical Properties of Blood

6.1. Viscosity. Blood viscosity refers to its thickness and resistance to flow. It is influenced by the number of RBCs and plasma proteins. Increased viscosity can impair circulation and is commonly associated with conditions like polycythemia or dehydration.

6.2. Plasma Osmotic Pressure. Plasma osmotic pressure is mainly maintained by albumin and is responsible for keeping water in the bloodstream, preventing edema. Changes in osmotic pressure can lead to fluid imbalances between the blood and tissues.

6.3. Erythrocyte Sedimentation Rate (ESR). ESR measures the rate at which RBCs settle at the bottom of a tube over one hour. It is a nonspecific test used to detect inflammation. Elevated ESR may indicate conditions such as infections, autoimmune disorders, or cancers.

III. Physical and Chemical Properties of the Blood

- Gravity
  - Blood: 1.05-1.60
  - Plasma: 1.025-1.030
- Suspension Stability of the Red Cells and Erythrocyte sedimentation rate (ESR).
- Viscosity
- Plasma Osmotic Pressure

Suspension Stability of the Red Cells

- The erythrocytes are very stable in suspension due to the repelling force by the same (negative) charge of the red cells.
- When the blood is anticoagulated and added in a narrow tube, rouleaux of the red cells are formed and then its sediment gradually takes place.
  - The length of sedimentation of the red cells within one hour is termed erythrocyte sedimentation rate (ESR).

Erythrocyte sedimentation rate (ESR).

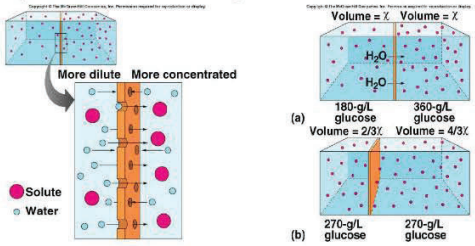
- The normal range
  - 0-3 mm per hour in men,
  - 0 - 10 mm per hour in women.
- depends mainly on the relative concentration of the plasma protein (Albumins and Globulins).
- Globulin and fibrinogen enhances the formation of the rouleaux.
- Almost all the infections (especially the tuberculosis and rheumatism) that are accompanied by a rise of globulin can accelerate ESR.

Viscosity

- The frictional force between the elements in the blood.
- The relative viscosity of the blood is 4-5, which is greater than that in plasma (1.6 - 2.4) and water (1).
- The higher the red cell concentration and the amount of plasma protein, the greater the viscosity of the blood.
- Increase of the viscosity can enhance the peripheral blood resistance, decreasing the blood supply to tissue.

Plasma Osmotic Pressure

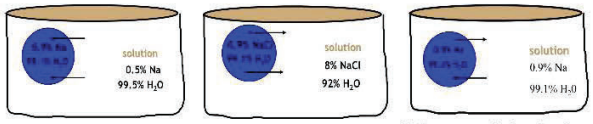
- Osmosis: Diffusion of the water across a semipermeable membrane to a region in which there is a higher concentration of solute



H20 moves by osmosis into the lower [H20] until equilibrium is reached.

Osmotic pressure.

- In clinical practice, it is common to substitute the term tonicity for osmolarity when referring to solutions.
- A solution is isotonic (isosmotic) if a normal cell does not change its volume when exposed to it.
  - This solution has a same osmotic pressure as that of the plasma.



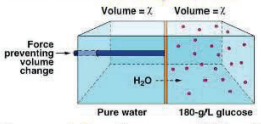
A solution that causes the cell to swell is termed hypotonic (hypoosmotic) solution.

A solution that causes shrinkage of the cell is called hypertonic (hyperosmotic) solution.

A 0.9 percent solution of sodium chloride, called physiological saline, or a 5 percent glucose solution is isotonic

Osmotic pressure.

- The osmosis of the water molecules can be opposed by applying a pressure in direction opposite that of the osmosis.
- The precise amount of pressure required to prevent the osmosis is called the osmotic pressure



- The total plasma osmotic pressure :
  - 313 mOsm/L or 708.9 kPa (5330 mmHg).
- It consists of two parts.
  - The plasma crystal osmotic pressure
  - The plasma colloid osmotic

Plasma crystal osmotic pressure: 5305 mmHg (99.5%), formed from the crystal substances and in the plasma, plays an important role in maintaining water equilibrium between the plasma and the intracellular fluid.

Plasma colloid osmotic pressure: 25 mmHg (0.5%).
formed from the colloid substances and plasma proteins in the plasma
important to maintain the water equilibrium between the plasma and the interstitial fluid.

Hemostasis

- In normal condition when a small blood vessel is severed or ruptured,
  - the injury can initiate a series of events that stop the bleeding automatically within a few minutes
- The process to arrest the bleeding is called hemostasis.

7. Hemostasis and Blood Clotting. Hemostasis is the process that prevents excessive blood loss when vessels are injured. It involves three main steps:

7.1. Vascular Constriction. Upon injury, vasoconstriction (narrowing of blood vessels) reduces blood flow to the site of injury, minimizing blood loss.

7.2. Platelet Plug Formation. Platelets adhere to exposed collagen at the injury site, become activated, and aggregate to form a platelet plug, providing temporary blockage of blood flow.

7.3. Blood Coagulation. Blood coagulation is the final step in hemostasis, where a series of enzymatic reactions result in the conversion of fibrinogen to fibrin, creating a stable clot that seals the injury. This process involves clotting factors, calcium, and vitamin K.

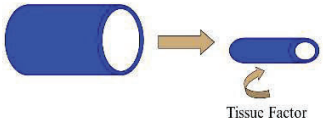
Mechanisms of Hemostasis

- vascular constriction (neural, myogenic and humoral)
- formation of a platelet plug;
- formation of a blood clot as a result of blood coagulation
- anticoagulation and fibrinolysis as a result of dissolution of the blood clot.

1. Vascular Constriction

- Nervous reflex;
- Local myogenic spasm
- Local humoral factors from the traumatized tissue and blood platelets.
  - Such as 5-HT, endothelin and thromboxane A2.

- Last for many minutes or even hours,
  - during this time the ensuing processes of platelet plugging and blood coagulation can take place



Formation of platelets plug and blood coagulation

- Platelet adhesion
- First phase of platelet aggregation
- Platelet release
- Second phase of aggregation.

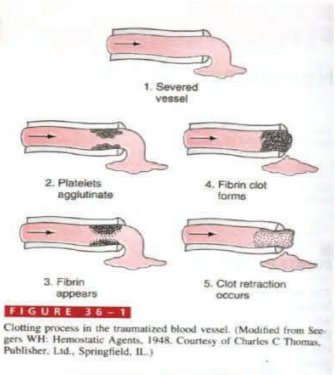
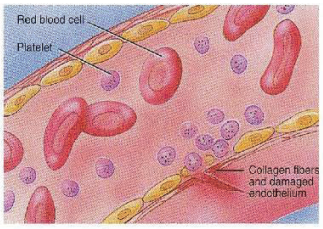


FIGURE 36–1

Clotting process in the traumatized blood vessel. (Modified from Seegers WH: Hemostatic Agents, 1948. Courtesy of Charles C Thomas, Publisher, Ltd., Springfield, IL.)

Platelet adhesion

- Adhere to the damaged vascular wall
  - the collagen fibers in the vascular wall
  - or even damaged endothelial wall

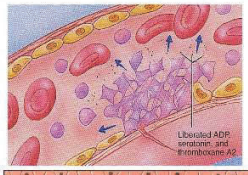


First phase of platelet aggregation

- ADP released from the damaged tissue
- the platelet adhere together loosely
- Reversible aggregation

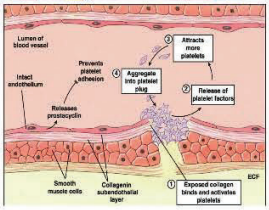
Platelet Release

- After the first phase (reversible) of aggregation
- the contractile proteins in the platelet contract forcefully and cause the release of granules
  - that contain multiple active factors including the ADP and thromboxane A_2



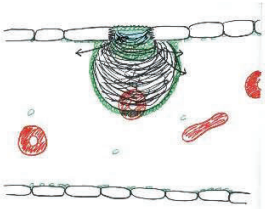
Second phase of aggregation

- ADP and thromboxane A2 in turn act on nearby platelets
- Cause the platelets to adhere to the originally activated platelets.
- Irreversible aggregation



3. Blood Coagulation in the Ruptured Vessel

- The clot begins to develop
  - in 15 to 20 seconds if the trauma of the vascular wall is severed
  - in 1 to 2 minutes if the trauma is minor.
- With 3 to 6 minutes after rupture, if the vessel opening is not too large, the entire opening or broken end of the vessel is filled with clot.
- Bleeding time, 1-3min



8. Blood Typing and Transfusion Reactions

8.1. ABO Blood Group System

Blood types are determined by the presence or absence of antigens (A and B) on the surface of RBCs:

- Type A: A antigen present, B antibodies in plasma.
- Type B: B antigen present, A antibodies in plasma.
- Type AB: Both A and B antigens present, no antibodies in plasma (universal recipient).
- Type O: No A or B antigens, both A and B antibodies present (universal donor).

8.2. Rh Factor

The Rh factor is another antigen present on RBCs. Individuals with the Rh antigen are Rh-positive (e.g., A+), while those without it are Rh-negative (e.g., A-). Incompatibility between Rh-positive and Rh-negative individuals during transfusions or pregnancy can lead to hemolytic reactions.

8.3. Transfusion Reactions

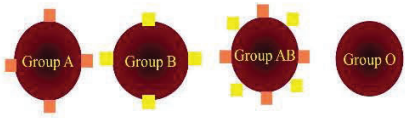
Transfusion reactions occur when incompatible blood is transfused, leading to the immune system attacking the foreign RBCs. This can cause hemolysis, fever, kidney failure, and, in severe cases, death.

ABO Blood

- classifications depend on the presence or absence of the **agglutinogens** (antigens) on the surface of the red cell membranes

Agglutinogens

- Two antigens- type A and type B occur on the surface of the red blood cells.
- These antigens are called **agglutinogens** because they often cause blood cell agglutination, causing blood transfusion reactions

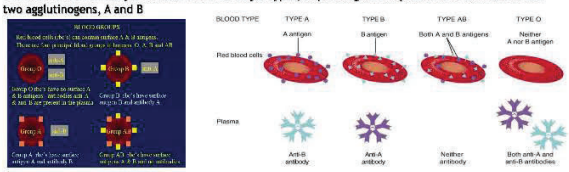


Agglutinins

- The agglutinins are gamma globulin in the plasma.
- When type A agglutinogen is not present in a person's red blood cells, antibodies known as anti-A agglutinins develop in the plasma.
- when type B agglutinogen is not present in the blood cells, antibodies known as anti-B agglutinins develop in the plasma.

Major types of ABO blood group

The bloods are normally classified into four major types, depending on the presence of absence of the two agglutinogens, A and B



ABO blood group

- **Two genes, one on each of two paired chromosomes, determine the ABO blood groups.**
- **They are allelomorphic genes that can be any one of three types but only one type on each chromsome: type O, A, B.**
- **The type O gene is either functionless or almost functionless, so that it causes no significant type O agglutinogen on the cells.**
- **the type A and type B genes do cause strong agglutinogens on the cells.**

Genotype	Blood Type	Agglutinogen	Agglutinin
OO	O	--	Anti-A, Anti-B
OA or AA	A	A	Anti - B
OB or BB	B	B	Anti-A
AB	AB	A and B	--

9. Practical Experiments and Demonstrations

9.1. Hematocrit Measurement

Students will measure their own hematocrit levels by centrifuging blood samples and calculating the proportion of RBCs to total blood volume.

9.2. Blood Typing

Students will perform blood typing by mixing blood samples with anti-A, anti-B, and anti-Rh antibodies to observe agglutination and determine blood types.

9.3. Coagulation Time

Students will measure coagulation time by observing the time it takes for a blood sample to clot after exposure to air. This experiment demonstrates the efficiency of the blood clotting process.

10. Clinical Case Studies

- Anemia:
  Anemia is a condition characterized by a reduced ability of the blood to carry oxygen due to low RBC count or hemoglobin levels. It can result from iron deficiency, chronic disease, or genetic disorders such as sickle cell anemia.

Coagulation Disorders:

Disorders such as hemophilia (a deficiency in clotting factors) and thrombocytopenia (low platelet count) result in impaired blood clotting and an increased risk of excessive bleeding.

Course 5: The Cardiovascular System
Sub-topic: Structure, Function, Circulation, and Regulation

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1. Overview of the Cardiovascular System
2. Structure of the Heart
2.1. Heart Chambers
2.2. Heart Valves

---

3. The Cardiac Cycle
3.1. Phases of the Cardiac Cycle
- Systole
- Diastole

3.2. Electrical Activity and Conduction
- Sinoatrial (SA) Node
- Atrioventricular (AV) Node
- Bundle of His and Purkinje Fibers:

3.3. Mechanical Events of the Cardiac Cycle

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4. Systemic and Pulmonary Circulation
4.1. Systemic Circulation
4.2. Pulmonary Circulation

---

5. Blood Flow and Resistance
5.1. Blood Flow (Q):
5.2. Factors Affecting Blood Flow

---

6. Blood Pressure and Its Regulation
6.1. Formation of Blood Pressure
6.2. Mean Arterial Pressure (MAP):
6.3. Regulation of Arterial Pressure

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7. Venous Return and Central Venous Pressure
7.1. Factors Affecting Venous Return
7.2. Central Venous Pressure:

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8. Microcirculation and Capillary Exchange
8.1. Capillary Structure and Function
8.2. Mechanisms of Exchange

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9. Lymphatic System
9.1. Functions of Lymphatic System
9.2. Role in Edema Prevention

Practical Session 6: Electrocardiography (ECG)

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1. Introduction to Electrocardiography

---

2. Anatomy of the Heart's Conduction System

---

3. The ECG Waveform Components

---

4. Lead Placement and ECG Leads

---

5. Voltage and Time Calibration

---

6. Rate and Rhythm Calculation

---

7. ECG Interpretation and Analysis
   - Arrhythmias
   - Ischemia and Infarction
   - Hypertrophy and Dilation

---

8. Practical Experiments and Demonstrations

---

9. Clinical Relevance

---

10. Blood Pressure and Pulse

10.1. Blood Pressure

- Definition
- Factors Influencing Blood Pressure

10.2. Pulse

- Definition
- Pulse Points

---

11. Practical Experiments and Demonstrations

11.1. Measurement of Blood Pressure

- Auscultatory Method:

Using a sphygmomanometer and stethoscope, the systolic and diastolic pressures are determined by listening to Korotkoff sounds as the cuff is deflated.

11.2. Pulse Rate and Quality

- Measurement of Pulse Rate:

o Measuring the pulse rate at rest and after physical activity, assessing the effects of exercise on cardiovascular function.

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12. Clinical Relevance

- Hypertension:
- Arrhythmias:
- Heart Failure:

Course 5: The Cardiovascular System
Sub-topic: Structure, Function, Circulation, and Regulation
1. Overview of the Cardiovascular System
The cardiovascular system is essential for maintaining homeostasis by ensuring the transport of nutrients, gases, hormones, and waste products to and from the cells. It consists of three major components:

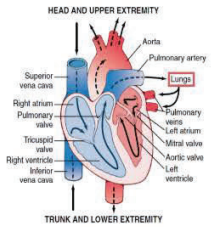
- The heart, which acts as a pump to propel blood.
- Blood vessels, which serve as conduits for blood flow.
- Blood, the fluid that carries oxygen, nutrients, hormones, and waste products.

Functions of the cardiovascular system include:

- Oxygen and nutrient delivery to tissues.
- Carbon dioxide and waste removal from cells.
- Temperature regulation by redistributing heat.
- Transport of hormones to target organs and tissues.
- Maintenance of blood pressure to ensure adequate perfusion of tissues.

2. Structure of the Heart
The heart is a muscular organ enclosed in a protective sac called the pericardium. It is divided into four chambers: two atria and two ventricles, separated by the interatrial and interventricular septa. The heart is composed of specialized cardiac muscle fibers capable of conducting electrical impulses and sustaining rhythmic contractions.
2.1. Heart Chambers

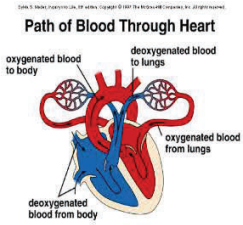
- Right atrium: Receives deoxygenated blood from the body via the superior and inferior venae cavae and pumps it to the right ventricle.
- Right ventricle: Pumps deoxygenated blood to the lungs through the pulmonary artery for oxygenation.
- Left atrium: Receives oxygenated blood from the lungs via the pulmonary veins and pumps it to the left ventricle.
- Left ventricle: The strongest and thickest chamber, responsible for pumping oxygenated blood into the systemic circulation via the aorta.



The heart is composed of three major types of cardiac muscle: atrial muscle, ventricular muscle, and specialized excitatory and conductive muscle fibers. The atrial and ventricular types of muscle contract in much the same way as skeletal muscle, except that the duration of contraction is much longer. The specialized excitatory and conductive fibers, however, contract only feebly because they contain few contractile fibrils; instead, they exhibit either automatic rhythmical electrical discharge in the form of action potentials or conduction of the action potentials through the heart, providing an excitatory system that controls the rhythmical beating of the heart.

B. Heart Chambers

- **1. Right Heart**
  - **receives venous blood from systemic circulation**
    - **via superior and inferior vena cava into right atrium**
    - **pumps blood to pulmonary circulation from right ventricle**



- **2. Left Heart**
  - **receives oxygenated blood from pulmonary circulation**
  - **pumps blood into systemic circulation**

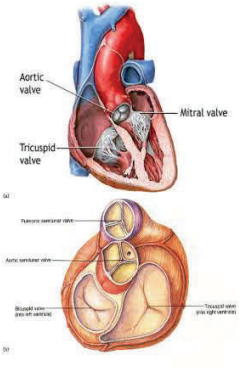
2.2. Heart Valves
Valves ensure unidirectional blood flow and prevent backflow during the cardiac cycle. There are four main valves:

- Atrioventricular valves:
  - Tricuspid valve: Between the right atrium and right ventricle.
  - Mitral (bicuspid) valve: Between the left atrium and left ventricle.
- Semilunar valves:
  - Pulmonary valve: Between the right ventricle and the pulmonary artery.
  - Aortic valve: Between the left ventricle and the aorta.

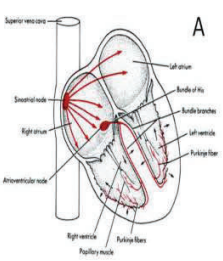
The synchronized opening and closing of these valves allow for the efficient pumping of blood throughout the body.

C. Heart Valves

- 1. Atrioventricular
  - tricuspid--between RA and RV; three leaflets
  - mitral--between LA and LV; two leaflets
- 2. Semilunar
  - pulmonic--three leaflets
  - aortic--three leaflets
- Prevent backward regurgitation
- Provide low resistance to forward flow



- The cardiac events that occur from the beginning of one heart beat to the beginning of the next.
- Each cycle is initiated by spontaneous generation of an action potential in the sinus node.
- The action potential travels from here rapidly through both atria and then through the A-V bundle into the ventricles.
- The conducting from the atria into the ventricles - there is a delay of more than 0.1 seconds during the passage of the cardiac impulse from the atria into the ventricles.
- This allows the atria to contract ahead of ventricular contraction, thereby pumping blood into the ventricles before the strong ventricular contraction begins. Thus, the atria act as primer pumps for the ventricles, and the ventricles in turn provide the major source of power for moving blood through the body's vascular system.



3. The Cardiac Cycle

The cardiac cycle encompasses all events associated with one heartbeat, involving both electrical and mechanical activities. It consists of two primary phases: systole and diastole.

3.1. Phases of the Cardiac Cycle

- Systole: The period of ventricular contraction where blood is ejected from the ventricles into the pulmonary artery (right ventricle) and the aorta (left ventricle).
- Diastole: The relaxation phase, where the heart chambers refill with blood. During this phase, the atrioventricular valves are open, and blood flows passively from the atria into the ventricles.

3.2. Electrical Activity and Conduction

The heart's electrical conduction system generates and transmits impulses that coordinate heartbeats. Key components include:

- Sinoatrial (SA) node: The primary pacemaker located in the right atrium, initiating the electrical impulse that spreads through the atria, causing contraction.
- Atrioventricular (AV) node: Delays the impulse to allow complete atrial contraction and ventricular filling.
- Bundle of His and Purkinje fibers: These rapidly transmit the impulse through the ventricles, ensuring coordinated and powerful ventricular contractions.
-

3.3. Mechanical Events of the Cardiac Cycle

Mechanical events during the cardiac cycle are synchronized with electrical impulses:

- Isovolumetric contraction: The ventricles contract without any change in volume, as all valves are closed.
- Ventricular ejection: Blood is ejected from the ventricles when the pressure exceeds that in the arteries, causing the semilunar valves to open.
- Isovolumetric relaxation: The ventricles relax without a change in volume, as all valves are closed again.
- Ventricular filling: The atrioventricular valves open, and blood flows passively from the atria to the ventricles.

---

4. Systemic and Pulmonary Circulation

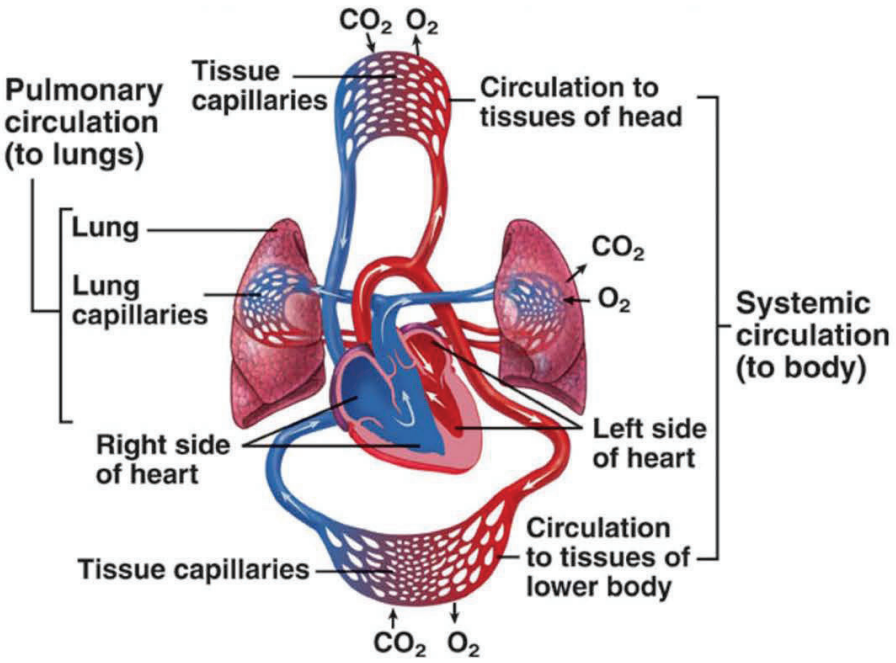
The heart powers two circuits of blood flow:

4.1. Systemic Circulation

Systemic circulation carries oxygenated blood from the left ventricle through the aorta and to the tissues of the body. Deoxygenated blood is returned to the right atrium via the superior and inferior venae cavae.

4.2. Pulmonary Circulation

Pulmonary circulation transports deoxygenated blood from the right ventricle to the lungs via the pulmonary arteries. Oxygenated blood is returned to the left atrium through the pulmonary veins. This ensures oxygenation of the blood and removal of carbon dioxide.



5. Blood Flow and Resistance

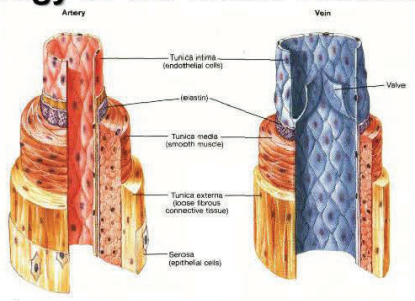
5.1. Blood Flow (Q)

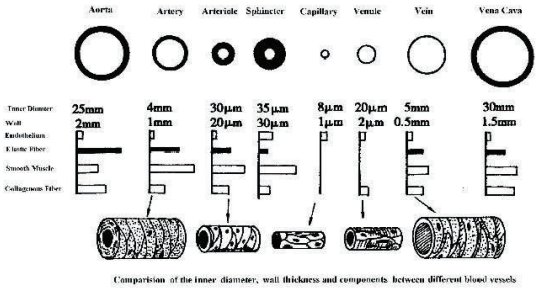
Blood flow refers to the volume of blood passing through a vessel or organ per unit time. It is driven by pressure gradients created by the heart and resisted by factors such as blood vessel diameter and viscosity.

5.2. Factors Affecting Blood Flow

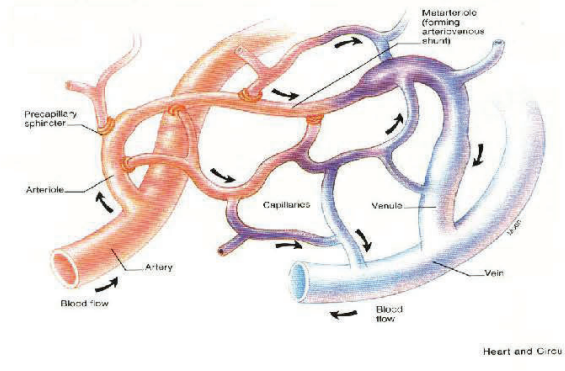
- Blood viscosity: Increased viscosity raises resistance to flow.
- Vessel diameter: Vasoconstriction increases resistance, while vasodilation decreases it.
- Vessel length: Longer vessels present more resistance.
- Pressure gradients: Blood moves from regions of high pressure to low pressure, ensuring circulation.

•Physiology of the Blood Vessels

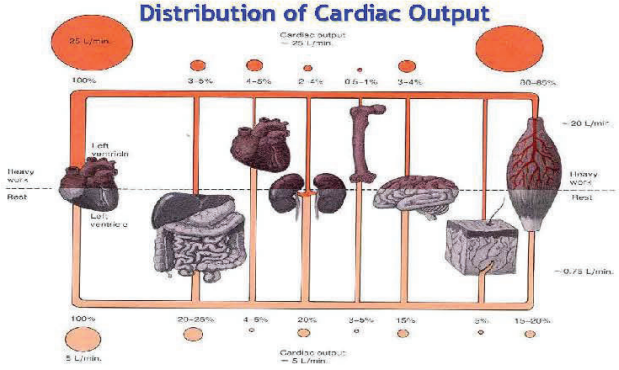




Comparision of the inner diameter, wall thickness and components between different blood vessels

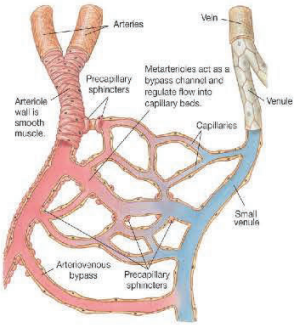


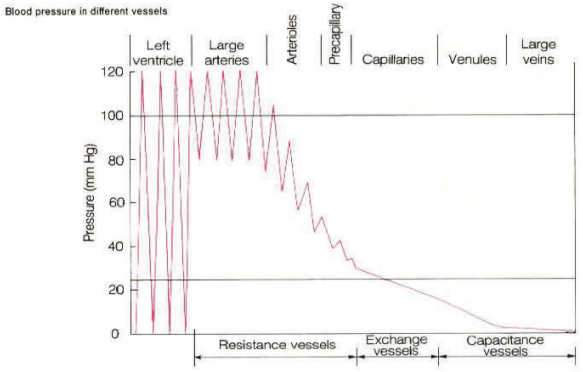
Heart and Circu



Precapillary Resistance Vessels – Small arteries and arterioles

- Less elastic than the larger arteries
- Have a thicker layer of smooth muscle.
- Provide the greatest resistance to blood flow through the arterial system
  - since they have narrow lumina.



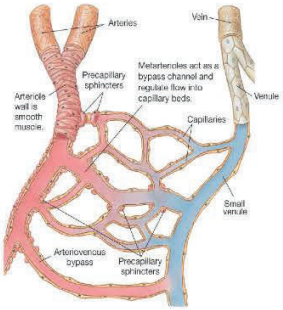


1. Blood Flow (Q)

- **Concept: The quantity of blood that passes a given point in the circulation in a given period of time.**
- **The overall blood flow in the systemic circulation is identical to the cardiac output**

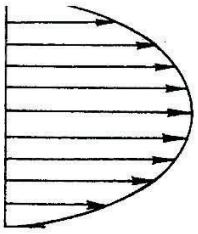
Precapillary Sphincter muscle

- **Partially determines the amount of blood flowing through a particular capillary bed**
  - **Allow only 5% - 10% of the capillary in bed skeletal muscles to be open at rest.**



Laminar flow and turbulent flow

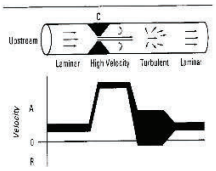
- **Laminar flow – blood flows in streamlines with each layer of blood remaining the same distance from the wall**



Laminar flow

Laminar flow and turbulent flow

- **Turbulent flow – blood flow in all directions in the vessel and continually mixes within the vessel.**
- **because of**
  - **the velocity of blood flow is too great**
  - **is passing by an obstruction**
  - **making a sharp turn,**
  - **passing over a rough surface**



C, constriction;
A, anterograde;
R, retrograde

6. Blood Pressure and Its Regulation

6.1. Formation of Blood Pressure

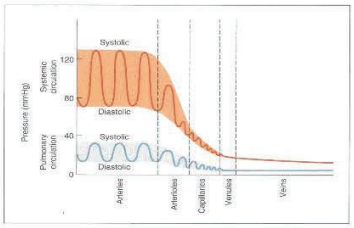
Blood pressure is the force exerted by circulating blood on the walls of blood vessels. It is generated by ventricular contraction and is necessary to maintain adequate tissue perfusion.

6.2. Mean Arterial Pressure (MAP)

Mean arterial pressure (MAP) is the average pressure within the arteries during one cardiac cycle. It is a critical determinant of blood flow and is maintained by balancing cardiac output and vascular resistance.

Blood pressure

- **the force exerted by the blood against the vessel wall**
- **stored energy (potential energy)**

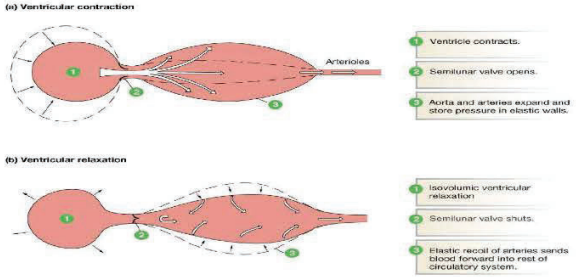


Formation of the blood pressure:

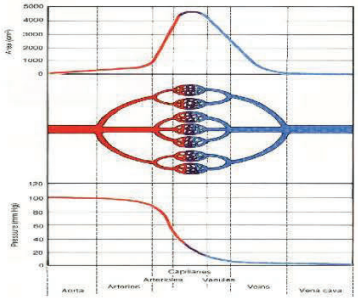
Cardiac pumping

- **Energy released from heart contraction is transferred into parts**
  - **1) kinetic energy (1% of the total)**
  - **2) potential energy (pressure) (99% of the total)**
- **most part of energy used to create the blood pressure**

Blood Pressure:
Generated by Ventricular Contraction



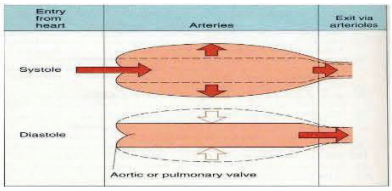
Physical Characteristics of the Systemic Circulation



- (1) The velocity: inversely proportional to its cross-sectional area.

Formation of the blood pressure:

- (4) Elasticity of Windkessel vessel
  - ① diastolic blood pressure
  - ② continuous blood flow in diastole
  - ③ buffering blood pressure



- (2) Pressure and resistance.
  - The decrease in pressure in each part of the systemic circulation is directly proportional to the vascular resistance.

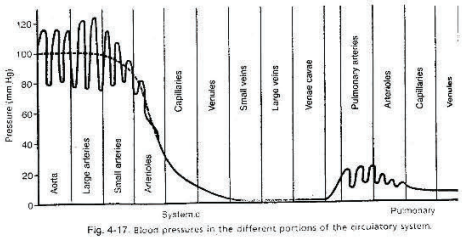


Fig. 4-17. Blood pressures in the different portions of the circulatory system.

Arterial Pressure

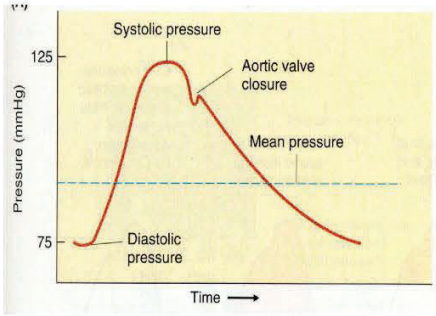
1. Concept of Arterial Pressure

- Blood pressure in the aorta and other big arterials.

2. Normal Range of Arterial Pressure

- Systolic pressure (Ps) – the maximum of the pressure during systole
- Diastole pressure (Pd) – the minimum pressure during diastole
- Pulse pressure – the difference between Ps and Pd
- Mean arterial pressure – the average pressure throughout each cardiac cycle.
  - Mean arterial pressure (Pm) = Pd + Pulse pressure / 3

Mean arterial pressure



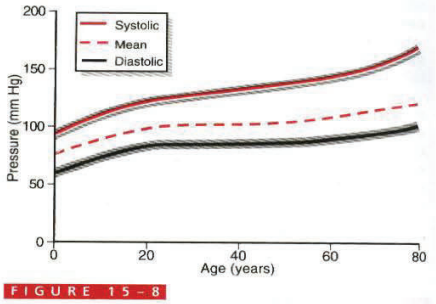
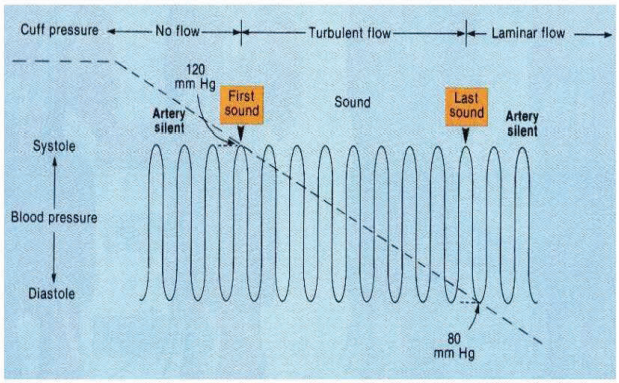


FIGURE 15-8
Changes in systolic, diastolic, and mean arterial pressures with age. The shaded areas show the approximate normal range.

6.3. Regulation of Arterial Pressure

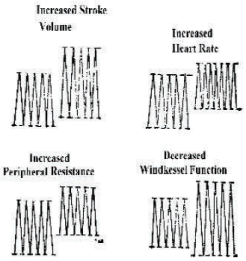
Several mechanisms regulate blood pressure:

- Baroreceptors in the aortic arch and carotid sinuses detect changes in blood pressure and adjust cardiac output and vessel diameter accordingly.
- Renin-Angiotensin-Aldosterone System (RAAS) adjusts blood volume and vascular tone.
- Sympathetic nervous system increases heart rate and contractility in response to low blood pressure, while the parasympathetic nervous system reduces heart rate during rest.



3. Factors Determining Arterial Pressure

- Stroke volume ---- Ps
- Heart rate ---- Pd
- Total peripheral resistance (Pd)
- Action of Windkessel vessel (aorta and other large arteries) - Pulse pressure
- Mean circulatory filling pressure



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7. Venous Return and Central Venous Pressure

7.1. Factors Affecting Venous Return

Venous return is the flow of blood back to the heart. Factors influencing venous return include:

- Venous tone: Degree of constriction of veins.
- Skeletal muscle pump: Muscle contractions compress veins and push blood toward the heart.
- Respiratory pump: During inhalation, negative pressure in the thoracic cavity promotes venous return.

7.2. Central Venous Pressure (CVP)

Central venous pressure (CVP) is the pressure in the thoracic vena cava near the right atrium. It reflects the volume of blood returning to the heart and the heart's ability to pump it into the arterial system.

Venous Pressure

- **Central venous pressure**
  - The pressure in the right atrium.
    - Normally about 0 mmHg.
  - Regulated by a balance between
    - the ability of the right ventricle to pump blood out
    - the tendency of blood to flow from the peripheral back into the right atrium.
  - Clinical importance:
    - the hemorrhage
    - right heart failure
- **Peripheral venous pressure**
  - Venous pressure in the organs
  - Properties
    - Low pressure
    - Affected by the hydrostatic pressure
    - Usually veins are collapsed (Why?)

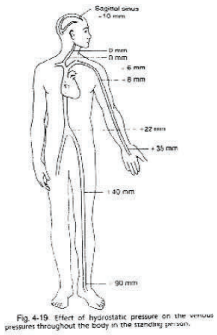


Fig. 4-19 Effect of hydrostatic pressure on the venous pressures throughout the body in the standing person.

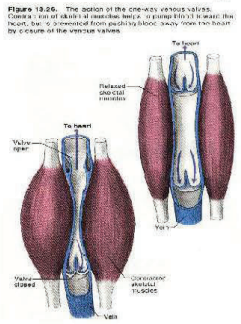
Factors affecting venous return

- 1) Mean systemic filling pressure
- 2) Cardiac contractility

  Cardiac contractility - stroke volume - ventricular pressure in diastole period - blood from atria and large veins to ventricle - venous return
- 3) Position of the body

  From lying to standing - increase of the blood in veins - dilation of veins in the lower part of the body - decrease of venous return

Factors affecting venous return

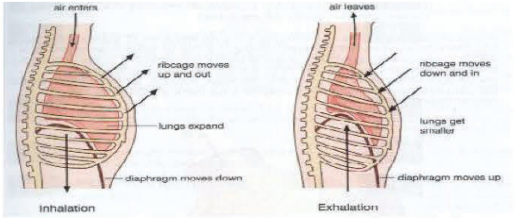


- 4) Action of "muscular pump" (or venous pump)

Factors affecting venous return

- *(5) respiration movement*.

Negative pressure in the thoracic cavity that changes with respiratory movement - dilation of venae cave - increase of venous return



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8. Microcirculation and Capillary Exchange

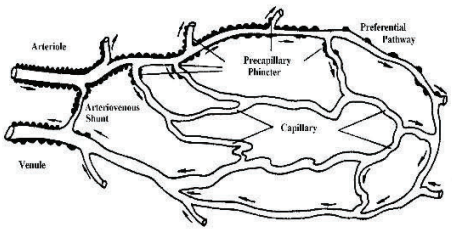
8.1. Capillary Structure and Function

Capillaries are the smallest blood vessels where gas, nutrient, and waste exchange occur. Their thin walls allow for efficient diffusion of oxygen, carbon dioxide, glucose, and other substances.

8.2. Mechanisms of Exchange

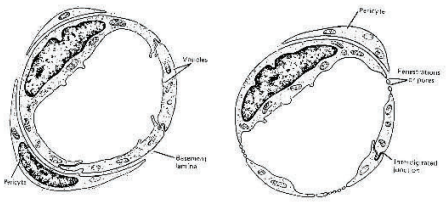
- Diffusion: Gases like oxygen and carbon dioxide passively diffuse across the capillary walls according to their concentration gradients.
- Filtration: Fluid and solutes move out of the capillaries into the interstitial space due to hydrostatic pressure.
- Reabsorption: Fluid is drawn back into capillaries by osmotic pressure created by plasma proteins.

1.Functional anatomy of the microcirculation



Microcirculation

2. "pores" in the capillary membrane



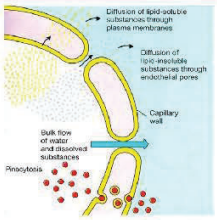
A, Continuous Capillaries B, Fenestrated Capillary

2. "pores" in the capillary membrane

- Structurally, capillaries have no smooth muscle in their walls.
- They are lined by only a single layer of endothelial cells.
- There are gaps between endothelial cells to allow for exchange of nutrients and metabolites.

3. Capillary pressure.

Capillaries



- Arterial end 30 - 40 mmHg;
- Venous end, 10 - 15 mmHg;
- Middle part 25 mmHg

4. Exchange of nutrients and other substances between the blood and interstitial fluid

- (1) Diffusion through the capillary membrane
  - Lipid-solute substance
    - diffuse directly
  - Water-soluble, liquid-insoluble substance
    - diffuse only through the capillary pores.

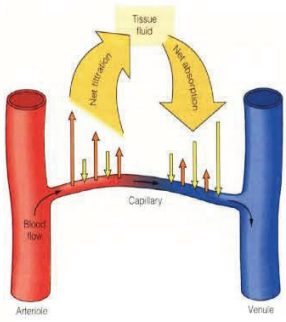
4. Exchange of nutrients and other substances between the blood and interstitial fluid

- (2) Proteins and large molecular: by pinocytosis.
- (3) Water and dissolved substance: filtration down a pressure gradient

VI The Interstitial Fluid

- Water within the body accounts for 60% of the total body weight (body fluid)
  - 2/3 intracellular compartment
  - 1/3 extracellular compartment
    - 80%, interstitial fluid;
    - 20%, blood plasma

- The distribution of extracellular fluid: dynamic equilibrium
- a continuously circulating medium
- Provide the glucose and other to the cells



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9. Lymphatic System

9.1. Functions of the Lymphatic System

The lymphatic system collects excess fluid from the interstitial spaces and returns it to the bloodstream. It also plays a vital role in immune defense by filtering pathogens through lymph nodes.

9.2. Role in Edema Prevention

Lymphatic vessels help prevent the buildup of excess fluid (edema) by draining interstitial fluid and maintaining proper fluid balance.

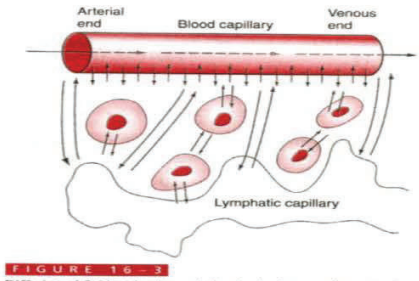
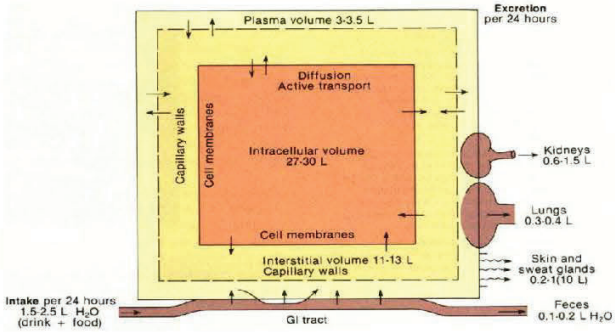
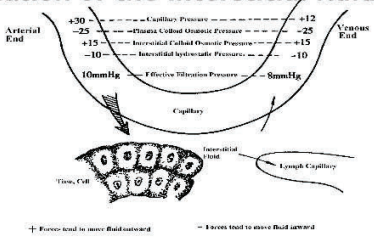


FIGURE 16-3
Diffusion of fluid molecules and dissolved substances between the capillary and interstitial fluid spaces.



1. Formation of the interstitial fluid



- Effective Filtration Pressure = (Capillary Pressure + Interstitial Colloid Osmotic Pressure) - (Plasma Colloid Osmotic Pressure + Interstitial Hydrostatic Pressure)

2. Factors Determining Formation of the Interstitial Fluid (Mechanism of Edema)

- Edema is an abnormally large collection of fluid in the interstitial space.
- From the physiology of capillaries and lymphatics

Mechanism of Edema

- (1) Capillary pressure
  - Right heart failure -systemic edema
  - Left heart failure - pulmonary edema
  - Late pregnancy - edema in legs and foot (pressure of uterus on inferior vena cava)
- (2) Plasma colloid osmotic pressure
  - Protein malnutrition, liver disease (inadequate albumin synthesis) or renal disease (protein loss in urine) - hypoproteinemia - low plasma colloid osmotic pressure
- (3) Permeability of capillary wall
  - Inflammation or allergy - leakage of abnormally large quantities of proteins from capillaries

Mechanism of Edema

- Lymphatic drainage: lymphatics
  - the second circulatory system.
  - a network of blind-ended thin endothelial tubes.
  - the endothelial lining is not fenestrated,
    - the intercellular junctions are permeable to large molecules.

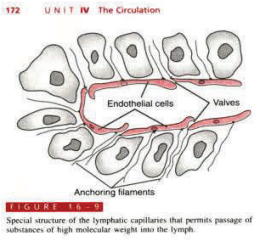


FIGURE 16-9
Special structure of the lymphatic capillaries that permits passage of substances of high molecular weight into the lymph.

Mechanism of Edema

- Lymphatic drainage: lymphatics collect proteins, lipids and other large molecules which leak out of capillaries into the interstitial space,
  - to prevent the osmotic pressure of interstitial space from rising,
    - prevent abnormal accumulation of fluid in the interstitial space.
  - Reduced lymphatic drainage, e.g. in filariasis, or involvement of lymph nodes in malignancy
    - - local or systemic edema.

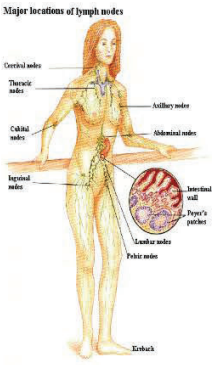
Figure 14.8. Parasitic larvae that block lymphatic drainage produce tissue edema, resulting in elephantiasis.



In the tropical disease *filariasis*, mosquitoes transmit a nematode worm parasite to humans. The larvae of these worms invade lymphatic vessels and block lymphatic drainage. The edema that results can be so severe that the tissues swell to produce an elephantlike appearance, with thickening and cracking of the skin. This condition is thus aptly named **elephantiasis** (fig. 14.8).

The function of lymph

- Removing protein from interstitial fluid.
- Regulating balance between plasma and interstitial fluid (reabsorption 10% of filtration fluid).
- Absorption of nutrients (80%~90% of fat) from gastrointestinal tract.
- Removing the particles such as RBC, bacteria, lymphatic cell, tissue cell in the interstitium.
- Defense function (to ingest bacteria and to produce antibodies)



Practical Session 6: Electrocardiography (ECG)

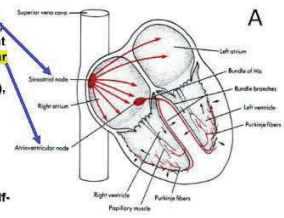
1. Introduction to Electrocardiography

Electrocardiography (ECG or EKG) is a diagnostic tool used to record the electrical activity of the heart. The ECG traces the depolarization and repolarization of the heart's atria and ventricles during each heartbeat. By placing electrodes on the skin, electrical impulses generated by the heart can be detected, measured, and displayed as a waveform on graph paper or a monitor. Analyzing the ECG waveform provides valuable information about heart rate, rhythm, and the presence of any abnormal conditions such as arrhythmias or ischemia.

ELECTROCARDIOGRAM

- At the heart level, depolarization is initiated by a peace-maker - this is normally the sinoatrial node (SAN) - and then taken over by other myocardial cells;
- The atria are gradually depolarized starting with Right Atrium (RA); the stimulus reaches the Atrio-Ventricular Node (AVN) (normally the only electrical communication pathway between atria and ventricles), then into His bundle, branches, Purkinje cells, ventricular myocytes.
- The physiological peace-maker is SAN - it contains cells that have the capacity for self-depolarization → automaticity; normal self-depolarization frequency 60-100 / minute.

Also AVS cells or Purkinje systems are capable of self-depolarization but they have lower download frequencies than SAN and are therefore depolarized by the stimulus coming from the higher frequency peace maker.

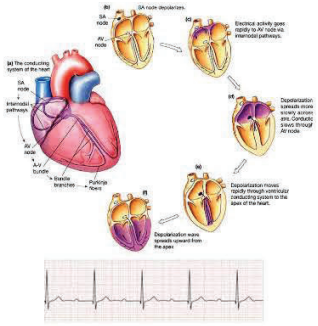


ELECTROCARDIOGRAM

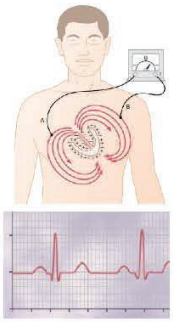
Detailed analysis of the differences in cardiac potential recorded at the level of the body surface, allows assessments regarding: anatomical orientation of the heart, its electrical activity, the thickness of the cardiac walls, the presence of rhythm disorders, etc.

The electrocardiogram is useful for diagnosis of:

- ARRHYTHMIAS
- Electrical driving disorders (Pacemaker)
- Myocardial ischemia
- Hypertrophy and dilation of the heart cavities
- The effect of some drugs (digitalis - heart failure, class 1 and 3 antiarrhythmics, psychotropic drugs, etc.).
- Dyselectrolithemias - electrolytic and metabolic abnormalities (Ca, K, Mg, pH, etc.)

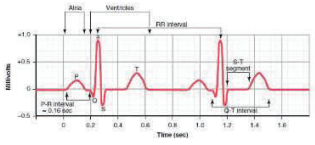


When the cardiac impulse passes through the heart, electrical current also spreads from the heart into the adjacent tissues surrounding the heart. A small portion of the current spreads all the way to the surface of the body. If electrodes are placed on the skin on opposite sides of the heart, electrical potentials generated by the current can be recorded; the recording is known as an electrocardiogram.



- The normal electrocardiogram is composed of a P wave, a QRS complex, and a T wave.
- The QRS complex is often, but not always, three separate waves: the Q wave, the R wave, and the S wave.
- The P wave is caused by electrical potentials generated when the atria depolarize before atrial contraction begins.
- The QRS complex is caused by potentials generated when the ventricles depolarize before contraction, that is, as the depolarization wave spreads through the ventricles.
- Therefore, both the P wave and the components of the QRS complex are depolarization waves.

- The T wave is caused by potentials generated as the ventricles recover from the state of depolarization. This process normally occurs in ventricular muscle 0.25 to 0.35 second after depolarization, and the T wave is known as a repolarization wave.
- Thus, the electrocardiogram is composed of both depolarization and repolarization waves.

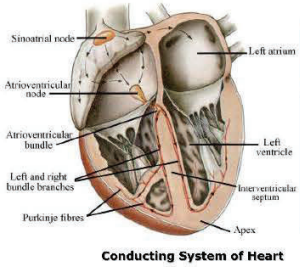


2. Anatomy of the Heart's Conduction System

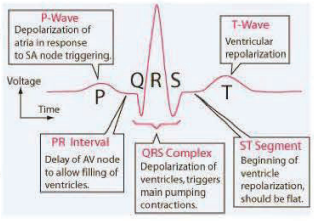
The conduction system of the heart is responsible for initiating and coordinating the contraction of the heart muscle. It consists of specialized tissues that generate and propagate electrical impulses throughout the heart. The major components include:

- Sinoatrial (SA) Node: The primary pacemaker of the heart located in the right atrium. It generates electrical impulses that initiate each heartbeat.
- Atrioventricular (AV) Node: Located at the junction of the atria and ventricles, the AV node delays the electrical signal before it passes to the ventricles, allowing time for the atria to contract and fill the ventricles with blood.
- Bundle of His: A pathway of fibers that conducts the electrical impulses from the AV node to the ventricles.
- Purkinje Fibers: Specialized fibers that rapidly transmit the electrical signal throughout the ventricles, ensuring coordinated contraction.

Anatomy of Heart and ECG signal



Conducting System of Heart



Normal ECG signal

Voltage and Time Calibration of the Electrocardiogram

- All recordings of electrocardiograms are made with appropriate calibration lines on the recording paper. Either these calibration lines are already ruled on the paper, as is the case when a pen recorder is used, or they are recorded on the paper at the same time that the electrocardiogram is recorded, which is the case with the photographic types of electrocardiographs.
- The vertical calibration lines are arranged so that 10 of the small line divisions upward or downward in the standard electrocardiogram represent 1 millivolt, with positivity in the upward direction and negativity in the downward direction.
- The horizontal lines on the electrocardiogram are time calibration lines. A typical electrocardiogram is run at a paper speed of 25 millimeters per second, although faster speeds are sometimes used. Therefore, each 25 millimeters in the horizontal direction is 1 second, and each 5-millimeter segment, indicated by the dark vertical lines, represents 0.20 second. The 0.20-second intervals are then broken into five smaller intervals by thin lines, each of which represents: 1mm = 0.04 second

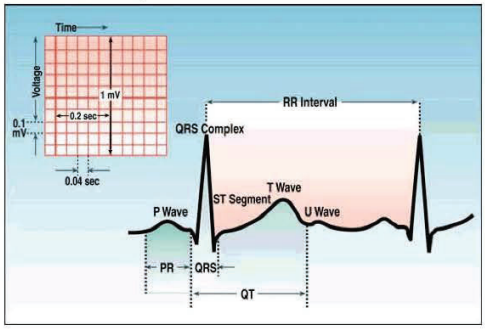
3. The ECG Waveform Components

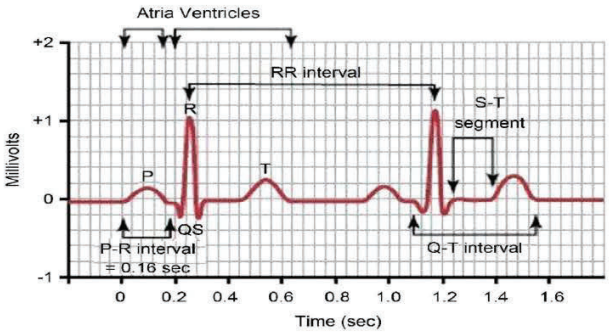
The ECG waveform represents the electrical events that occur during the cardiac cycle. Each wave corresponds to a specific phase of depolarization or repolarization of the heart muscle.

- P Wave:
  Represents atrial depolarization, which leads to atrial contraction.
- QRS Complex:
  Represents ventricular depolarization, which triggers ventricular contraction. It is the largest deflection on the ECG because the ventricles generate a stronger electrical signal than the atria.
- T Wave:
  Represents ventricular repolarization, the recovery phase after the ventricles have contracted.
- U Wave:
  Sometimes seen after the T wave, the U wave is less understood but is thought to represent late repolarization of the ventricles or the Purkinje fibers.
- Intervals and Segments:
  - PR Interval: The time between the onset of the P wave and the start of the QRS complex, representing the delay in the AV node.
  - QRS Duration: The time taken for ventricular depolarization, normally less than 120 milliseconds.
  - QT Interval: Represents the total time for ventricular depolarization and repolarization.
  - ST Segment: The period between the end of ventricular depolarization and the start of repolarization. ST elevation or depression can indicate ischemia or myocardial infarction.

Normal Voltages in the Electrocardiogram

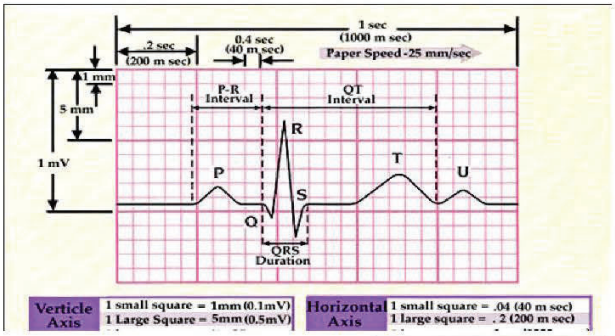
- The recorded voltages of the waves in the normal electrocardiogram depend on the manner in which the electrodes are applied to the surface of the body and how close the electrodes are to the heart. When one electrode is placed directly over the ventricles and a second electrode is placed elsewhere on the body remote from the heart, the voltage of the QRS complex may be as great as 3 to 4 millivolts. Even this voltage is small in comparison with the monophasic action potential of 110 millivolts recorded directly at the heart muscle membrane. When electrocardiograms are recorded from electrodes on the two arms or on one arm and one leg, the voltage of the QRS complex usually is 1.0 to 1.5 millivolts from the top of the R wave to the bottom of the S wave; the voltage of the P wave is between 0.1 and 0.3 millivolts; and that of the T wave is between 0.2 and 0.3 millivolts.
- P-Q or P-R Interval. The time between the beginning of the P wave and the beginning of the QRS complex is the interval between the beginning of electrical excitation of the atria and the beginning of excitation of the ventricles. This period is called the P-Q interval. The normal P-Q interval is about 0.16 second. (Often this interval is called the P-R interval because the Q wave is likely to be absent.)
- Q-T Interval. Contraction of the ventricle lasts almost from the beginning of the Q wave (or R wave, if the Q wave is absent) to the end of the T wave. This interval is called the Q-T interval and ordinarily is about 0.35 second.





Rate of Heartbeat from the Electrocardiogram

- **The rate of heartbeat can be determined easily from an electrocardiogram because the heart rate is the reciprocal of the time interval between two successive heartbeats.**
- **If the interval between two beats as determined from the time calibration lines is 1 second, the heart rate is 60 beats per minute.**
- **The normal interval between two successive QRS complexes in the adult person is about 0.83 second. This is a heart rate of 60/0.83 times per minute, or 72 beats per minute.**



- Standard electrocardiography consists of recording 12 leads.
- A lead represents the spatial relationship between the two electrode placement points and is characterized by:
  - Two potential collection points;
  - An axis of the lead, which unites the 2 points and is polarized depending on the location of the electrodes (positive or negative)
- In the frontal plane of the body were defined 6 common leads: I, II, III, aVR, aVL, aVF
- Precordial leads - unipolar leads (noted using V), the axes of these leads making a transverse plane,6 leads: V1, V2, V3, V4, V5, V6

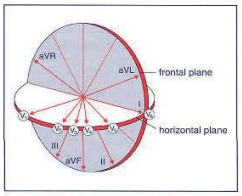


Figure 11-4 Frontal and horizontal planes.

4. Lead Placement and ECG Leads

4.1. Standard 12-Lead ECG. The 12-lead ECG provides a comprehensive view of the heart's electrical activity from different angles. The leads are categorized into:

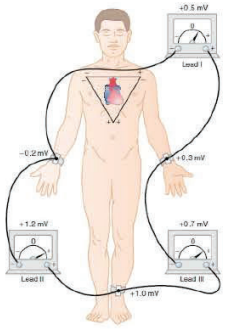
- Limb Leads: Lead I, II, III, aVR, aVL, and aVF provide views of the heart in the frontal plane.
- Precordial (Chest) Leads: V1 to V6 provide views of the heart in the horizontal plane.

Lead Placement: Limb leads are placed on the arms and legs, while precordial leads are positioned on the chest. Each lead captures electrical activity from a different part of the heart, offering a detailed assessment of its function.

I. Limb leads: I, II, III

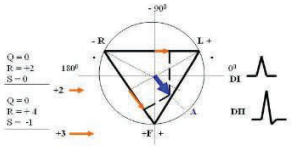
Bipolar leads, imagined by Einthoven, the electrocardiograph is recording the difference of potential between electrodes .

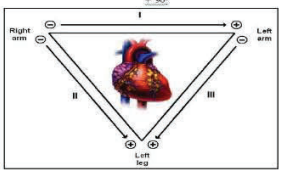
- **Lead I - the negative electrode is placed on the right arm and the positive one on the left arm + R-L**
- **Lead II - the negative electrode is placed on the right arm and the positive one on the left leg - R + F**
- **Lead III - the negative electrode is placed on the left arm and the positive one on the left leg**



Einthoven's Triangle - is drawn around the area of the heart. This illustrates that the two arms and the left leg form apices of a triangle surrounding the heart. The two apices at the upper part of the triangle represent the points at which the two arms connect electrically with the fluids around the heart, and the lower apex is the point at which the left leg connects with the fluids.

Einthoven's Law states that if the electrical potentials of any two of the three bipolar limb electrocardiographic leads are known at any given instant, the third one can be determined mathematically by simply summing the first two. Note, however, that the positive and negative signs of the different leads must be observed when making this summation.



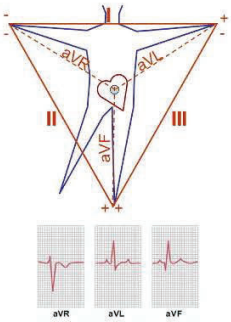


II. The unipolar leads

- These are the leads in which one electrode (the positive one) is an exploration electrode and the other electrode (indifferent) is placed in a zero potential terminal.

The leads are noted as follows:

- **aVR**: exploratory electrode on the right arm, and the indifferent one is at the foot
- **aVL**: exploratory electrode on the left arm, and the indifferent one on the foot
- **avF**: exploratory electrode at the level of the left foot, and the one indifferent at the level of the foot

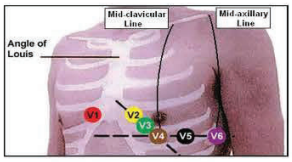


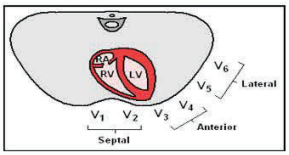
III. Precordial leads

These are unipolar leads (noted using V), the axes of these leads making a transverse plane.

The explorer electrode is applied in six points on the chest, corresponding to the 6 leads:

- **V1: the 4th intercostal space, right parasternal**
- **V2: the 4th intercostal space, left parasternal**
- **V3: the halfway distance between V2 and V4**
- **V4: the 5th intercostal space, on the medioclavicular line (heart tip)**
- **V5: the 5th intercostal space, on the anterior axillary line**
- **V6: the 5th intercostal space, on the middle axillary line**





5. Voltage and Time Calibration

Voltage Calibration: The vertical axis of the ECG paper represents voltage, where each 10 mm corresponds to 1 mV. This allows for the measurement of the amplitude of electrical signals, such as the size of the QRS complex or T wave.

Time Calibration: The horizontal axis represents time. Each small square (1 mm) equals 0.04 seconds, and each large square (5 mm) equals 0.20 seconds. This helps in determining the duration of each ECG component, such as the PR interval, QRS duration, and QT interval.

---

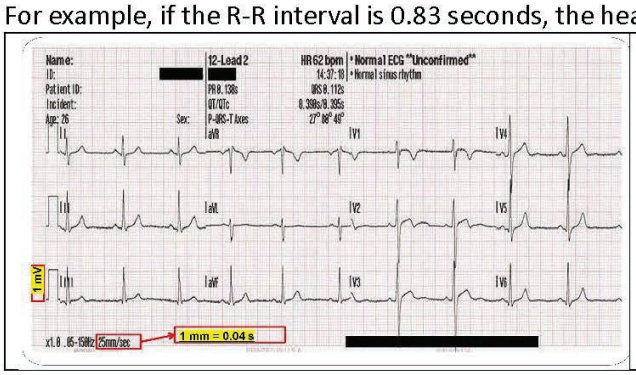
6. Rate and Rhythm Calculation

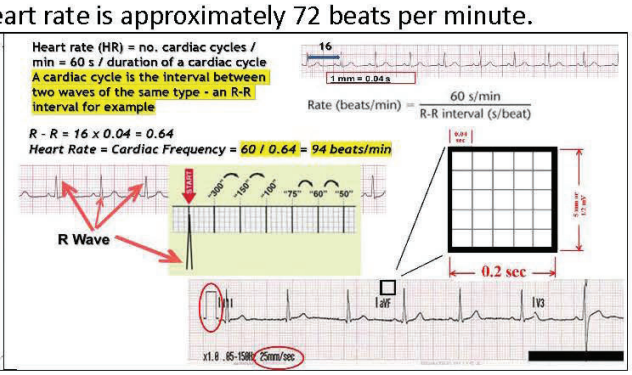
Heart Rate Determination:

$$\text{Heart Rate (beats per minute)} = \frac{60}{R - R\,\text{Interval (in seconds)}}$$

Heart rate is calculated by measuring the R-R interval (the distance between two successive R waves). The formula for heart rate is:

For example, if the R-R interval is 0.83 seconds, the heart rate is approximately 72 beats per minute.





Rhythm Analysis:

Rhythm is assessed by examining the consistency of the ECG waveforms:

- Check for the presence of P waves before each QRS complex.
- Measure the PR interval to determine whether the rhythm is sinus (normal) or irregular.
- Regularity of the R-R interval is also evaluated to identify any arrhythmias.

7. ECG Interpretation and Analysis

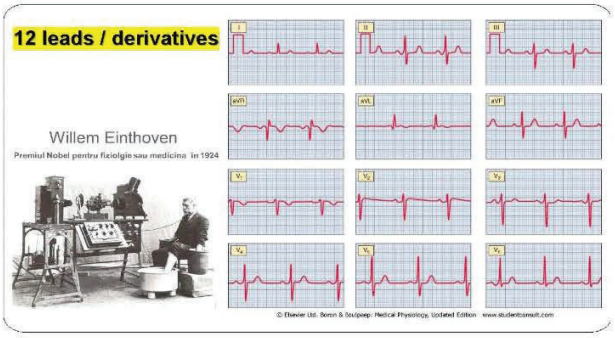
7.1. Steps in ECG Interpretation

A systematic approach is used to interpret the ECG and identify potential abnormalities:

1. Check Calibration:
   Ensure that 1 mV = 10 mm on the ECG paper for proper voltage calibration.
2. Determine Heart Rate and Rhythm:
   Evaluate the R-R intervals for consistency and regularity. Calculate the heart rate based on the R-R interval.
3. Analyze the P, QRS, and T Waves:
   Examine the shape, duration, and amplitude of each wave. For instance, a prolonged QRS complex could indicate ventricular hypertrophy or a bundle branch block.
4. Examine Intervals and Segments:
   Measure the PR interval, QRS duration, and QT interval to ensure they fall within normal ranges. Abnormal intervals may indicate conduction delays or electrolyte imbalances. The ST segment should be assessed for any elevation or depression, which can be a sign of myocardial ischemia or infarction.

7.2. Clinical Interpretation

- Arrhythmias: Arrhythmias are disturbances in the heart's rhythm and can range from benign to life-threatening. Examples include atrial fibrillation (irregular rhythm with no discernible P waves) and ventricular tachycardia (rapid, life-threatening rhythm originating in the ventricles).
- Ischemia and Infarction: ST segment depression or T wave inversion can suggest ischemia, while ST segment elevation may indicate an acute myocardial infarction.
- Hypertrophy and Dilation: Enlarged heart chambers can alter the amplitude and duration of the ECG waves. Left ventricular hypertrophy often results in a taller R wave, while atrial enlargement can cause an abnormally large P wave.



Electrocardiography analysis

1. Checking the recording technique
- the amplification used (check the standard signal so that 1 mV = 1 cm);
- the electrodes should not be reversed;
- It is checked if the largest waves in amplitude have not been amputated by the limits of the registration;

2. Position
- Usually, after recording the electrocardiogram, the recorded derivations, the name and the age of the patient are noted, which implicitly shows the "position" of the ECG;
- If these notations are missing, the position of the standard signal, which is always positive and placed at the left end of the path, will be taken into account;
- If this is also missing, the relations between the P and T waves with respect to the QRS complex are taken into account:
  - QRS is a large and multi-phase complex;
  - P is a small wave (below 2 mm) before QRS (left);
  - T is a larger and wider wave than P, located after QRS (right).

Electrocardiography analysis

3. Appreciation of the basic rhythm of the heart

The normal sinus rhythm of the heart is recognized according to the following criteria:
- There are P-waves in all cardiac revolutions and in all recorded derivatives;
- P waves are located in front of the QRS complex;
- P waves have normal vector duration, amplitude and orientation;
- P waves have a constant form in all revolutions of the same lead;
- The P-Q interval (between the beginning of the P wave and the beginning of the QRS complex) is constant in all leads and revolutions;
- The P-Q range is within normal duration limits: 0.12"-0.21".

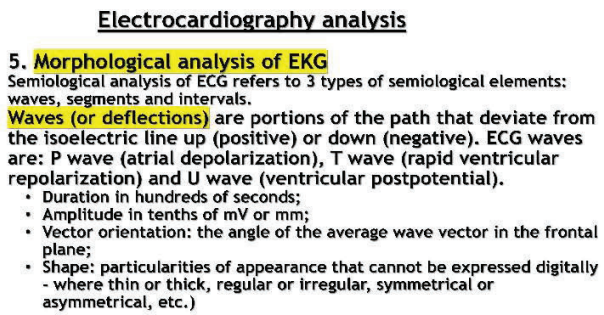
Electrocardiography analysis

4. Heart rate calculation

i.Direct method using calculation rules. The rulers have a common principle of use:
- A mark is set on the ruler next to a mark chosen from the read path: the tip of a wave (P, R, S) or the beginning of a wave (P, QRS etc.)
- The heart rate is read after 2, 3 or 4 cardiac revolutions against a landmark of the same type as the one previously fixed (the rulers are calculated for 2,3 or 4 cardiac cycles)
- There are calculation rules for the paper roll speed of 25 mm/s.

ii.Indirect methods
- The number of intervals of 0.20 s (marked by thicker lines on the route) between two QRS complexes:

* one interval fr-300 / min ** two intervals fr-150 / min, *** three intervals-100 / min, **** four intervals fr-75 / min, ***** five intervals fr-60 / min, ****** six intervals fr-50 / min
- The number of QRS complexes in a range of 6 sec: for example, if within the 6 s interval there are 8 QRS complexes and approximately another half interval, the frequency will be about 85 / min.



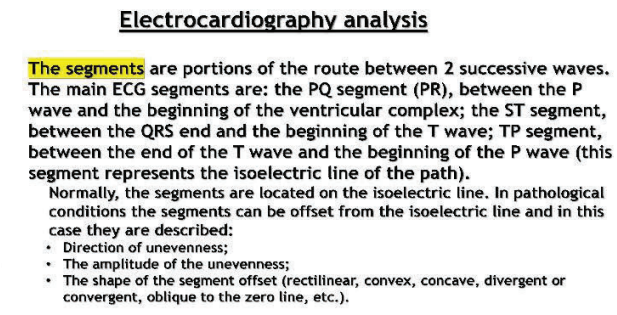
Electrocardiography analysis

5. Morphological analysis of EKG

Semiological analysis of ECG refers to 3 types of semiological elements: waves, segments and intervals.

Waves (or deflections) are portions of the path that deviate from the isoelectric line up (positive) or down (negative). ECG waves are: P wave (atrial depolarization), T wave (rapid ventricular repolarization) and U wave (ventricular postpotential).

- Duration in hundreds of seconds;
- Amplitude in tenths of mV or mm;
- Vector orientation: the angle of the average wave vector in the frontal plane;
- Shape: particularities of appearance that cannot be expressed digitally - where thin or thick, regular or irregular, symmetrical or asymmetrical, etc.)

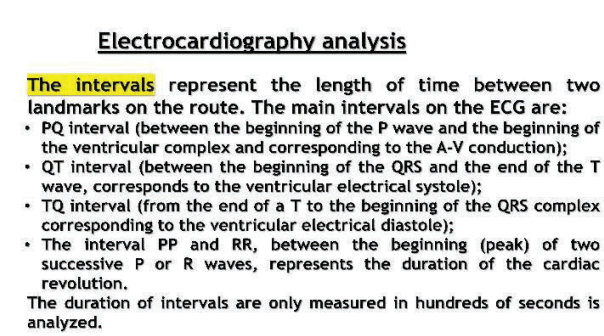


Electrocardiography analysis

The segments are portions of the route between 2 successive waves. The main ECG segments are: the PQ segment (PR), between the P wave and the beginning of the ventricular complex; the ST segment, between the QRS end and the beginning of the T wave; TP segment, between the end of the T wave and the beginning of the P wave (this segment represents the isoelectric line of the path).

Normally, the segments are located on the isoelectric line. In pathological conditions the segments can be offset from the isoelectric line and in this case they are described:

- Direction of unevenness;
- The amplitude of the unevenness;
- The shape of the segment offset (rectilinear, convex, concave, divergent or convergent, oblique to the zero line, etc.).

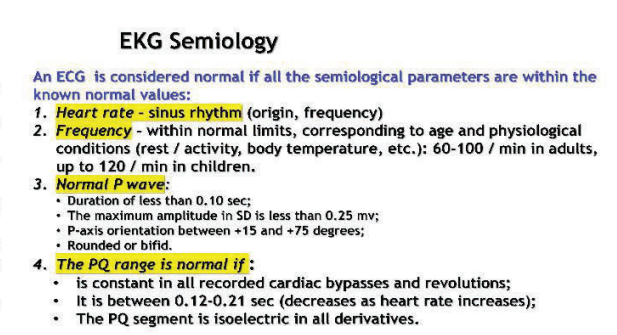


Electrocardiography analysis

The intervals represent the length of time between two landmarks on the route. The main intervals on the ECG are:

- PQ interval (between the beginning of the P wave and the beginning of the ventricular complex and corresponding to the A-V conduction);
- QT interval (between the beginning of the QRS and the end of the T wave, corresponds to the ventricular electrical systole);
- TQ interval (from the end of a T to the beginning of the QRS complex corresponding to the ventricular electrical diastole);
- The interval PP and RR, between the beginning (peak) of two successive P or R waves, represents the duration of the cardiac revolution.

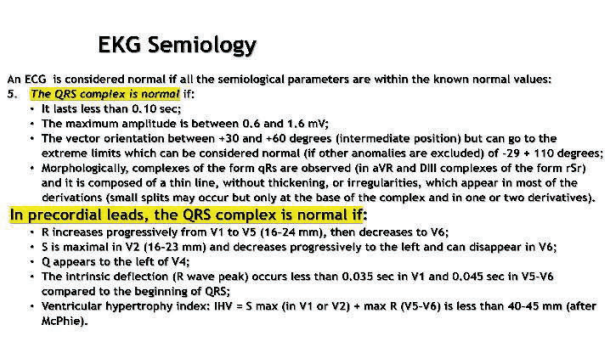
The duration of intervals are only measured in hundreds of seconds is analyzed.



EKG Semiology

An ECG is considered normal if all the semiological parameters are within the known normal values:

1. ***Heart rate*** - sinus rhythm (origin, frequency)
2. ***Frequency*** - within normal limits, corresponding to age and physiological conditions (rest / activity, body temperature, etc.): 60-100 / min in adults, up to 120 / min in children.
3. ***Normal P wave***:
   - Duration of less than 0.10 sec;
   - The maximum amplitude in SD is less than 0.25 mv;
   - P-axis orientation between +15 and +75 degrees;
   - Rounded or bifid.
4. ***The PQ range is normal if*** :
   - is constant in all recorded cardiac bypasses and revolutions;
   - It is between 0.12-0.21 sec (decreases as heart rate increases);
   - The PQ segment is isoelectric in all derivatives.



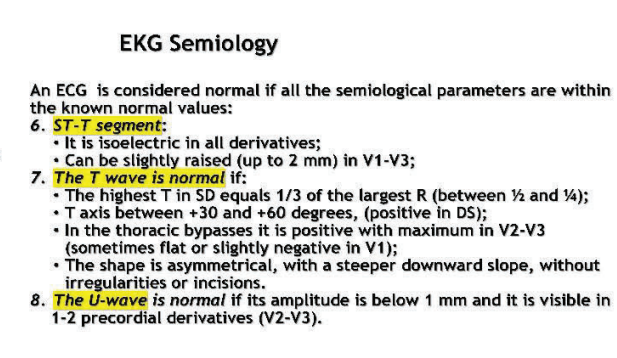
EKG Semiology

An ECG is considered normal if all the semiological parameters are within the known normal values:

5. ***The QRS complex is normal*** if:
   - It lasts less than 0.10 sec;
   - The maximum amplitude is between 0.6 and 1.6 mV;
   - The vector orientation between +30 and +60 degrees (intermediate position) but can go to the extreme limits which can be considered normal (if other anomalies are excluded) of -29 + 110 degrees;
   - Morphologically, complexes of the form qRs are observed (in aVR and DIII complexes of the form rSr) and it is composed of a thin line, without thickening, or irregularities, which appear in most of the derivations (small splits may occur but only at the base of the complex and in one or two derivatives).

In precordial leads, the QRS complex is normal if:

- R increases progressively from V1 to V5 (16-24 mm), then decreases to V6;
- S is maximal in V2 (16-23 mm) and decreases progressively to the left and can disappear in V6;
- Q appears to the left of V4;
- The intrinsic deflection (R wave peak) occurs less than 0.035 sec in V1 and 0.045 sec in V5-V6 compared to the beginning of QRS;
- Ventricular hypertrophy index: IHV = S max (in V1 or V2) + max R (V5-V6) is less than 40-45 mm (after McPhie).



EKG Semiology

An ECG is considered normal if all the semiological parameters are within the known normal values:

6. ***ST-T segment***:
   - It is isoelectric in all derivatives;
   - Can be slightly raised (up to 2 mm) in V1-V3;
7. ***The T wave is normal*** if:
   - The highest T in SD equals 1/3 of the largest R (between ½ and ¼);
   - T axis between +30 and +60 degrees, (positive in DS);
   - In the thoracic bypasses it is positive with maximum in V2-V3 (sometimes flat or slightly negative in V1);
   - The shape is asymmetrical, with a steeper downward slope, without irregularities or incisions.
8. ***The U-wave is normal*** if its amplitude is below 1 mm and it is visible in 1-2 precordial derivatives (V2-V3).

8. Practical Experiments and Demonstrations

8.1. Recording of ECG

Students will perform ECG recordings on themselves or peers, learning how to place electrodes properly, capture the heart's electrical activity, and interpret the waveforms.

8.2. Analysis of Heart Rate and Rhythm

Students will calculate the heart rate and assess rhythm regularity by measuring the R-R intervals and analyzing the P, QRS complexes, and T waves.

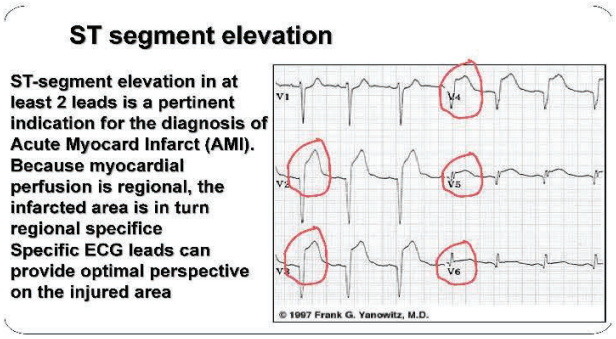
8.3. Interpretation of ECG Findings

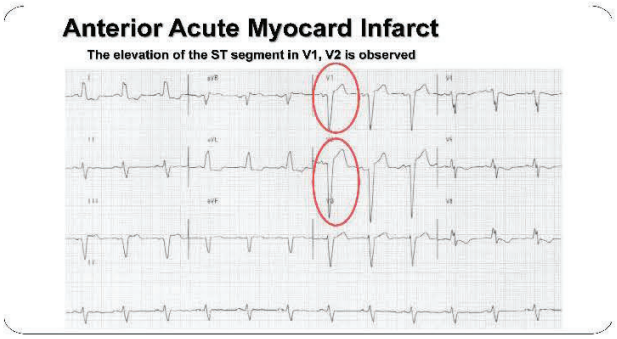
Students will interpret pre-recorded ECGs to identify common abnormalities such as arrhythmias, ischemia, and hypertrophy. This hands-on practice will enhance their ability to detect and analyze key patterns in the ECG waveform.

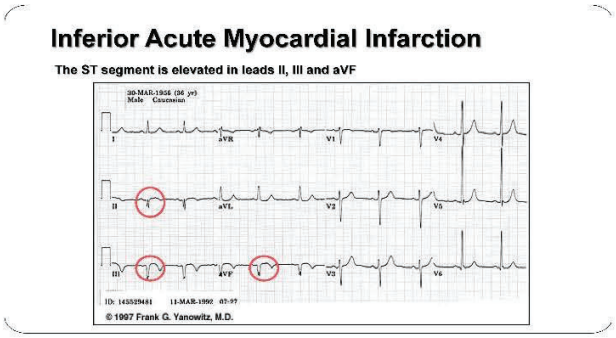
9. Clinical Relevance

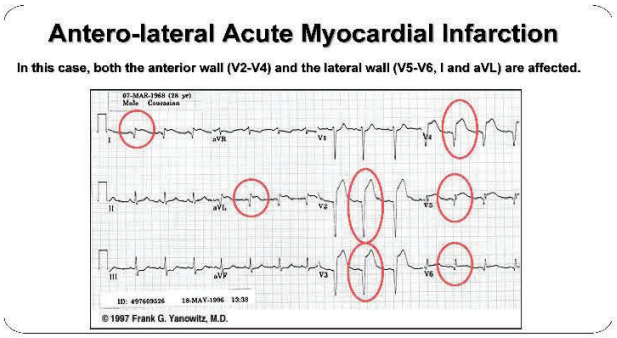
- Arrhythmias:
  Early detection and treatment of arrhythmias are critical in preventing complications such as stroke, heart failure, or sudden cardiac arrest. Conditions like atrial fibrillation or ventricular tachycardia may require medical or electrical intervention.
- Ischemia and Infarction:
  ECG is the primary tool for diagnosing myocardial ischemia and infarction. Prompt recognition of ST segment elevation myocardial infarction (STEMI) allows for rapid intervention, reducing the risk of heart muscle damage and improving patient outcomes.

- Hypertrophy and Dilation:
  Changes in the size of the heart chambers, such as left ventricular hypertrophy due to chronic hypertension, can be identified on the ECG and prompt further investigation or treatment to prevent heart failure.





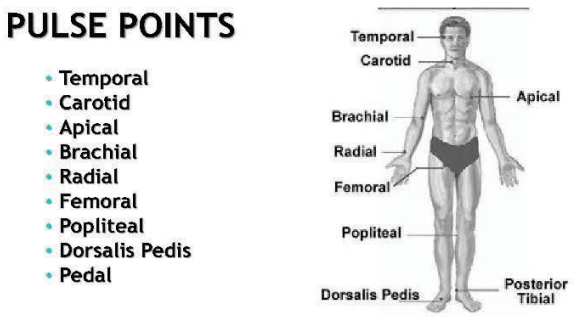


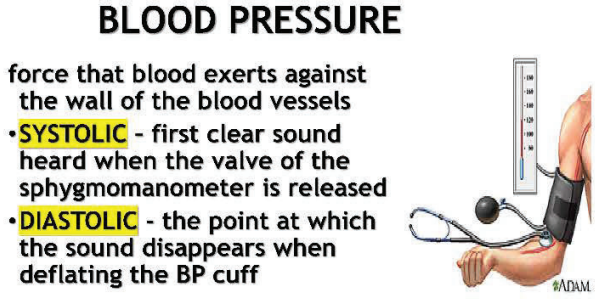


10. Blood Pressure and Pulse

10.1. Blood Pressure

- Definition:
  Blood pressure is the force exerted by circulating blood on the walls of the arteries. It is expressed as two numbers: systolic pressure (pressure during heart contraction) over diastolic pressure (pressure during heart relaxation). Normal blood pressure is around 120/80 mm Hg.
- Factors Influencing Blood Pressure:
  - Cardiac Output: The amount of blood the heart pumps per minute. Higher output increases blood pressure.
  - Peripheral Resistance: The resistance to blood flow in the arteries. Narrow or stiff arteries increase resistance, leading to higher blood pressure.
  - Blood Volume: A higher blood volume increases pressure on the arterial walls.
  - Hormonal and Neural Control: Hormones like adrenaline and the autonomic nervous system play a role in regulating blood pressure.





INTRODUCTION

The circulatory system consists of the heart, the central organ that pumps blood - and a closed system of vessels, consisting of arteries - capillaries - veins.

The heart is, from an anatomical point of view, a muscular, cavity organ that rhythmically pumps blood into the body. Structurally, it is a striated muscle, with common functional properties and other tissues, but also with specific properties. Blood propulsion is provided by the ventricular contraction, the most important being the left ventricle; the blood is pushed at each contraction, but flows in DC, due to the elasticity of the arterial walls.

Blood pressure / blood tension

Blood pressure is one of the obligatory investigations of any patient.

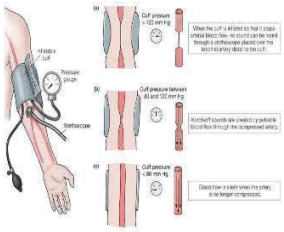
Blood pressure measurement can be done through

- direct method
- indirect methods

BP determination technique:

Apply the pneumatic sleeve to the arm.
The pulse is felt at the level of the radial artery.
The air is pumped with the rubber valve with the valve closed until the pulse is heard at the radial artery.
Then slowly open the valve.

The palpatory method measures only the systolic pressure, by perceiving the first pulse of the radial artery at the progressive decompression of the cuff applied around the forearm.
The appearance of the first pulse is perceived by the palpation of the artery downstream of the model



Normal values

- ✓ The maximum / systolic pressure in the large and medium arteries in adults is 120-140 mmHg
- ✓ Normal value can be calculated according to the formula; TA max = 100 + age in years, without exceeding 160 mmHg in persons over 60 years
- ✓ The minimum / diastolic pressure in the large and medium arteries in adults is 60-90 mmHg
- ✓ Normal value can be calculated according to the formula;
- ✓ TA max = 10 + TAmax / 2
- ✓ In adults as a normal upper limit of diastolic pressure, 90 mmHg is allowed in women and 95 mmHg in men, or 100 mmHg after 60 years, regardless of sex.

Blood pressure

It represents the value of blood pressure on the arterial walls and is determined by three factors

- Cardiac factor - cardiac output depending on the degree or force of contraction, frequency and venous return;
- Vascular factor - the condition of the arterial walls and the peripheral resistance;
- Blood factor - viscosity and blood mass

The walls of the arteries are resistant, which causes the blood to be under a certain tension, called blood pressure (TA).

TA varies by age, sex, time of day and degree of activity. High values represent hypertension, and low values - hypotension.

Normal values:
In children and young people: 90 - 110 / 60 - 70 mmHg;
Adult: 120 - 130 / 70 - 80 mm Hg.



HOLTER BP

It is a method used in patients suspected of high blood pressure - for confirmation of diagnosis.

Apply the pneumatic sleeve to the arm with the stethoscope at the elbow envelope. The patient returns to the doctor after 24 hours, during which time he is instructed to perform his daily activity.

As a result, a table with blood pressure values of 24 hours will be printed.

Normal range of arterial pressure

Age	Systolic		Diastolic		Age	Systolic		Diastolic	
	Men	Women	Men	Women		Men	Women	Men	Women
1 day	70				16 years	118	116	73	72
3 days	72				17 years	121	116	74	72
9 days	73				18 years	120	116	74	72
3 weeks	77				19 years	122	116	75	71
3 months	86				20–24 years	123	116	76	72
6–12 months	89	93	60	62	25–29 years	126	117	78	74
1 year	96	95	66	65	30–34 years	126	120	79	75
2 years	99	92	64	60	35–39 years	127	124	80	78
3 years	100	100	67	64	40–44 years	129	127	81	80
4 years	99	99	65	66	45–49 years	130	131	82	82
5 years	92	92	62	62	50–54 years	135	137	83	84
6 years	94	94	64	64	55–59 years	138	139	84	84
7 years	97	97	65	66	60–64 years	142	144	85	85
8 years	100	100	67	68	65–69 years	143	154	83	85
9 years	101	101	68	69	70–74 years	145	159	82	85
10 years	103	103	69	70	75–79 years	146	158	81	84
11 years	104	104	70	71	80–84 years	146	157	82	83
12 years	105	106	71	72	85–89 years	145	154	79	82
13 years	108	108	72	73	90–94 years	145	150	78	79
14 years	110	110	73	74	95–106 years	146	149	78	81
15 years	112	112	75	76					

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10.2. Pulse

- Definition:
  The pulse is the palpable beat of the heart, felt in arteries where blood pressure waves pass through. It reflects the heart's rate and rhythm.
- Pulse Points:
  The pulse can be felt at various locations, including the radial artery (wrist), carotid artery (neck), femoral artery (groin), and dorsalis pedis (foot).

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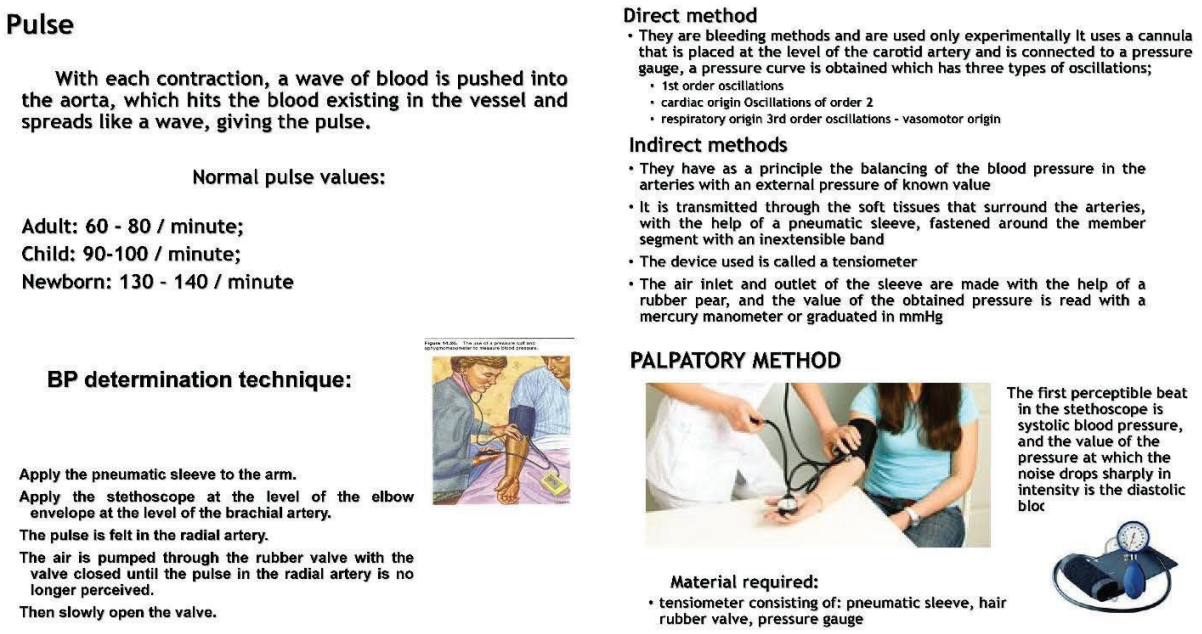
11. Practical Experiments and Demonstrations
11.1. Measurement of Blood Pressure

- Auscultatory Method:
  Blood pressure is measured using a sphygmomanometer and a stethoscope. The cuff is inflated to restrict blood flow, and as it deflates, the systolic and diastolic pressures are determined by listening to Korotkoff sounds. The first sound indicates systolic pressure, and the disappearance of the sound marks diastolic pressure.

11.2. Pulse Rate and Quality

- Measurement of Pulse Rate:
  Students will measure their pulse rate at rest and after physical activity. This demonstrates how the cardiovascular system adapts to exercise by increasing heart rate and stroke volume to meet the increased oxygen demand of muscles.



12. Clinical Relevance

- Hypertension: Chronic high blood pressure can lead to damage in blood vessels, increasing the risk of heart attack, stroke, and kidney disease. Managing blood pressure is crucial for preventing cardiovascular complications.
- Arrhythmias: Abnormal heart rhythms can result from issues with the heart's electrical system. Arrhythmias can range from benign (e.g., occasional premature beats) to life-threatening (e.g., ventricular fibrillation).
- Heart Failure: Heart failure occurs when the heart is unable to pump blood effectively, leading to symptoms like shortness of breath, fatigue, and fluid retention. It can result from damage to the myocardium due to hypertension, coronary artery disease, or myocardial infarction.

Course 6: Regulation of the Cardiovascular System
Sub-topic: Neural, Hormonal, and Local Mechanisms

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1. Overview of Cardiovascular Regulation
- Purpose of Regulation

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2. Neural Regulation of the Cardiovascular System
2.1. Cardiac Innervation
- Sympathetic Innervation
- Parasympathetic Innervation (Vagal Tone)

2.2. Innervation of Blood Vessels
- Sympathetic Vasoconstrictor Fibers
- Sympathetic Vasodilator Fibers
- Parasympathetic Fibers to Blood Vessels:
  - These fibers primarily innervate vessels in specific regions like the brain, liver, and salivary glands, influencing blood flow in these organs during special situations.

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3. Hormonal Regulation of the Cardiovascular System
3.1. Epinephrine and Norepinephrine
3.2. Angiotensin II
3.3. Vasopressin (Antidiuretic Hormone, ADH)
3.4. Nitric Oxide (NO)

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4. Reflex Regulation of Circulation
4.1. Baroreceptor Reflex
4.2. Chemoreceptor Reflex
4.3. CNS Ischemic Response

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5. Local Regulation of Blood Flow
5.1. Autoregulation
5.2. Endothelial Factors

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6. Cardiovascular Centers in the Brain
6.1. Medulla Oblongata
6.2. Higher Brain Centers

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7. Practical Applications and Clinical Implications
7.1. Hypertension
7.2. Heart Failure
7.3. Shock

Examination and Assessment

Course 6: Regulation of the Cardiovascular System
Sub-topic: Neural, Hormonal, and Local Mechanisms

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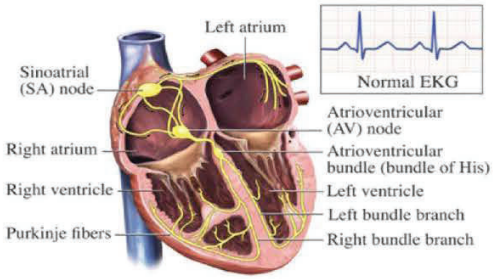
1. Overview of Cardiovascular Regulation

Cardiovascular regulation is essential for maintaining adequate tissue perfusion and ensuring that blood pressure remains within an optimal range to meet the body's metabolic demands. It involves a complex interaction of neural, hormonal, and local mechanisms that adapt to both short-term and long-term changes in the body's physiological state.

- Purpose of Regulation:
  - Maintaining Blood Pressure: Ensuring that mean arterial pressure (MAP) remains sufficient to perfuse all organs, especially the brain and heart.
  - Cardiac Output Adjustment: Regulation of heart rate and stroke volume to ensure adequate blood flow during varying physiological states, such as rest, exercise, and stress.
  - Vascular Resistance Control: Adjusting the tone of arterioles to control blood flow distribution across different organs depending on metabolic needs.
  - Blood Volume Regulation: Control of fluid balance to maintain venous return, preload, and cardiac output, ensuring stable perfusion.

Cardiac Cycle

- **Cardiac Cycle: Each complete heartbeat consisting of systole and diastole of both atria plus systole and diastole of both ventricles.**
- **Systole: The contraction of the heart muscle, especially the ventricle**
- **Diastole: The relaxation of the heart muscle.**



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2. Neural Regulation of the Cardiovascular System

Neural regulation is primarily mediated by the autonomic nervous system (ANS), which has two components: the sympathetic and parasympathetic systems. These systems influence heart rate, contractility, and the diameter of blood vessels, allowing for rapid adjustments in response to physiological stimuli such as changes in blood pressure, blood volume, and activity level.

2.1. Cardiac Innervation

The heart is innervated by both sympathetic and parasympathetic fibers that regulate its activity:

- Sympathetic Innervation:
  - Sympathetic nerves release norepinephrine, which binds to beta-1 adrenergic receptors on the heart, leading to:
    - Increased heart rate (positive chronotropy): By increasing the firing rate of the sinoatrial (SA) node.
    - Enhanced contractility (positive inotropy): By increasing calcium influx into cardiac muscle cells, leading to more forceful contractions.
    - Increased conduction velocity (positive dromotropy): By accelerating the speed of action potential propagation through the atrioventricular (AV) node and the His-Purkinje system.
  - Sympathetic activation is crucial during exercise, stress, or emergencies (fight-or-flight responses), where enhanced cardiac output is required to supply working muscles with oxygen and nutrients.
- Parasympathetic Innervation (Vagal Tone):

- The vagus nerve (cranial nerve X) provides parasympathetic innervation to the heart, primarily affecting the SA node and AV node by releasing acetylcholine.
- Acetylcholine binds to muscarinic receptors (M2), leading to:
  - Decreased heart rate (negative chronotropy): Parasympathetic activity reduces the firing rate of the SA node.
  - Reduced conduction velocity (negative dromotropy): Slowing of the AV node conduction.
- At rest, parasympathetic (vagal) tone predominates, keeping the heart rate lower than the intrinsic pacemaker rate of the SA node (~100 beats per minute). Vagal tone can lower the resting heart rate to as low as 60-70 beats per minute in healthy individuals.

Regulation of the Heart

- **Intrinsic Regulation**
  - Modifies stroke volume (SV) through the functional characteristics of cardiac muscle cells
  - According to Starling's law of the heart, a critical factor controlling the SV is how much the cardiac cells are stretched just before they contract. The important factor stretching the heart muscle is the *venous return*.
    - Anything that will increase the venous return will increase the SV. (ex. a slow heart beat allows more time for the ventricles to fill)

- Parasympathetic stimulation is supplied by the vagus nerve
  - Decreases heart rate.
  - Giving more time heart to rest during noncrisis time
  - Postganglionic neurons secrete acetylcholine, which increases membrane permeability to K^+.
- Sympathetic stimulation is supplied by the cardiac nerves
  - Increases heart rate and the force of contraction (stroke volume)
  - Postganglionic neurons secrete norepinephrine, which increases membrane permeability to Ca^{2+}.
  - More oxygen and glucose are made available to the cells during stress.

- **Extrinsic Regulation**
  - Modifies heart rate and stroke volume through nervous and hormonal mechanisms
    - The cardioregulatory center in the medulla oblongata regulates the parasympathetic and sympathetic nervous control of the heart
    - Epinephrine and norepinephrine are released into the blood from the adrenal medulla as a result of sympathetic stimulation. They increase the rate and force of heart contraction

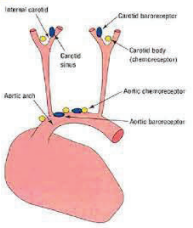
- Various hormones and ions have a dramatic effect on heart activity
- Epinephrine and thyroxin mimic the effect of the sympathetic nerves and increase the heart rate.
- Age, gender, and exercise influence the heart rate.
  - Resting heart rate is fastest in the fetus (140-160 bpm)
  - Average heart rate is faster in females (72-80 bpm) than in males (64-72 bpm).

Effect of Ions and Body Temperature

- A deficit of potassium ion K+ in the blood, causes the heart to beat feebly, and abnormal heart rhythms appear.
- Reduced level of Ca2+ in the blood depressed the heart, whereas hypercalcemia causes such as prolonged contractions that the heart may stop entirely.
- Heart rate increases when body temperature increases, and it decreases when body temperature decreases

The Heart and Homeostasis

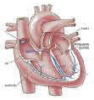
- Effect of pH, Carbon Dioxide, and Oxygen
  - Carotid body and aortic chemoreceptor receptors monitor blood oxygen levels
  - Chemoreceptors monitor blood pH and carbon dioxide levels
  - Chemoreceptors are not important for the normal regulation of the heart, but are important in the regulation of respiration and blood vessel constriction



Effect of Blood Pressure

- Baroreceptors monitor blood pressure and the cardio-regulatory center modifies heart rate and stroke volume
- In response to a decrease in blood pressure, the baroreceptor reflexes increase heart rate and stroke volume
- When blood pressure increases, the baroreceptor reflexes decrease heart rate and stroke volume

- Sinoatrial Node (SAN) myocytes set the rhythm and rate of cardiac chamber contraction.



- "Pacemaker" cells generate repetitive action potentials at a constantly controlled rate by their inherited property of their membrane : spontaneous Na+ leak generating the prepotential or pace maker potential

- This prepotential propagates in the conducting system of the heart causing the contractile cardiac fibers to depolarise to generate the action potential with plateau

2.2. Innervation of Blood Vessels

Most blood vessels are innervated primarily by sympathetic fibers, with limited parasympathetic input. Neural control of vascular tone is critical for regulating peripheral resistance and blood pressure.

- Sympathetic Vasoconstrictor Fibers:
  - These fibers release norepinephrine, which binds to alpha-1 adrenergic receptors on vascular smooth muscle cells, causing vasoconstriction. This results in:
    - Increased systemic vascular resistance (SVR), contributing to higher blood pressure.
    - Vasoconstriction is particularly important in non-essential organs (skin, kidneys, gastrointestinal tract) during states of sympathetic activation, allowing more blood to be directed to vital organs like the brain, heart, and skeletal muscles during exercise or stress.
- Sympathetic Vasodilator Fibers:
  - Sympathetic vasodilation occurs primarily in skeletal muscle and coronary vessels, where beta-2 adrenergic receptors mediate vasodilation in response to norepinephrine or epinephrine, particularly during exercise. This ensures adequate blood supply to active muscles.
  - Additionally, local metabolites produced by exercising muscles (e.g., lactic acid, CO_2, and H^+) further enhance vasodilation, overriding sympathetic vasoconstriction.
- Parasympathetic Fibers to Blood Vessels:
  - Parasympathetic innervation of blood vessels is rare but does exist in specialized regions, such as the cerebral vasculature, salivary glands, and genital organs. These fibers promote vasodilation, primarily through the release of nitric oxide (NO) from endothelial cells in response to acetylcholine.

Regulation of the blood flow of organs to fit their metabolic requirement in different conditions.

- **The regulation of blood flow is of three major types:**
  - **Neural**
  - **Humoral**
  - **Local**

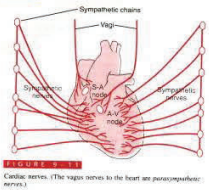
I. Neural Regulation of the Circulation

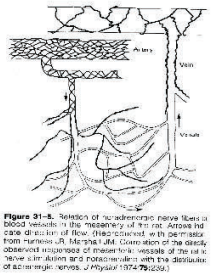
1. Innervation of the Circulatory System

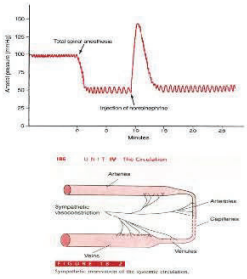
- **Cardiac innervation**
- **Innervation of blood vessels**
  - **Sympathetic vasoconstrictor fiber**
  - **Sympathetic vasodilator fiber**
  - **Parasympathetic nerve fiber to peripheral vessels**

Cardiac innervation

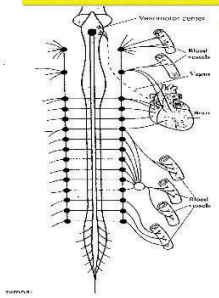
- **Sympathetic nerve - noradrenergic fiber**
  - **increase the cardiac rate (positive chronotropic effect)**
  - **Increase the force of cardiac contraction (positive inotropic effect).**
- **Parasympathetic nerve - cholinergic fiber**
  - **Cholinergic vagal cardiac fibers decrease the heart rate.**
- **At rest**
  - **moderate amount of tonic discharge in the cardiac sympathetic nerves**
  - **a good deal of tonic vagal discharge (vagal tone)**
    - **When the vagi are cut in experiment animals, the heart rate rises**







Innervation of blood vessels



- **Sympathetic vasoconstrictor fiber**
  - **Distribution: Almost all segments of the circulation.**
  - **The innervation is powerful in the kidneys, gut, spleen and skin,**
    - **is less potent in both skeletal and cardiac muscle and in the brain.**
  - **Almost all vessels, such as arteries, arterioles, venules and veins are innervated,**
    - **except the capillaries, precapillary sphincters and most of the metarterioles.**
  - **Tone: Usually the sympathetic vasoconstrictor fibers keep tonic.**

Innervation of blood vessels

- **2) Sympathetic vasodilator fiber**
  - **The sympathetic nerves to skeletal muscles carry sympathetic vasodilator fibers as well as constrictor fibers.**
  - **release acetylcholine at their endings and cause vasodilation.**
  - **Importance: increase the blood flow in skeletal muscle during exercise and stress.**

Innervation of blood vessels

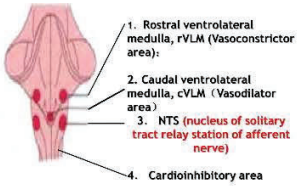
- 3) Parasympathetic nerve fiber to peripheral vessels
  - Parasympathetic nerve fibers innervate vessels of the blood vessels in
    - Meninges
    - the salivary glands
    - the liver
    - the viscera in pelvis
    - the external genitals
  - Importance: Regulate the blood flow of these organs in some special situations.

Cardiovascular centers of the brainstem

- Medulla oblongata is essential to Cardiovascular centers.

Cardiovascular centers of the brainstem

- vasoconstrictor-area
- vasodilator area
- cardioinhibitory area
- relay station of afferent nerve



3. Reflex Regulation of the Circulation

- Baroreceptor reflexes
- Reflex involving arterial chemoreceptors
- CNS ischemic response

Carotid sinus

- At the bifurcation of the common carotid arteries
  - the root of internal carotid artery shows a little bulge
- has stretch receptors in the adventitia
- are sensitive to arterial pressure fluctuations
- Afferent nerves travel in the carotid sinus nerve
  - a branch of the glossopharyngeal nerve. (IXth cranial nerve)

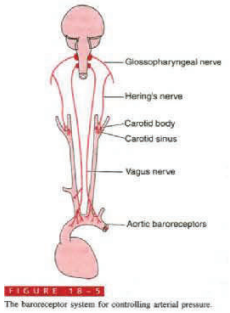
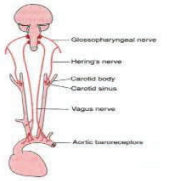
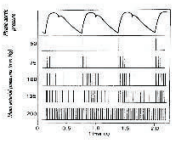


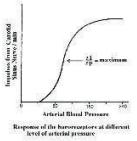
FIGURE 18-5
The baroreceptor system for controlling arterial pressure.

2) buffer nerves

- Buffer nerves
  - The carotid sinus nerves and vagal fibers from the aortic arch
- At normal blood pressure levels, the fibers discharge at a low rate.
  - When the pressure rises, the discharge rate increases
  - when the pressure falls, the rate declines





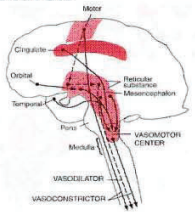


Response of the baroreceptors at different level of arterial pressure

- At 0 - 60 mmHg, no sensitive (aortic baroreceptors, 0-30mmHg).
- Between 60 to 80 mmHg: respond progressively more and more strongly.
- At 100 mmHg: The response is the greatest
- Above 180 mmHg: no further increase in response .

2 Cardiovascular Center

- The control center of cardiovascular activities is the nucleus groups at different levels
  - spinal cord
  - brain stem
  - hypothalamus
  - limbic system
  - cerebral cortex
  - cerebellum

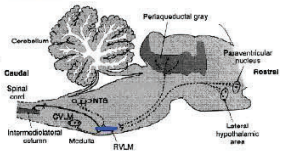


1). vasoconstrictor-area (rVLM) (neurotransmitter: NE neurons)
(l) the cardiac sympathetic center
(2) the sympathetic vasoconstrictor center

2). vasodilator area (cVLM) (NE neurons)
to inhibit action of rVLM area → vasodilation

3). cardioinhibitory area
(dorsal vagal nucleus and nucleus ambigulus) the cardial vagus center

4). relay station of afferent nerve
NTS (nucleu of solitary tract) to accept and integrate afferent impulses and then affect other centers



(1) Baroreceptor reflexes

- 1) Physiological anatomy of the baroreceptors.

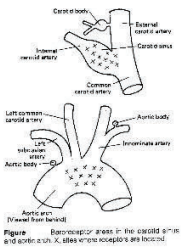
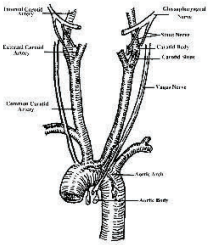


Figure Baroreceptor areas in the carotid sinus and aortic arch. X, sites where receptors are located.



Aortic arch

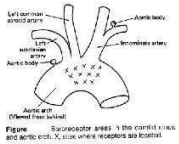
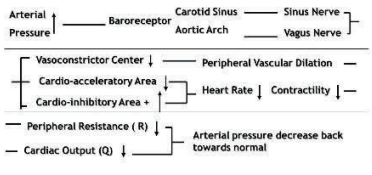


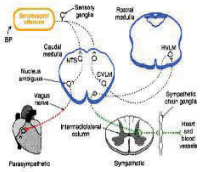
Figure Baroreceptor areas in the carotid sinus and aortic arch. X, sites where receptors are located.

- baroreceptors
  - in the adventitia of the arch of aorta
- Function
  - similar to the carotid sinus receptors.
- afferent nerve fibers travel in the aortic nerve,
  - a branch of the vagus nerve. (Xth cranial nerve)

4) Concept and mechanism of baroreceptor reflex

- Any drop in systemic arterial pressure decreases the discharge in the buffer nerves,
  - there is a compensatory rise in blood pressure and cardiac output.





(5) Importance of the baroreceptor reflex

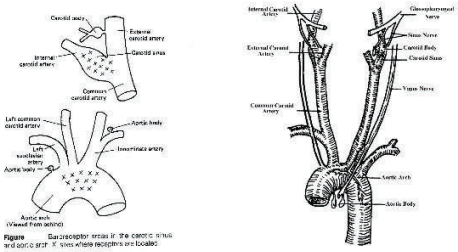
- Tonic regulation of blood pressure
  - keep the arterial pressure relatively constant
  - Pressure buffer system - reduce the blood pressure fluctuation during the daily events, such as changing of the posture, respiration, excitement, and so forth.

(6) Baroreceptor Resetting

- Baroreceptor will adapt to the long term change of blood pressure.
  - if the blood pressure is elevated for a long period of time, several days or years, the set point will transfer to the elevated mean blood pressure.
- baroreceptor reflex is not a long term control system.
  - unimportant for long-term regulation of arterial pressure

(2) Reflex involving arterial chemoreceptors

- Chemoreceptors: situated in the carotid body and aortic body



Reflex involving arterial chemoreceptors

- have a very rich blood supply,
  - ideal for sampling chemical changes in the blood.
- sensitive to the decreased Po_2, increased PCO_2 and increased hydrogen ion concentration in the plasma.
- Afferent:
  - carotid body afferent fiber - carotid sinus nerve ---glossopharyngeal nerve.
  - Aortic body afferent fiber - aortic nerve - vagus nerve
- Response: Stimulation of chemoreceptors leads to a reflex increase in vasomotor tone,
- causes generalized vasoconstriction and hence a rise in blood pressure.
- Importance: is important in regulation of blood pressure when it fall below the range in which baroreceptors act (70 mmHg).

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3. Hormonal Regulation of the Cardiovascular System

Hormonal regulation involves circulating hormones that influence vascular tone, blood volume, and heart rate. These hormones allow for both rapid and long-term adjustments in cardiovascular function.

3.1. Epinephrine and Norepinephrine

- Epinephrine and norepinephrine are catecholamines secreted by the adrenal medulla in response to sympathetic stimulation (particularly during stress or exercise).
  - Epinephrine:
    - Binds to beta-1 adrenergic receptors on the heart, increasing heart rate and contractility.
    - Binds to beta-2 adrenergic receptors on skeletal muscle blood vessels, causing vasodilation and increasing blood flow to active tissues.
  - Norepinephrine:
    - Primarily binds to alpha-1 adrenergic receptors on blood vessels, causing widespread vasoconstriction and increasing systemic vascular resistance (SVR), which raises blood pressure.

3.2. Angiotensin II

- Angiotensin II is a powerful vasoconstrictor produced through the Renin-Angiotensin-Aldosterone System (RAAS). It has several effects:
  - Vasoconstriction: Increases blood pressure by constricting arterioles.
  - Aldosterone Release: Stimulates the adrenal cortex to release aldosterone, which promotes sodium and water retention in the kidneys, increasing blood volume and pressure.
  - Thirst and ADH Release: Angiotensin II stimulates thirst and antidiuretic hormone (ADH) secretion, further enhancing water retention.

3.3. Vasopressin (Antidiuretic Hormone, ADH)

- ADH is secreted by the posterior pituitary gland in response to low blood volume, high plasma osmolarity, or significant blood loss (hemorrhage).
  - It promotes water reabsorption in the kidneys, increasing blood volume.
  - ADH also acts as a vasoconstrictor at high concentrations, contributing to blood pressure regulation during hypovolemia or shock.

3.4. Nitric Oxide (NO)

- Nitric oxide (NO) is synthesized by endothelial cells from the amino acid L-arginine and is a key regulator of vascular tone.
    - NO causes vasodilation by increasing cyclic GMP (cGMP) in vascular smooth muscle, leading to relaxation.
    - NO plays an important role in regulating blood flow during periods of increased demand (e.g., exercise) and counteracting excessive vasoconstriction to protect tissues from ischemia.

(3) CNS ischemic response

- Chemoreceptor reflex:
    - useful in regulation of blood pressure when it falls to a level between 40 and 70 mmHg.
- But if the blood pressure below 40 mmHg, the last ray of hope for survival is the central nervous system (CNS) ischemia response.
- evoked by ischemia (poor blood flow) of the central nervous system.
- Reduction in blood flow leads to
- reduced Po2
- elevated Pco2

II Chemical and hormonal control of cardiovascular function

- Various hormones, chemicals
- Start at a low pace,
- Have long-lasting influences
- Classification
    - Vasoconstrictors
    - Vasodilators

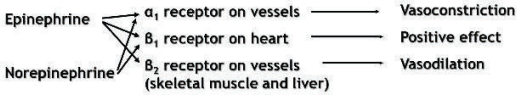
Vasoconstrictors and Vasodilators

- Vasoconstrictors
    - Epinephrine and Norepinephrine
    - Angiotensin II
    - Vasopressin
- Vasodilators
    - NO

Epinephrine and Norepinephrine

- The adrenal medulla secrete both epinephrine (80%) and norepinephrine (20%)
- carried by blood flow to everywhere in the body.
- In the blood, only a little norepinephrine comes form the endings of the adrenergic fibers.

Adrenergic receptors



Effect

- On heart in vitro (contractility and automaticity).
    - both increase the force and rate of contraction of the isolated heart.
    - mediated by B1 receptors.

Effect

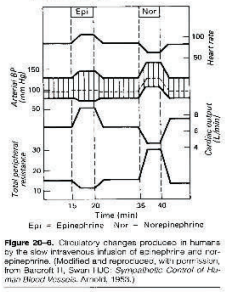
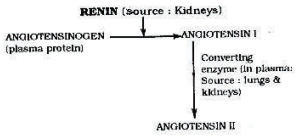


Figure 20–6. Circulatory changes produced in humans by the slow intravenous infusion of epinephrine and norepinephrine. (Modified and reproduced, with permission, from Bacroft H, Swan I UO: *Sympathetic Control of Human Blood Vessels.* Arnold, 1953.)

- Norepinephrine produces vasoconstriction in most if not all organs via α1 receptors
    - Ps increase - baroreceptor reflex - bradycardia
    - the heart rate and cardiac out falls.
    - Epinephrine dilates the blood vessels in skeletal muscle and the liver via B2 receptors
        - overbalances the vasoconstriction produced by epinephrine elsewhere
        - the total peripheral resistance drops
        - causes a widening of the pulse pressure
        - baroreceptor stimulation is insufficient to obscure the direct effect of the hormone on the heart,
        - cardiac rate and output increase.

Angiotensin II

- very potent vasoconstrictor
- formed in the plasma through a chain reaction.
    - triggered by a substance, renin, released form kidneys.
    - Renin is released from kidneys in response to renal ischemia, which may be due to a fall in blood pressure.



Vasopressin

- antidiuretic hormone (ADH),
    - formed in the hypothalamus (mainly)
    - secreted through the posterior pituitary gland.

  more powerful than angiotensin as a vasoconstrictor.
- during hemorrhage - increased vasopressin - raise the arterial pressure as much as 40 to 60 mmHg.

Vasopressin

- **Vasoconstriction has not a physiological function**
  - **does not increase blood pressure when small doses are injected in vivo**
  - **In healthy person, the plasma concentration is too low to induce vasoconstrion**
- **Acts on the brain to cause a decrease in cardiac output.**
  - **in the area of postrema**
- **Acts on the kidney - physiological (ADH)**

Effect of NO

- **Relax the vascular smooth muscle directly**
- **Mediate vascular dilator effect of some hormones and transmitters (Ach, bradykinin, VIP, substance P)**
- **Inhibit the tonic excitation of some neurons in the vasomotor centre.**
- **Inhibit the norepinephrine release from the sympathetic postganglionic fiber.**

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4. Reflex Regulation of Circulation

Reflex mechanisms provide rapid adjustments to blood pressure and cardiac output in response to short-term changes in the cardiovascular system, such as sudden changes in posture, blood volume, or oxygen demand.

4.1. Baroreceptor Reflex

- Baroreceptors are stretch-sensitive mechanoreceptors located in the carotid sinus and aortic arch.
  - When blood pressure rises, increased stretch of these receptors sends signals to the cardiovascular centers in the medulla oblongata, activating parasympathetic pathways and inhibiting sympathetic output. This results in:
    - Reduced heart rate (via vagal stimulation).
    - Vasodilation of peripheral blood vessels.
  - Conversely, when blood pressure falls, baroreceptor activity decreases, leading to increased sympathetic stimulation, raising heart rate and causing vasoconstriction to restore normal blood pressure.

4.2. Chemoreceptor Reflex

- Chemoreceptors located in the carotid bodies and aortic bodies respond to changes in arterial oxygen (O_2), carbon dioxide (CO_2), and pH levels.
  - Low O_2 or high CO_2 levels stimulate the respiratory centers, increasing ventilation, heart rate, and sympathetic outflow to improve oxygen delivery and CO_2 removal.
  - This reflex is particularly important during hypoxia or hypercapnia, such as during exercise or respiratory distress.

4.3. CNS Ischemic Response

- The CNS ischemic response is activated by severe reductions in cerebral blood flow, such as during hemorrhage or extreme hypotension.
  - If cerebral perfusion falls below critical levels, the medullary vasomotor center initiates massive sympathetic outflow, leading to intense vasoconstriction and tachycardia in an effort to raise blood pressure and restore cerebral perfusion.

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5. Local Regulation of Blood Flow

Local control mechanisms allow tissues to regulate their own blood flow based on metabolic needs, ensuring that blood supply is matched to demand without relying solely on neural or hormonal inputs.

5.1. Autoregulation

- Autoregulation refers to the intrinsic ability of organs and tissues to regulate their blood flow despite changes in arterial pressure.
    - In the brain, heart, and kidneys, autoregulation ensures constant perfusion over a range of pressures, preventing ischemia or over-perfusion.
    - Autoregulation involves myogenic mechanisms (smooth muscle contraction in response to stretch) and metabolic factors (vasodilators like adenosine, CO_2, and low oxygen).

5.2. Endothelial Factors

- The endothelium plays a critical role in local blood flow regulation by producing various vasoactive substances:
    - Vasodilators: Besides nitric oxide (NO), other endothelial vasodilators include prostacyclin and endothelium-derived hyperpolarizing factor (EDHF).
    - Vasoconstrictors: The endothelium also produces vasoconstrictors such as endothelin-1, which plays a role in conditions like hypertension and heart failure when produced in excess.

III Autoregulation of Local Blood Pressure

- **Role of Vasodilator Substances.**
    - **CO_2, Lactic acid, Adenosine, Adenosine phosphate compounds, Histamine, K^+ and H^+**
- **Myogenic Activity**
    - **Heterometric autoregulation**

---

6. Cardiovascular Centers in the Brain

6.1. Medulla Oblongata

- The medulla oblongata houses the cardiovascular control centers, including:
    - The vasomotor center, which regulates sympathetic activity to blood vessels.
    - The cardioinhibitory center, which controls parasympathetic (vagal) activity to the heart.
    - The medulla receives input from baroreceptors, chemoreceptors, and higher brain centers to modulate cardiovascular responses.

6.2. Higher Brain Centers

- The hypothalamus and cerebral cortex influence cardiovascular function in response to emotional stimuli (e.g., stress, fear) and physical exertion. These higher centers can modulate autonomic output, affecting heart rate, blood pressure, and vasodilation.

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7. Practical Applications and Clinical Implications

7.1. Hypertension

- Hypertension results from increased systemic vascular resistance, elevated cardiac output, or a combination of both. It can be driven by overactive sympathetic nervous system activity, abnormal RAAS function, or endothelial dysfunction.
    - Chronic hypertension increases the risk of stroke, heart attack, heart failure, and kidney disease.
    - Treatments target neural (beta-blockers), hormonal (ACE inhibitors, ARBs), and local mechanisms (calcium channel blockers) to reduce blood pressure.

7.2. Heart Failure

- Heart failure occurs when the heart cannot pump effectively to meet the body's needs, often due to increased afterload (hypertension), impaired contractility (post-myocardial infarction), or volume overload (kidney disease).
    - Understanding neural, hormonal, and local regulation helps guide treatment with diuretics, ACE inhibitors, and beta-blockers to reduce workload on the heart and improve cardiac function.

7.3. Shock

- Shock is a life-threatening condition where tissue perfusion is inadequate, leading to cellular dysfunction and organ failure.
    - Hypovolemic shock results from fluid loss (e.g., hemorrhage).
    - Cardiogenic shock occurs due to heart failure.
    - Septic shock involves systemic vasodilation due to infection.
    - Treatment aims to restore blood volume (fluid resuscitation) and enhance cardiac output (vasopressors, inotropes).

Examination and Assessment

1	Cardiac Conduction System includes:	
a.	Sinus node (SA)	True
b.	Internodal pathways	True
c.	Atrioventricular node	True
d.	Bundle of His	True
e.	Purkinje fibers	True
f.	Right atrium	False
g.	Right ventricle	False
h.	Left atrium	False
i.	Left ventricle	False
j.	Na+ -K+ pumps	False

2	A pacemaker is:	
a.	a small, battery-operated electronic device	True
b.	a device which is inserted under the skin to help the heart beat regularly	True
c.	a device which is inserted under the skin to help the heart beat at an appropriate rate	True
d.	has leads that travel through a large vein to the heart, where the wires are anchored.	True
e.	electrical impulses to the heart to tell it to beat	True
f.	a big battery-operated electronic device	False
g.	a device which is inserted under the skin to help the heart slow down	False
h.	a device which is inserted under the skin to help the heart stop beating	False
i.	the pacemaker has leads that travel through a large vein to the brain	False
j.	the electrical impulses to the lungs	False

3	Main functions of the circulatory system:	
a.	Transport and distribute essential substances to the tissues.	True
b.	Remove metabolic byproducts.	True
c.	Adjustment of oxygen and nutrient supply in different physiologic states.	True
d.	Regulation of body temperature.	True
e.	Humoral communication	True
f.	Extrinsic regulation	False
g.	Protein secretion	False
h.	Behavioral regulation	False
i.	Meta-regulation	False
j.	Lipid oxidation	False

4	Heart Valves	
a.	tricuspid--between RA and RV; three leaflets	True
b.	mitral--between LA and LV; two leaflets	True
c.	pulmonic- three leaflets	True
d.	aortic- three leaflets	True
e.	Prevent backward regurgitation	True
f.	Provide high resistance to forward flow	False
g.	tricuspid--between LA and LV; two leaflets	False
h.	mitral--between RA and RV; three leaflets	False
i.	pulmonic- two leaflets	False
j.	aortic- two leaflets	False

5	Cardiac Cycle	
a.	The cardiac events that occur from the beginning of one heart beat to the beginning of the next	True
b.	Each cycle is initiated by spontaneous generation of an action potential in the sinus node.	True
c.	The impulse travels from SA node through both atria and then through the A-V bundle into the ventricles.	True
d.	The conducting from the atria into the ventricles - there is a delay of more than 0.1 seconds	True
e.	Atria contract ahead of ventricles	True
f.	The cardiac events that occur from the end of contraction to the beginning of the relaxation	False
g.	Each cycle is initiated by spontaneous generation of an action potential in the Atrio-ventricular node.	False
h.	The impulse travels from SA node through both ventricles and then through the A-V bundle into the atria.	False
i.	The conducting from the ventricles into the atria - there is a delay of more than 1 seconds	False
j.	Atria contract after ventricles	False

6	The total duration of the cardiac cycle	
a.	includes systole and diastole	True
b.	is the reciprocal of the heart rate	True
c.	Normal heart rate is 72 beats/min	True
d.	Normal duration of the cardiac cycle is 1/72 beats/min	True
e.	Normal duration of the cardiac cycle is 0.0139 minutes per beat, or 0.833 second per beat	True
f.	includes only the systole	False
g.	is the reciprocal of the diastole duration	False
h.	Normal heart rate is 102 beats/min	False
i.	Normal duration of the cardiac cycle is 1/102 beats/min	False
j.	Normal duration of the cardiac cycle is 0.5 minutes per beat, or 1.833 second per beat	False

7	Cardiac Cycle definition:	
a.	complete heartbeat	True
b.	systole and diastole of both atria and ventricles	True
c.	systole and diastole of both atria plus systole and diastole of both ventricles	True
d.	contraction and relaxation cycle of the heart muscle	True
e.	Cycle of systole - contraction and diastole - relaxation of the heart muscle	True
f.	The cardiac events that occur from the end of contraction to the beginning of the relaxation	False
g.	Each cycle is initiated by spontaneous generation of an action potential in the Atrio-ventricular node.	False
h.	The impulse travels from SA node through both ventricles and then through the A-V bundle into the atria.	False
i.	The conducting from the ventricles into the atria - there is a delay of more than 1 seconds	False
j.	Atria contract after ventricles	False

8	Cardiac reserve:	
a.	Normal cardiac output 5.25 L /min	True
b.	Maximal diastole volume 160 ml	True
c.	Maximal systole residual volume 20 ml	True
d.	Maximal heart rate (without the stroke volume decrease) 180 beats/min	True
e.	Maximal cardiac output (160 – 20) X 180 = 25.2 L/min	True

f.	Normal cardiac output 25 L /min	False
g.	Maximal diastole volume 10 ml	False
h.	Maximal systole residual volume 100 ml	False
i.	Maximal heart rate 60 beats/min	False
j.	Maximal cardiac output 5 L/min	False

9	Electrocardiogram – ECG – includes:	
a.	P wave- shows how atria contract	True
b.	QRS complex- shows how ventricles contract	True
c.	T wave- shows how ventricle relax	True
d.	P-R Interval	True
e.	Q-T Interval	True
f.	A dynamometer	False
g.	Tensiometer	False
h.	Blood pressure	False
i.	Pulse points	False
j.	Cardiac factor	False

10	Regarding the electrical (conductive) system of the heart:	
a.	The human heart beats about 100,000 times a day	True
b.	Atrial and ventricular cells involved in this contractile activity, referred to as "working myocytes"	True
c.	SAN myocytes set the rhythm and rate of cardiac chamber contraction	True
d.	Pacemaker" cells generate repetitive action potentials at a constantly controlled rate	True
e.	Prepotential propagates in the conducting system causing the contractile cardiac fibers to depolarise	True
f.	Modifies stroke volume (SV) through the functional characteristics of cardiac muscle cells	False
g.	Modifies heart rate	False
h.	Includes the cardiac reserve	False
i.	Includes heart valves	False
j.	Has an antiregulation system	False

11	Big blood vessels, arteries and veins, wals structure includes:	
a.	Tunica intima (endothelial cells)	True
b.	Elastin	True
c.	Tunica media (smooth muscle)	True
d.	Tunica externa	True
e.	Serosa	True
f.	Laminar flow	False
g.	Turbulent flow	False
h.	A muscular pump	False
i.	A venous pump	False
j.	A microcirculatory system	False

12	Distribution of Cardiac Output during rest includes:	
a.	20-25 % to digestive system	True
b.	20 % to the kidney	True
c.	15-20 % to skeletal muscular system	True
d.	3-5% to bones	True

e.	15 % to the brain	True
f.	3-5 % to digestive system	False
g.	2-4 % to the kidney	False
h.	80-85 % to skeletal muscular system	False
i.	0,5-1% to bones	False
j.	3-4 % to the brain	False

13	Distribution of Cardiac Output during heavy work includes:	
a.	3-5 % to digestive system	True
b.	2-4 % to the kidney	True
c.	80-85 % to skeletal muscular system	True
d.	0,5-1% to bones	True
e.	3-4 % to the brain	True
f.	20-25 % to digestive system	False
g.	20 % to the kidney	False
h.	15-20 % to skeletal muscular system	False
i.	3-5% to bones	False
j.	15 % to the brain	False

14	Precapillary Resistance Vessels – Small arteries and arterioles	
a.	Less elastic than the larger arteries	True
b.	Have a thicker layer of smooth muscle	True
c.	Provide the greatest resistance to blood flow	True
d.	They have narrow lumina	True
e.	Precapillary sphincter muscle partially determines the amount of blood flowing through a capillary bed	True
f.	Precapillary sphincter muscle allows 20% of the capillary in bed skeletal muscles to be open at rest	False
g.	Precapillary sphincter muscle allows 30% of the capillary in bed skeletal muscles to be open at rest	False
h.	Precapillary sphincter muscle allows 40% of the capillary in bed skeletal muscles to be open at rest	False
i.	Precapillary sphincter muscle allows 50% of the capillary in bed skeletal muscles to be open at rest	False
j.	Precapillary sphincter muscle allows 60% of the capillary in bed skeletal muscles to be open at rest	False

15	Blood Flow (Q)	
a.	The quantity of blood that passes a given point in the circulation in a given period of time	True
b.	The overall blood flow in the systemic circulation is identical to the cardiac output	True
c.	Laminar flow – blood flows in streamlines with each layer of blood remaining the same distance from the wall	True
d.	Turbulent flow – blood flow in all directions in the vessel and continually mixes within the vessel	True
e.	Blood flow can be laminar or turbulent	True
f.	The quantity of blood that passes a given point in the circulation by electrocardiogram	False
g.	The overall blood flow in the systemic circulation is oposite to the cardiac output	False
h.	Laminar flow – blood flows in all directions in the vessel and continually mixes within the vessel	False
i.	Turbulent flow – blood flow in streamlines with each layer of blood remaining the same distance from the wall	False

j.	Blood flow can be fluid or virulent	False

16	Blood pressure	
a.	the force exerted by the blood against the vessel wall	True
b.	stored energy (potential energy) in the circulatory system	True
c.	Energy released from heart contraction is transferred into potential energy (pressure) (99% of the total)	True
d.	Generated by Ventricular Contraction	True
e.	Decrease in pressure in each part of the systemic circulation is directly proportional to the vascular resistance	True
f.	The quantity of blood that passes a given point in the circulation by electrocardiogram	False
g.	The overall blood flow in the systemic circulation is oposite to the cardiac output	False
h.	Laminar flow – blood flows in all directions in the vessel and continually mixes within the vessel	False
i.	Turbulent flow – blood flow in streamlines with each layer of blood remaining the same distance from the wall	False
j.	Blood flow can be fluid or virulent	False

17	Factors Determining Arterial Pressure:	
a.	Stroke volume	True
b.	Heart rate	True
c.	Total peripheral resistance	True
d.	Action of Windkessel vessel (aorta and other large arteries) – Pulse pressure	True
e.	Mean circulatory filling pressure	True
f.	Central venous pressure	False
g.	Venous pressure in the organs	False
h.	The pressure in the right atrium	False
i.	hydrostatic pressure	False
j.	Carbon dioxide content	False

18	Factors affecting venous return:	
a.	Mean systemic filling pressure	True
b.	Cardiac contractility	True
c.	Position of the body	True
d.	Action of “muscular pump”	True
e.	respiration movement	True
f.	Protein secretion	False
g.	Lipid oxidation	False
h.	Water transport in the body	False
i.	Intracellular movement of materials	False
j.	Control electrical charges in the organism	False

19	“pores” in the capillary membrane:	
a.	Are specific to fenestrated capillaries	True
b.	Structurally, capillaries have no smooth muscle in their walls.	True
c.	“pores” are gaps in the calillary membrane	True
d.	“pores” are gaps between endothelial cells	True
e.	“pores” allow for exchange of nutrients and metabolites	True
f.	Are specific to continuous capillary	False

g.	Structurally, capillaries have smooth muscle in their walls.	False
h.	They are lined by only a single layer of pericytes	False
i.	“pores” are gaps between pericytes	False
j.	“pores” allow for exchange of blood elements	False

20	The function of lymph	
a.	Removing protein from interstitial fluid.	True
b.	Regulating balance between plasma and interstitial fluid (reabsorption l0% of filtration fluid).	True
c.	Absorption of nutrients (80%~90% of fat) from gastrointestinal tract.	True
d.	Removing the particles such as RBC, bacteria, lymphatic cell, tissue cell in the interstitium.	True
e.	Defense function (to ingest bacteria and to produce antibodies)	True
f.	Daily intake and excretion of body water	False
g.	Inflammation or allergy – leakage of abnormally large quantities of proteins	False
h.	Abnormal accumulation of fluid in the interstitial space.	False
i.	Local edema	False
j.	Systemic edema	False

21	Intrinsic Regulation of the Heart:	
a.	Modifies stroke volume (SV) through the functional characteristics of cardiac muscle cells	True
b.	Is according to Starling’s law of the heart	True
c.	A slow heart beat allows more time for the ventricles to fill	True
d.	The important factor stretching the heart muscle is the venous return	True
e.	Anything that will increase the venous return will increase the SV	True
f.	Modifies heart rate and stroke volume through nervous mechanisms	False
g.	Modifies heart rate and stroke volume through hormonal mechanisms	False
h.	Parasympathetic nervous control of the heart	False
i.	Sympathetic nervous control of the heart	False
j.	Various hormones and ions have a dramatic effect on heart activity	False

22	Extrinsic Regulation of the Heart:	
a.	Modifies heart rate and stroke volume through nervous mechanisms	True
b.	Modifies heart rate and stroke volume through hormonal mechanisms	True
c.	Parasympathetic nervous control of the heart	True
d.	Sympathetic nervous control of the heart	True
e.	Various hormones and ions have a dramatic effect on heart activity	True
f.	Modifies stroke volume (SV) through the functional characteristics of cardiac muscle cells	False
g.	Is according to Starling’s law of the heart	False
h.	A slow heart beat allows more time for the ventricles to fill	False
i.	The important factor stretching the heart muscle is the venous return	False
j.	Anything that will increase the venous return will increase the SV	False

23	The Heart and Homeostasis	
a.	Carotid body and aortic chemoreceptor receptors monitor blood oxygen levels	True
b.	Chemoreceptors monitor blood pH and carbon dioxide levels	True
c.	Chemoreceptors are important in the regulation of respiration and blood vessel constriction	True
d.	Baroreceptors monitor blood pressure and the cardio-regulatory center modifies heart rate and stroke volume	True

e.	When blood pressure increases, the baroreceptor reflexes decrease heart rate and stroke volume	True
f.	Carotid body and aortic chemoreceptor receptors monitor blood hormon levels	False
g.	Chemoreceptors monitor blood oxygen levels	False
h.	Chemoreceptors are important in the normal heart regulation	False
i.	Baroreceptors monitor stroke volume	False
j.	When blood pressure increases, the baroreceptor reflexes increase heart rate	False

24	Regulation of the blood flow of organs to fit their metabolic requirement in different conditions involves	
a.	Cardiac innervation	True
b.	Innervation of blood vessels	True
c.	Parasympathetic nerve fiber to peripheral vessels	True
d.	Control centers of cardiovascular activities	True
e.	Sympathetic vasodilator fiber	True
f.	Daily intake and excretion of body water	False
g.	Inflammation or allergy – leakage of abnormally large quantities of proteins	False
h.	Abnormal accumulation of fluid in the interstitial space.	False
i.	Local edema	False
j.	Systemic edema	False

25	Sympathetic vasodilator fiber	
a.	The sympathetic nerves to skeletal muscles carry sympathetic vasodilator fibers as well as constrictor fibers	True
b.	release acetylcholine	True
c.	increase the blood flow in skeletal muscle during exercise	True
d.	increase the blood flow in skeletal muscle during stress	True
e.	cause vasodilation	True
f.	The sympathetic nerves to skeletal muscles carry only constrictor fibers	False
g.	release epinephrine	False
h.	decrease the blood flow in skeletal muscle during exercise	False
i.	decrease the blood flow in skeletal muscle during stress	False
j.	cause constriction	False

26	Parasympathetic nerve fibers innervate vessels of the blood vessels in:	
a.	Meninges	True
b.	the salivary glands	True
c.	the liver	True
d.	the viscera in pelvis	True
e.	the external genitals	True
f.	Muscles	False
g.	Bones	False
h.	Fingers	False
i.	Legs	False
j.	Upper extremities	False

27	The control center of cardiovascular activities is the nucleus groups at different levels:	
a.	Brainstem	True

b.	Hypothalamus	True
c.	Limbic system	True
d.	Cerebral cortex	True
e.	Cerebellum	True
f.	Pituitary gland	False
g.	Thalamus	False
h.	Internal ear	False
i.	Motor area	False
j.	Spinal cord	False

28	Reflex involving arterial chemoreceptors:	
a.	have a very rich blood supply,	True
b.	ideal for sampling chemical changes in the blood.	True
c.	sensitive to the decreased Po2, increased PCO2 and increased hydrogen ion concentration in the plasma.	True
d.	carotid body afferent fiber - carotid sinus nerve ---glossopharyngeal nerve.	True
e.	stimulation of chemoreceptors leads to a reflex increase in vasomotor tone	True
f.	have a very poor blood supply,	False
g.	ideal for sampling stroke volume of the heart	False
h.	sensitive to the increased Po2, decreased PCO2 and low level hydrogen ion concentration in the plasma.	False
i.	carotid body afferent fiber - carotid sinus nerve ---cochlear nerve.	False
j.	stimulation of chemoreceptors leads to a reflex increase in vasodilation	False

29	Effect of NO	
a.	Relax the vascular smooth muscle directly	True
b.	Mediate vascular dilator effect of some hormones and transmitters	True
c.	Inhibit the tonic excitation of some neurons in the vasomotor centre.	True
d.	Inhibit the norepinephrine release from the sympathetic postganglionic fiber	True
e.	Mediate vascular dilator effect of acetylcholine	True
f.	Contract the vascular smooth muscle directly	False
g.	Mediate vasculomotor contractive effect of some hormones and transmitters	False
h.	Stimulate the tonic excitation of some neurons in the vasomotor centre.	False
i.	Stimulate the norepinephrine release from the sympathetic postganglionic fiber	False
j.	Mediate vasculomotor contractive effect of acetylcholine	False

30	Autoregulation of Local Blood Pressure:	
a.	Role of vasodilator Substances	True
b.	CO2, Lactic acid, Adenosine	True
c.	Myogenic Activity	True
d.	Adenosine phosphate compounds, Histamine, K+ and H+	True
e.	Heterometric autoregulation	True
f.	Useful in regulation of blood pressure when it falls to a level between 40 and 70 mmHg	False
g.	Evoked by ischemia (poor blood flow) of the central nervous system	False
h.	In the blood, only a little norepinephrine comes form the endings of the adrenergic fibers	False
i.	Norepinephrine produces vasoconstriction in most if not all organs via α1 receptors	False
j.	Acts on the brain to create the sensation of thirst	False

Course 7: The Endocrine System
Sub-topic: Hormones, Glands, Functions, and Regulation

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1. Overview of the Endocrine System

- **Definition and Function**
- **Components of the Endocrine System**

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2. The Pituitary Gland
2.1. Anatomy and Function
2.2. Hormones of the Pituitary Gland:

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3. The Thyroid Gland
3.1. Anatomy and Function
3.2. Thyroid Hormones:
3.3. Disorders of Thyroid Function:

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4. The Parathyroid Glands
4.1. Anatomy and Function
4.2. Functions of Parathyroid Hormone:

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5. The Adrenal Glands
5.1. Anatomy and Function
5.2. Hormones of the Adrenal Glands:
5.3. Disorders of Adrenal Function:

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6. The Pancreas
6.1. Anatomy and Function
6.2. Hormones of the Pancreas:
6.3. Disorders of Pancreatic Function:

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7. The Gonads (Ovaries and Testes)
7.1. Ovaries (in females):
7.2. Testes (in males):

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8. Regulation of Endocrine Activity
8.1. Feedback Mechanisms
8.2. Hypothalamic-Pituitary Axis

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9. Practical Applications and Clinical Implications
9.1. Endocrine Disorders:

- **Disorders such as diabetes, hypothyroidism, hyperthyroidism, and Cushing's syndrome highlight the importance of hormone balance in maintaining health.**

9.2. Diagnostic Tools:

- **Blood tests to measure hormone levels (e.g., TSH, cortisol, insulin).**
- **Imaging techniques such as ultrasound and MRI to assess gland structure.**

Examination and Assessment

Practical Session 7: Endocrine System

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1. Introduction to the Endocrine System

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2. Concept of Hormones

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3. Endocrine System Control
3.1. Feedback Mechanisms
- Negative Feedback
- Positive Feedback

---

4. Hormonal Actions and Target Cells
4.1. Specificity of Hormones
4.2. Mechanisms of Action

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5. Hormonal Signaling and Second Messenger Systems
- Second Messengers:
  - These molecules mediate intracellular responses to hormonal signals. Examples include cyclic AMP (cAMP), calcium ions (Ca^{2+}), and inositol triphosphate (IP_3).
- Signal Amplification:
  - Hormonal binding to a receptor can activate a cascade of events, amplifying the signal and producing a significant biological effect even with low hormone concentrations.

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6. Endocrine Glands and Hormones
6.1. Pituitary Gland
- Anterior Pituitary:
  - Secretes hormones like growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), and gonadotropins (LH, FSH).
- Posterior Pituitary:
  - Releases oxytocin and antidiuretic hormone (ADH).

6.2. Thyroid Gland
- Produces thyroxine (T_4) and triiodothyronine (T_3), which regulate metabolism, and calcitonin, which helps regulate calcium levels.

6.3. Adrenal Glands
- Adrenal Cortex:
  - Secretes corticosteroids (cortisol, aldosterone) involved in stress response, immune function, and sodium-potassium balance.
- Adrenal Medulla:
  - Produces catecholamines (epinephrine, norepinephrine) involved in the "fight-or-flight" response.

6.4. Pancreas
- Islets of Langerhans:
  - Secretes insulin and glucagon, which regulate blood glucose levels.

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7. Practical Experiments and Demonstrations
7.1. Measuring Hormone Levels
7.2. Feedback Mechanism Simulation
7.3. Hormone Receptor Interaction
- Cellular Response to Hormones:

Course 7: The Endocrine System
Sub-topic: Hormones, Glands, Functions, and Regulation

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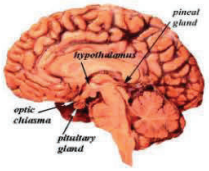
1. Overview of the Endocrine System
   - Definition and Function: The endocrine system is a network of glands that secrete hormones directly into the bloodstream to regulate various physiological processes. Hormones are chemical messengers that influence growth, metabolism, reproduction, and homeostasis.
   - Components of the Endocrine System:
     The endocrine system consists of major glands including the pituitary gland, thyroid gland, parathyroid glands, adrenal glands, pancreas, and gonads (ovaries and testes). Each of these glands secretes specific hormones with distinct regulatory functions.

---

2. The Pituitary Gland

Pituitary

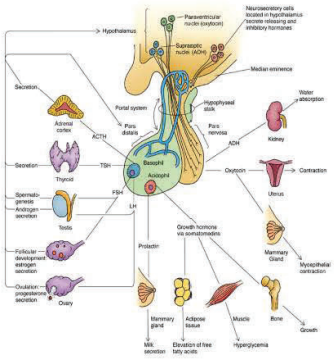
- **Pituitary gland is a round organ about the size of a pea (~1 cm in diameter), located behind the bridge of the nose at the base of the brain**
- **Secretes 9 different hormones, which affect many different areas of the body, including:**
  - **Growth**
  - **Blood pressure**
  - **Regulation of Pregnancy**
  - **Breast milk production**
  - **Sex organ functions in both men and women**
  - **Thyroid gland function**
  - **Metabolism**
  - **Water regulation in the body (kidneys)**
  - **Temperature regulation**



2.1. Anatomy and Function
   - The pituitary gland, also known as the "master gland," is located at the base of the brain and is divided into two parts:
     - Anterior Pituitary (Adenohypophysis): Secretes hormones that regulate growth, metabolism, and reproductive functions.
     - Posterior Pituitary (Neurohypophysis): Releases hormones in the hypothalamus that control water balance and uterine contractions.

2.2. Hormones of the Pituitary Gland
   - Anterior Pituitary Hormones:
     - Growth Hormone (GH): Stimulates growth and cell reproduction.
     - Thyroid-stimulating hormone (TSH): Regulates thyroid hormone secretion.
     - Adrenocorticotropic Hormone (ACTH): Stimulates the adrenal cortex to release cortisol.
     - Gonadotropins: Luteinizing Hormone (LH) and Follicle-Stimulating Hormone (FSH) regulate reproductive processes.
     - Prolactin: Promotes milk production.
   - Posterior Pituitary Hormones:
     - Antidiuretic Hormone (ADH): Regulates water balance by reducing urine output.
     - Oxytocin: Triggers uterine contractions during childbirth and milk ejection during breastfeeding.

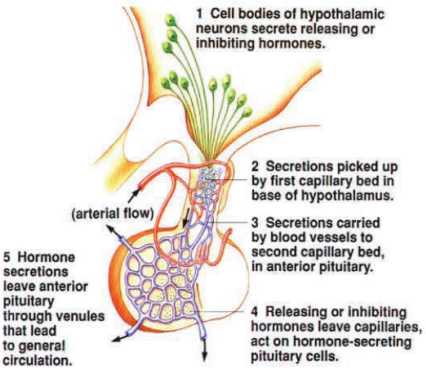
Pituitary and its Targets



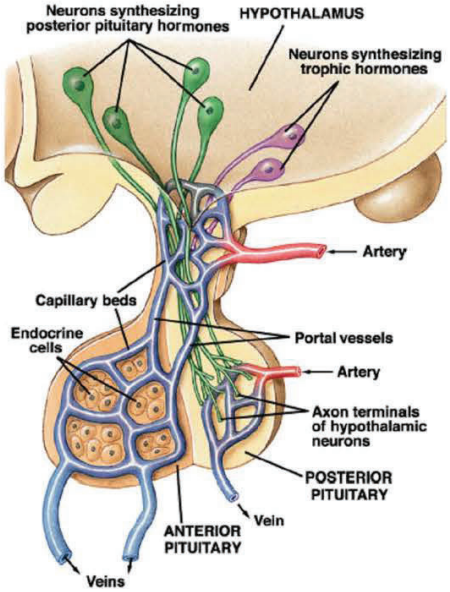
The pituitary gland and its target organs. ACTH, adrenocorticotropic hormone; ADH, antidiuretic hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone.

The **endocrine system,** consisting of **ductless glands,** distinct clusters of cells within certain organs of the body, and **diffuse neuroendocrine cells,** regulates metabolic activities in certain organs and tissues of the body, thereby helping to bring about homeostasis brought about by chemical substances called **hormones,** which are released into the bloodstream to influence target cells at remote sites.

The **pituitary gland** is connected to the brain by neural pathways; it also has a rich vascular supply from vessels that supply the brain, attesting to the inter coordination of the two systems in maintaining a physiological balance. Indeed, secretion of nearly all of the hormones produced by the pituitary gland is controlled by either hormonal or nerve signals from the hypothalamus. The main releasing and inhibitory hormones (factors) are: **Thyroid-stimulating hormone-releasing hormone (thyrotropin-releasing hormone [TRH])** stimulates the release of TSH; **Corticotropin-releasing hormone (CRH)** stimulates the release of adrenocorticotropin; **Somatotropin-releasing hormone (SRH)** stimulates the release of somatotropin **(growth hormone); Gonadotropin-releasing hormone (GnRH)** stimulates the release of luteinizing hormone **(LH)** and **FSH; Prolactin-releasing hormone (PRH)** stimulates the release of prolactin; **Prolactin inhibitory factor (PIF)** inhibits prolactin secretion.



Blood Supply of the Pituitary Gland



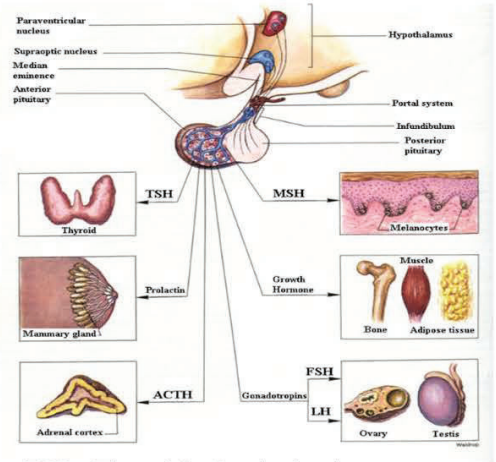
The pituitary gland and its circulatory system. ADH, antidiuretic hormone.

The arterial supply for the pituitary gland is provided from two pairs of vessels that arise from the internal carotid artery. The superior hypophyseal arteries supply the pars tuberalis and the infundibulum. They also form an extensive capillary network, the primary capillary plexus, in the median eminence. Inferior hypophyseal arteries primarily supply the posterior lobe, although they also send a few branches to the anterior lobe.

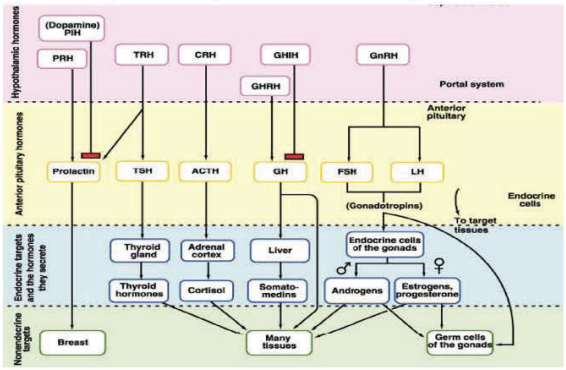
Hypophyseal portal veins drain the primary capillary plexus of the median eminence, which delivers its blood into the secondary capillary plexus, located in the pars distalis. Hypothalamic neurosecretory hormones, manufactured in the hypothalamus and stored in the median eminence, enter the primary capillary plexus and are drained by the hypophyseal portal veins, which connect to the secondary capillary plexus in the anterior lobe. Here the neurosecretory hormones leave the blood to stimulate or inhibit the parenchymal cells. Thus, the hypophyseal portal system is used for regulation of the pars distalis by the hypothalamus.

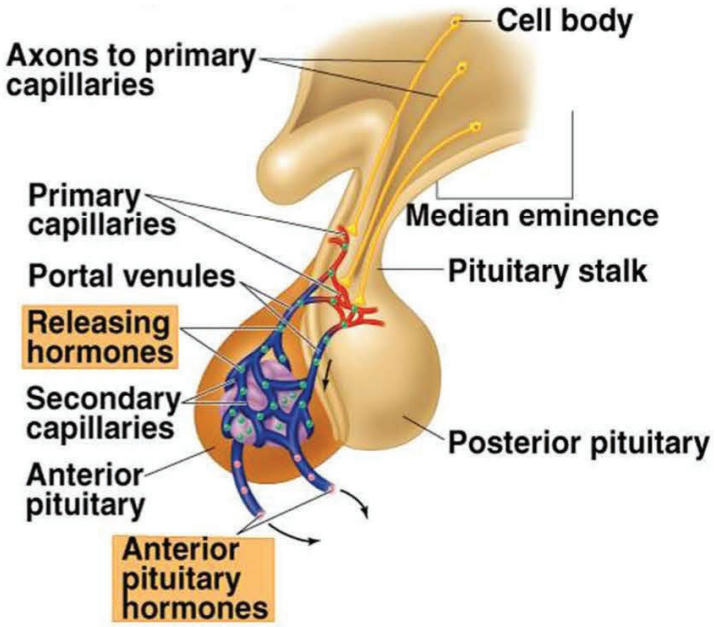
Axons of neurons that originate in various portions of the hypothalamus terminate around these capillary plexuses. The endings of these axons differ from other axons of the body, because instead of delivering a signal to another cell, they liberate either releasing or inhibiting hormones (factors) directly into the primary capillary bed. These hormones are taken by the hypophyseal portal system and delivered to the secondary capillary bed of the pars distalis, where they regulate secretion of various anterior pituitary hormones.

Anterior pituitary, also known as the adenohypophysis



TSH, Thyroid stimulating hormone
ACTH, Adrenocorticotropin hormone
FSH, Follicle-stimulating hormone
LH, Luteinizing hormone
MSH, Melanophore-stimulating hormone





GH, Growth Hormone; PRL, Prolactin

Growth Hormone

- Oversecretion of growth hormone:
  - Giantism in childhood and acromegaly in adults (bones of face, hands and feet enlarge)
- Undersecretion of growth hormone:
  - Dwarfism in childhood






Growth Hormone

Physiological functions.

Growth effect - stimulates cell division, especially in muscle and epiphyseal cartilage of long bones.
The result is muscular growth as well as linear growth.
GH also stimulates growth in several other tissues, e.g. skeletal muscle, heart, skin, connective tissue, liver, kidney, pancreas, intestines, adrenals and parathyroids.
Hypersecretion of GH leads to cause gigantism in children and acromegaly in adult.
Hyposection of GH results in dwarfism during childhood.

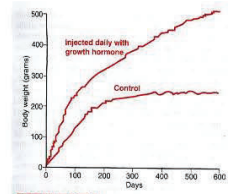


FIGURE 75–5
Comparison of weight gain of a rat injected daily with growth hormone with that of a normal littermate.

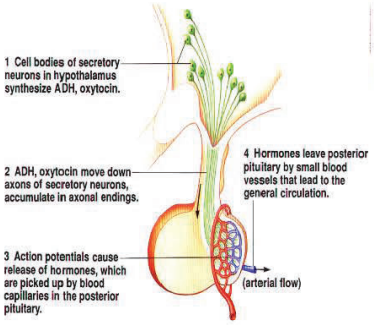
Growth Hormone Excess

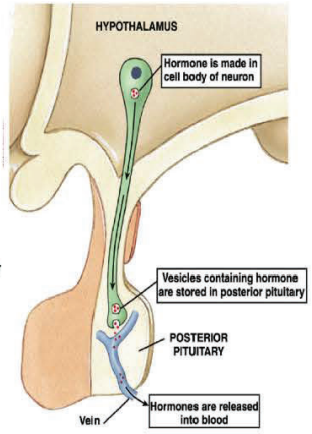
• in childhood leads to GIGANTISM



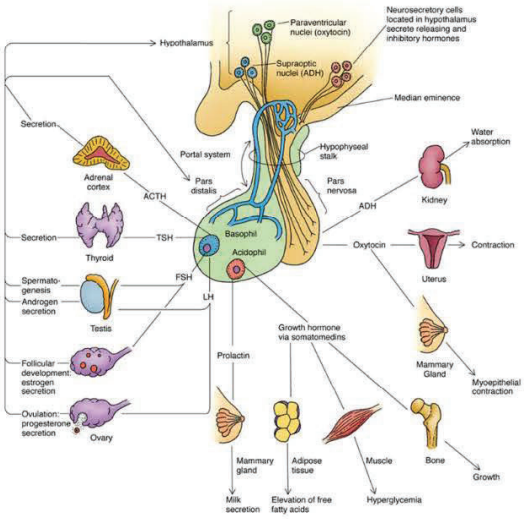
Hormones Secreted from the Posterior Pituitary

Vasopressin and oxytocin





Cells of the Pituitary Gland



The pituitary gland and its target organs. ACTH, adrenocorticotropic hormone; ADH, antidiuretic hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone.

The pituitary gland is divided into the adenohypophysis (composed of the pars distalis, pars intermedia, and the pars tuberalis) and the neurohypophysis (composed of the median eminence, infundibulum, and the pars nervosa).

The pars distalis possesses three types of cells, acidophils and basophils (together known as chromophils) and chromophobes.

The most abundant cells in the pars distalis are acidophils, possessing large, orange to red granules. There are two types of acidophils, somatotrophs and mammotrophs.

Somatotrophs secrete somatotropin (growth hormone); they are are stimulated by SRH and inhibited by somatostatin. Somatotropin has a generalized effect of increasing cellular metabolic rates. This hormone also induces liver cells to produce insulin-like growth factors I and II which stimulate the mitotic rates of epiphyseal plate chondrocytes and thus promote elongation of long bones and, hence, growth.

Mammotrophs release the hormone prolactin, which promotes mammary gland development during pregnancy as well as lactation after birth.

Basophils house granules that stain blue with basic dyes. There are three types of basophils, corticotrophs, thyrotrophs, and gonadotrophs.

Corticotrophs, are round to ovoid cells, each with an eccentric nucleus and relatively few organelles. They secrete adrenocorticotropic hormone (ACTH) and lipotropic hormone (LPH). Secretion is stimulated by CRH. ACTH stimulates cells of the suprarenal cortex to release their secretory products.

Thyrotrophs can be distinguished by their small secretory granules which contain TSH, also known as thyrotropin. Secretion is stimulated by TRH and inhibited by the presence of thyroxine (T4) and triiodothyronine (T3) (thyroid hormones) in the blood.

Gonadotrophs are round cells whose secretory granules vary in diameter from 200 to 400 nm. They secrete FSH and LH; sometimes LH is called interstitial cell-stimulating hormone (ICSH), because it stimulates steroid hormone production in interstitial cells of the testes. Secretion is stimulated by GnRH.

Chromophobes generally have less cytoplasm than chromophils do, and they may represent either nonspecific stem cells or partially degranulated chromophils.

The pars intermedia is characterized by many cuboidal cell-lined, colloid-containing cysts as well as by cords of basophils along the networks of capillaries. These basophils synthesize the prohormone proopiomelanocortin (POMC), which undergoes post-translational cleavage to form α-melanocyte-stimulating hormone (α-MSH), corticotropin, ß-lipotropin, and ß-endorphin. Although α-MSH stimulates melanin production in lower animals, in humans it may stimulate the release of prolactin and is therefore referred to as prolactin-releasing factor.

The distal terminals of the axons of the hypothalamohypophyseal tract end in the pars nervosa and store the neurosecretions that are produced by their cell bodies, which are located in the hypothalamus. These axons are supported by glia-like cells known as pituicytes. One population of axons contains membrane-bound granules of vasopressin and that another population contains oxytocin. These hormones are housed in dilatations of the axons called Herring bodies. The contents of these granules are released into the perivascular space near the fenestrated capillaries of the capillary plexus. Vasopressin acts on the nephron of the kidney and oxytocin facilitates contraction of the uterine myometrium.

3. The Thyroid Gland

3.1. Anatomy and Function

- Located in the neck, the thyroid gland regulates metabolism, growth, and development. It releases hormones that influence the body's metabolic rate, heart rate, and temperature regulation.

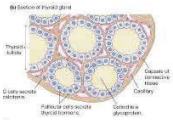
3.2. Thyroid Hormones

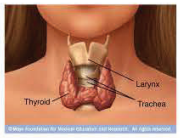
- Thyroxine (T_4) and Triiodothyronine (T_3): These hormones regulate the body's metabolism, growth, and development.
- Calcitonin: Helps regulate calcium levels by inhibiting bone resorption, lowering blood calcium levels.

3.3. Disorders of Thyroid Function

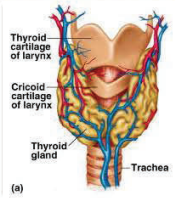
- Hypothyroidism: Characterized by insufficient thyroid hormone production, leading to fatigue, weight gain, and slow metabolism.
- Hyperthyroidism: Excess thyroid hormone production, causing increased metabolism, weight loss, and heat intolerance.
- Goiter: Enlargement of the thyroid gland, often due to iodine deficiency.

Thyroid





- Located in the neck
- Releases hormone thyroxin
- Function is to regulate rates of metabolism in the body
  - Essential for normal physical and mental development
- Oversecretion of thyroxin:
  - Results in nervousness and weight loss
- Undersecretion of thyroxin:
  - Results in cretinism (mental retardation, small size) in children



Thyroid

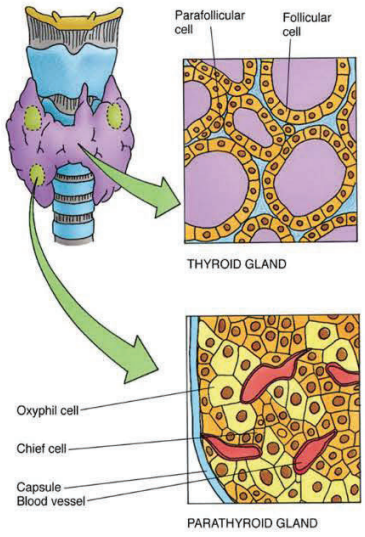


- Iodine deficiency in your diet results in goiter (enlargement of thyroid gland)





Thyroid Gland



The thyroid and parathyroid glands.

Unlike most of the endocrine glands, which store their secretory substances within the parenchymal cells, the thyroid gland stores its secretory substances in the lumina of follicles. These cyst-like structures, ranging from 0.2 to 0.9 mm in diameter, are composed of a simple cuboidal epithelium (composed of follicular cells and occasional parafollicular cells) surrounding a central colloid-filled lumen. Each follicle can store several weeks' supply of hormone within the colloid. The hormones T_4 and T_3 are bound to thyroglobulin a large secretory glycoprotein. When the hormones are to be released, the hormone-bound thyroglobulin is endocytosed by the follicular cells and the hormones are cleaved from it by lysosomal proteases.

Connective tissue septa derived from the capsule invade the parenchyma and provide a conduit for blood vessels, lymphatic vessels, and nerve fibers. Slender connective tissue elements, composed mostly of reticular fibers and housing a rich capillary plexus, surround each follicle but are separated from the follicular and parafollicular cells by a thin basal lamina. Occasionally, follicular cells of neighboring follicles may come into contact with each other and disrupt the continuity of the basal lamina.

Iodide is essential for the synthesis of the thyroid hormones (T3 and T4); iodination of tyrosine residues occurs in the follicles at the colloid-follicular cell interface.

Parafollicular cells make calcitonin (thyrocalcitonin), a peptide hormone that inhibits bone resorption by osteoclasts, thereby lowering calcium concentrations in blood.

Biological Actions of Thyroid Hormones

- T_3 and T_4 bind with nuclear receptor,
- activate and initiate genetic transcription. ---- mRNA
- protein synthesis in cytoplasmic ribosomes ----
- general increase in functional activity throughout the body.

On Metabolism

- Calorigenic action of thyroid hormones

increase O2 consumption of most tissues in the body, increasing heat production and BMR.

mechanism

A: Enhances Na+-K+ ATPase activity

B: Causes the cell membrane of most cells to become leaky to Na+ ions

On metabolism of protein

- Physiological level: stimulates synthesis of proteins and enzymes,
- Hyperthyroidism: catabolism of protein, leads weigh-loss and muscle weakness
- Hypothyroidism: myxedema develops because of deposition of mucoprotein binding with positive ions and water molecules in the interstitial spaces while protein synthesis decreases

On carbohydrate metabolism

- Increase absorption of glucose from the gastrointestinal tract
- Enhance glycogenolysis, and even enhanced diabetogenic effect of glucagon, cortisol and growth hormone.
- Enhancement of glucose utilization of peripheral tissues.

On fat metabolism

- Fatty acids:
  - accelerate the oxidation of free fatty acids
  - increase the effect of catecholamine on decomposition of fat.
- decrease plasma cholesterol concentration
  - promote synthesis
  - increase decomposition

Effects on Nervous System

- increase excitability of
  - central nervous system
  - sympathetic nervous system
- Hyperthyroidism:
  - extreme nervousness,
  - many psychoneurotic tendencies including anxiety complexes, extreme worry, paranoia and muscle tremor
- Hypothyroidism
  - fatigue
  - extreme somnolence
  - poor memory
  - slow mentation





Hyperthyroidism

Other Effects

- on cardiovascular system
  - increase heart rate and stroke volume,
    - (may through enhance calcium release from sarcoplasmic reticulum)
- on gastrointestinal tract
  - increase the appetite and food intake by metabolic rate increased.
  - increase both the rate of secretion of the digestive juices and the motility of the gastrointestinal tract.
  - Lack of thyroid hormone can cause constipation.

Regulation of Thyroid Hormone Secretion

- Hypothalamic Pituitary Thyroid Axis
- Feedback Mechanisms
- Autoregulation
- Effect of Autonomic Nervous System

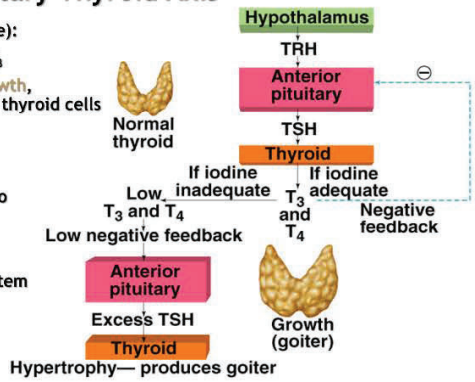
Hypothalamic Pituitary Thyroid Axis

TSH (throid-stimulating hormone):

- Increase secretion of T_4 and T_3
- Stimulate thyroid gland to growth, increasing size and number of thyroid cells

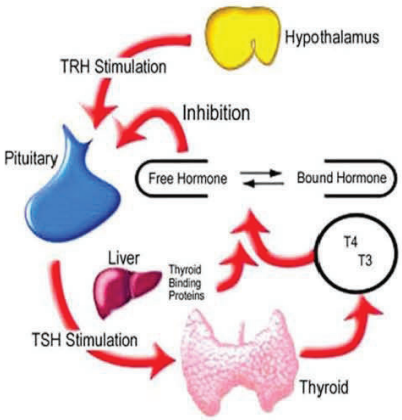
TRH (thyrotropin-releasing hormone)

- causes the anterior pituitary to produce and release of TSH.
- Cold and various emotional reactions can increase TRH secretion through nervous system



Feedback Mechanisms of Thyroid Hormones

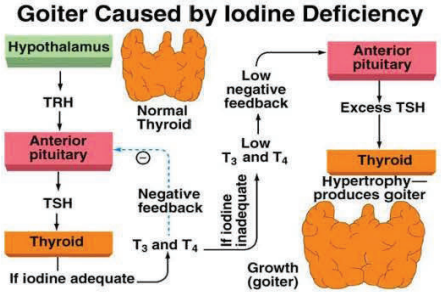
- T_3 and T_4 ⟶ inhibitory protein in anterior pituitary
  - reduces production and secretion of TSH
  - decrease response of pituitary to TRH
- Negative feedback



In the absence of sufficient dietary iodide the thyroid cannot produce adequate amounts of T_4 and T_3.

causes abnormally high level of the TSH secretion, which in turn stimulate the abnormal growth of the thyroid (a goiter).

Goiter Caused by Iodine Deficiency





Autoregulation of Thyroid Hormone Secretion

- thyroid gland adapt itself function to iodide uptake,
  - When iodine is insufficient, the thyroid gland increases formation of hormones
  - large doses of iodide act directly on the thyroid gland to produce a mild and transit inhibition of hormone synthesis.
- In patients with hyperthyroidism
  - iodides cause the vascularity of hyperplastic gland to decrease (Wolff-Chaikoff effect)
    - making iodide treatment considerable in preparing patients for surgery.

Effect of Autonomic Nervous System on Thyroid Activity

- The thyroid gland is innervated by both sympathetic nerve and parasympathetic nerve
  - sympathetic nerve increases formation of thyroid hormones
  - cholinergic fibers (vagus nerve) inhibits secretion of thyroid hormone

4. The Parathyroid Glands

4.1. Anatomy and Function

- The parathyroid glands are four small glands located on the posterior surface of the thyroid gland. They play a critical role in calcium homeostasis.

4.2. Functions of Parathyroid Hormone

- Parathyroid Hormone (PTH): Increases blood calcium levels by stimulating bone resorption, increasing intestinal calcium absorption, and promoting calcium reabsorption in the kidneys.

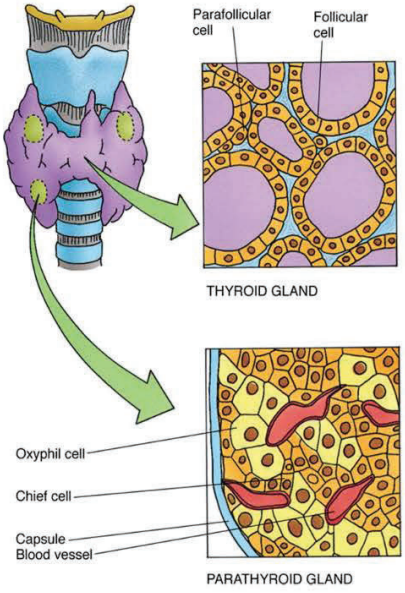


Parathyroid

Function is to control metabolism of calcium

- **Necessary for normal nerve and muscle function, blood clotting, healthy bones and teeth**
- **Located in back of thyroid gland (in neck)**
- **Hormone released is parathormone**
- **Undersecretion of parathormone results in nerve disorders, brittle bones and clotting problems**

Parathyroid Gland



The thyroid and parathyroid glands.

The parathyroid glands, usually four in number, are located on the posterior surface of the thyroid gland; each gland is enveloped in its own thin, collagenous connective tissue capsule.

The major functional parenchymal cells of the parathyroid glands are the slightly eosinophilic-staining chief cells which house PTH containing secretory granules. PTH acts on bone, kidneys, and the intestines in maintaining the optimal calcium concentrations in blood and interstitial tissue fluid.

The second cell type located in the parathyroid glands is the oxyphil cell. Its function is unknown, although it is believed that oxyphil cells and a third cell, described as an intermediate cell, probably represent inactive phases of a single cell type, with chief cells being the actively secreting phase.

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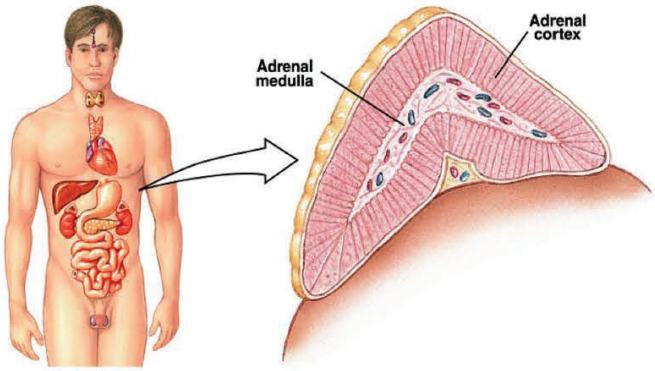
5. The Adrenal Glands

5.1. Anatomy and Function

- The adrenal glands are located above each kidney and consist of two main parts:
  - Adrenal Cortex: Produces corticosteroids that regulate metabolism, immune response, and stress.
  - Adrenal Medulla: Produces catecholamines (epinephrine and norepinephrine) involved in the fight-or-flight response.

Adrenal Gland

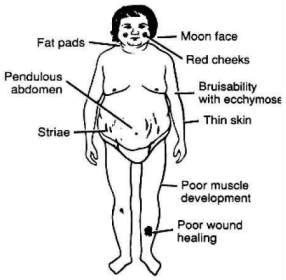


5.2. Hormones of the Adrenal Glands

- Cortisol: A glucocorticoid that regulates metabolism, reduces inflammation, and helps the body respond to stress.
- Aldosterone: A mineralocorticoid that regulates sodium and potassium balance, affecting blood pressure.
- Epinephrine (Adrenaline) and Norepinephrine: Mediate the body's fight-or-flight response, increasing heart rate, blood pressure, and energy supply.

5.3. Disorders of Adrenal Function

- Cushing's Syndrome: Results from excess cortisol production, leading to weight gain, hypertension, and muscle weakness.
- Addison's Disease: Caused by insufficient production of adrenal hormones, leading to fatigue, low blood pressure, and skin darkening.



CUSHING'S SYNDROME

Cushing's Syndrome

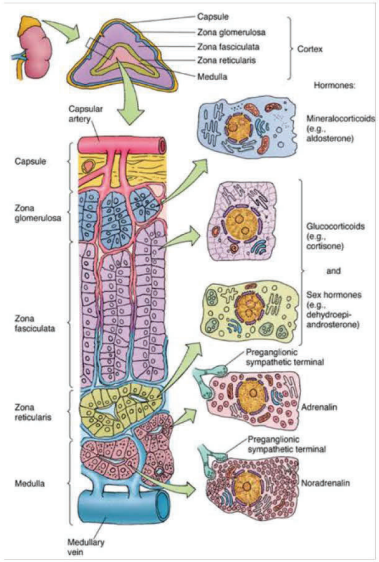
People with excess cortisol secretion

develop a peculiar type of obesity

excess deposition of fat in the chest and head regions of the body

a buffalo-like torso and a rounded "moon-face".

Suprarenal Glands



The suprarenal gland and its cell types.

The suprarenal gland is divided into two histologically and functionally different regions: an outer yellowish portion, called the suprarenal cortex, and a small, dark, inner portion called the suprarenal medulla. Although both entities are endocrine in function, each develops from a different embryological origin and performs a different role.

The suprarenal cortex is divided into three concentric regions, the outermost zona glomerulosa, the middle (and largest) zona fasciculata, and the innermost zona reticularis.

The zona glomerulosa, when stimulated by angiotensin II and ACTH, synthesize and release the hormones aldosterone and deoxycorticosterone.

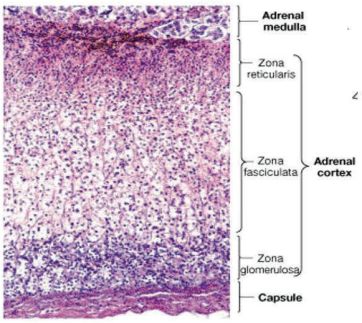
The zona fasciculata, whose cells are referred to as spongiocytes, when stimulated by ACTH, synthesize and release the hormones cortisol and corticosterone.

The zona reticularis, when stimulated by ACTH, synthesize and release dehydroepiandrosterone, androstenedione, and some glucocorticoids.

The suprarenal medulla is functionally related to and regulated by the sympathetic nervous system. Its parenchymal cells are known as chromaffin cells which are considered to be modified postganglionic sympathetic cell bodies. These chromaffin cells manufacture and release the neurotransmitter substances epinephrine and norepinephrine in response to preganglionic sympathetic splanchnic nerves.

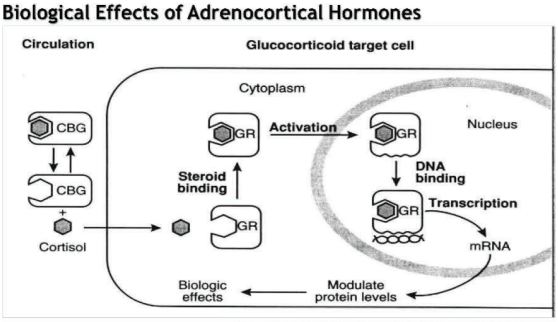
I. Adrenal Cortical Hormones

- **The mineralocorticoids are secreted by zona glomerulosa**
  - **regulates the concentration of the extracellular fluid.**
  - **Aldosterone is the principal mineralocorticoid.**



- **The glucocorticoids are secreted by both zona fasciculata and zona reticularis,**
  - **exhibiting an important effect on increasing blood glucose concentration**
  - **Cortisol is the principal glucocorticoid**
- **Small amounts of sex hormones are secreted by the zona reticularis.**

Biological Effects of Adrenocortical Hormones



CBG, corticosteroid-binding globulin; GR, glucocorticoid receptor

On metabolism

1) On carbohydrate metabolism.

A, Stimulation of gluconeogenesis by the liver cell

----activates DNA transcription in the liver cell nuclei and increase the synthesis of enzymes required for gluconeogenesis.

----causes mobilization of amino acids from extrahepatic tissues, mainly from muscle.

Result: a marked increase in glycogen storage in the liver cells.

B, Reduction of glucose utilization by the cells.

by inhibition of response of cells to insulin.

Elevate blood glucose concentration

2) On protein metabolism

A. mobilizes amino acids from the nonhepatic tissues and diminishes the tissue stores of protein.

B. decreases protein synthesis and increases catabolism of protein in many extrahepatic tissues especially in muscle and lymphoid tissue

In the presence of great excesses of cortisol, the muscles become weak and the immunity functions of lymphoid tissue decrease.

3) On fat metabolism

A. Promote mobilization of fatty acids from adipose tissue and increases the concentration of free acids in the plasma

B. Increases oxidation of fatty acids in the liver cells for energy.

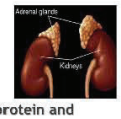
4) Effects on water and electrolytes

slight enhancement of sodium reabsorption and potassium excretion by distal tubules and colleting ducts in kidney.

increases the rate of renal blood flow and then glomerular filtration rates, facilitating water excretion

In patients with adrenal insufficiency, excretion of water is so slow that there is a danger of water intoxication and only glococorticoids can repair this deficit.

Adrenal Glands (Kidney Hats)



- Located at the top of each kidney
- Hormones released are cortisone and adrenaline
- Function of cortisone is to regulate carbohydrate, protein and fat metabolism
  - promotes conversion of fats and proteins to glucose
- Function of adrenaline is to raise blood sugar levels and increases heartbeat and breathing rates
- Undersecretion of adrenaline results in the inability to deal with stress



On blood cells

increase the production of red cells and platelets by stimulating bone marrow.

decrease the number of lymphocytes and eosinocytes

causes atrophy of the all lymphoid tissues and promotion of destruction of lymphocytes and eosinocytes.

On cardiovascular system

necessary for maintenance of normal blood pressure.

Cause permissive action, enhancing the response of vascular muscle to catecholamines.

Inhibit synthesis of prostaglandins that have vasodilator effect.

Reduces the permeability of capillaries, which is useful to maintenance of blood volume.

Effect on stress.

Almost any type of stress cause increase in ACTH secretion, and consequent cortisol secretion.

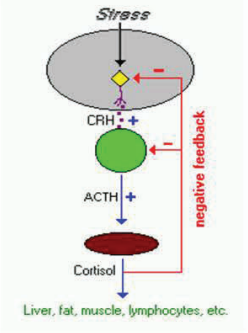
essential for survival.

Other effects.

increase production of HCl and pepsin,

promotion of synthesis of fetal surfactant.

pharmacological effects including anti-inflammatory, antiallergic and antishock



Regulation of Secretion of Adrenocortical Hormone

Hypothalamus - Anterior Pituitary - Adrenocortical Axis

1. Action of ACTH (adrenocorticotropin hormone)

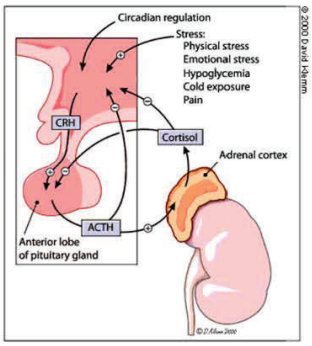
control of cortisol secretion

ACTH causes

formation of adrenocortical

adrenocortical secretion.

hypertrophy and proliferation of the adrenocorticol cells.



2. CRH (corticotropin releasing hormone)

A, Action of CRH

promote synthesis and release of ACTH

B, Regulation of CRH secretion

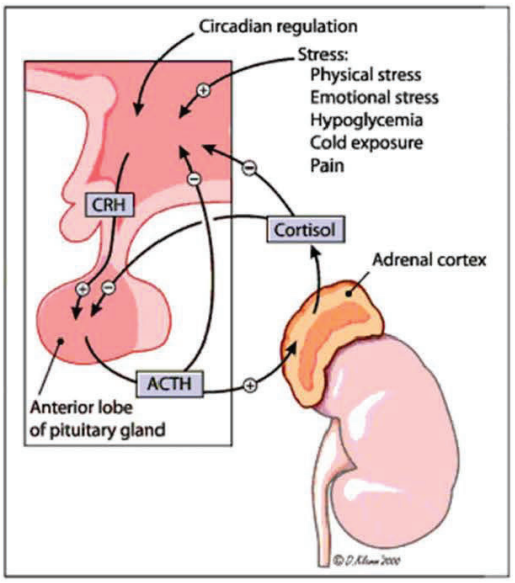
(3) Feedback mechanism

Cortisol has direct negative feedbacks on the hypothalamus to decrease formation of CRH

High circulating levels of cortisol inhibit secretion and formation of ACTH, decreasing response of anterior pituitary gland to CRH.

High levels of ACTH also inhibit CRH secretion by a negative feedback mechanism.

These feedbacks help regulate the plasma concentration of cortisol toward a normal control level.



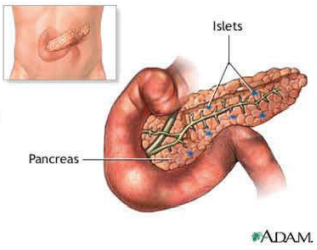
6. The Pancreas

6.1. Anatomy and Function

- The pancreas serves both endocrine and exocrine functions. The endocrine portion consists of the islets of Langerhans, which regulate blood sugar levels.

Islet of Langerhans

- **Located on the pancreas**
- **Hormones secreted are insulin and glucagon**
- **Insulin stimulates glucose uptake by cells**
- **Glucagon promotes conversion of glycogen (animal-based carbohydrate) to glucose**



6.2. Hormones of the Pancreas

- Insulin: Lowers blood glucose by promoting glucose uptake into cells and storage as glycogen.
- Glucagon: Increases blood glucose by stimulating glycogen breakdown in the liver.
- Somatostatin: Inhibits the secretion of both insulin and glucagon to regulate blood sugar balance.

6.3. Disorders of Pancreatic Function

- Diabetes Mellitus Type 1: Autoimmune destruction of insulin-producing beta cells, leading to insulin deficiency.
- Diabetes Mellitus Type 2: Insulin resistance where cells do not respond effectively to insulin, often associated with obesity.

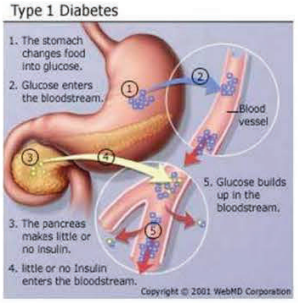
Blood Sugar Regulation

- **Oversecretion of insulin results in low blood sugar**
- **Undersecretion of insulin results in high blood sugar**
  - **This can lead to a condition known as diabetes**

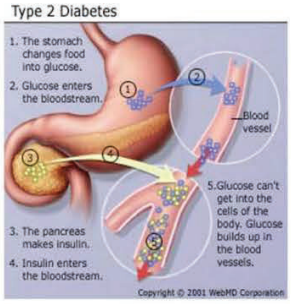
- **Type 1- Usually found in children and young adults; the body doesn't make enough insulin**
  - **Symptoms:**
    - **Frequent urination**
    - **Unusual thirst**
    - **Extreme hunger**
    - **Unusual weight loss**
    - **Extreme fatigue and Irritability**

- **Type 2- Either the body doesn't produce enough insulin, or the cells ignore it.**
  - **If you consume too much sugar over a long period of time, your body has to release large amounts of insulin. This can result in your cells building up a tolerance for insulin, which means they won't be affected by it.**
  - **Symptoms:**
    - **Any of the type 1 symptoms**
    - **Frequent infections**
    - **Blurred vision**
    - **Cuts/bruises that are slow to heal**
    - **Tingling/numbness in the hands/feet**
    - **Recurring skin, gum, or bladder infections**

Type 1 Diabetes



Type 2 Diabetes



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7. The Gonads (Ovaries and Testes)

7.1. Ovaries (in females)

- The ovaries produce estrogens and progesterone, which regulate the menstrual cycle, development of secondary sexual characteristics, and pregnancy maintenance.

7.2. Testes (in males)

- The testes produce testosterone, which is responsible for sperm production, development of male secondary sexual characteristics, and libido.

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8. Regulation of Endocrine Activity

8.1. Feedback Mechanisms

- Negative Feedback: A process that maintains hormone levels within a specific range. When hormone levels rise above a set point, feedback inhibits further hormone release (e.g., thyroid hormone regulation by TSH).

- Positive Feedback: Less common, this mechanism amplifies the release of hormones. An example is oxytocin during childbirth, where increasing contractions stimulate more oxytocin release.

8.2. Hypothalamic-Pituitary Axis

- The hypothalamus and pituitary gland are central regulators of endocrine function. The hypothalamus produces releasing and inhibiting hormones that control the anterior pituitary's hormone release. This axis regulates the thyroid, adrenal glands, and gonads through a series of feedback loops.

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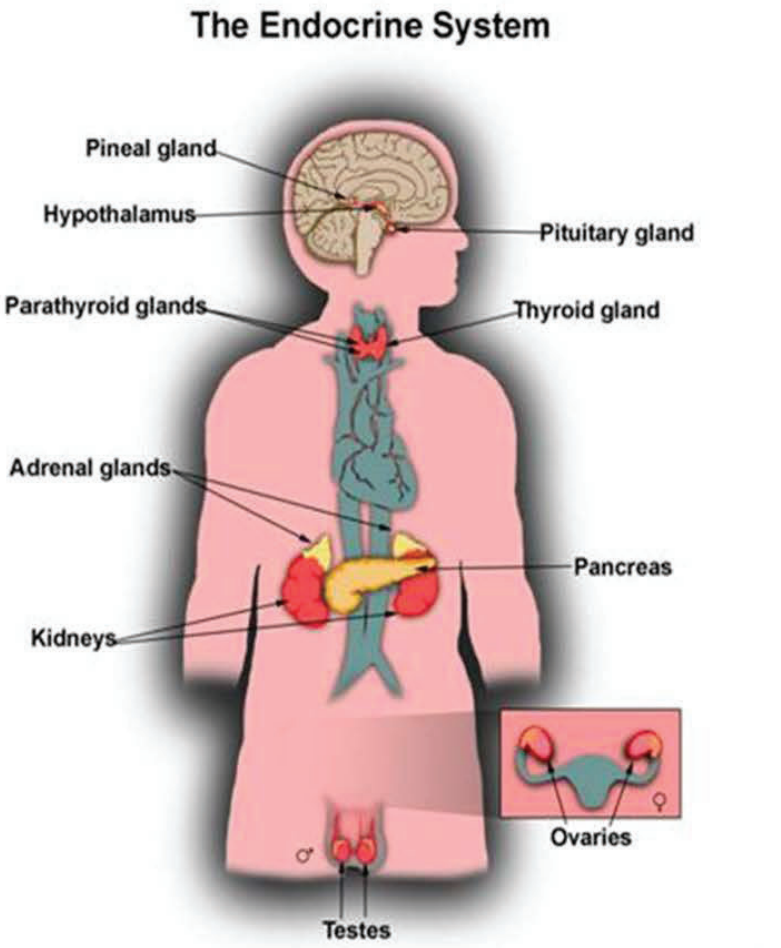
9. Practical Applications and Clinical Implications

9.1. Endocrine Disorders

- Diabetes Mellitus: A group of metabolic disorders characterized by high blood glucose due to insulin deficiency (Type 1) or insulin resistance (Type 2).
- Hypothyroidism and Hyperthyroidism: Conditions related to the underproduction or overproduction of thyroid hormones, affecting metabolism.
- Cushing's Syndrome: Caused by prolonged exposure to high levels of cortisol, leading to obesity, hypertension, and other metabolic disturbances.
- Addison's Disease: A disorder in which the adrenal glands do not produce enough cortisol or aldosterone, leading to fatigue, weight loss, and hypotension.



9.2. Diagnostic Tools

- Blood Tests: Measure hormone levels such as thyroid-stimulating hormone (TSH), cortisol, insulin, and glucose levels to diagnose endocrine imbalances.
- Imaging: Techniques like ultrasound, MRI, or CT scans are used to visualize endocrine glands and detect abnormalities such as tumors or structural changes.

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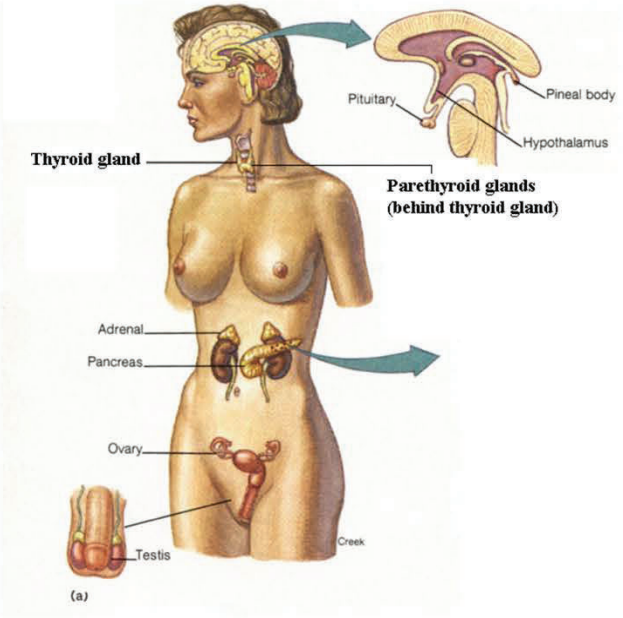
10. Review and Case Studies

- Case studies on endocrine disorders:
  Discuss real-life cases involving conditions like diabetes, hypothyroidism, and Cushing's syndrome, emphasizing the diagnostic process and treatment strategies.
- Clinical examples:
  Explore scenarios involving hormone replacement therapy, regulation of blood glucose in diabetes, and the role of hormone imbalances in growth and development.

Practical Session 7: Endocrine System

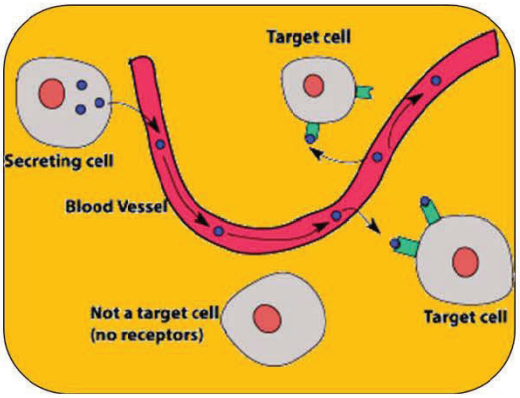


1. Introduction to the Endocrine System

The endocrine system is a network of glands that produce and secrete hormones, which are chemical messengers responsible for regulating a wide range of physiological processes, including metabolism, growth, reproduction, and homeostasis. Unlike the nervous system, which uses electrical signals for fast responses, the endocrine system uses hormones that travel through the bloodstream, allowing for slower, but longer-lasting effects. Endocrine glands are ductless, meaning their hormones are released directly into the bloodstream to reach distant target organs.

2. Concept of Hormones

Hormones are biochemical substances that act as messengers between endocrine glands and target cells. Hormones regulate various bodily functions by binding to specific receptors on or inside target cells, triggering specific physiological responses. There are several types of hormones:

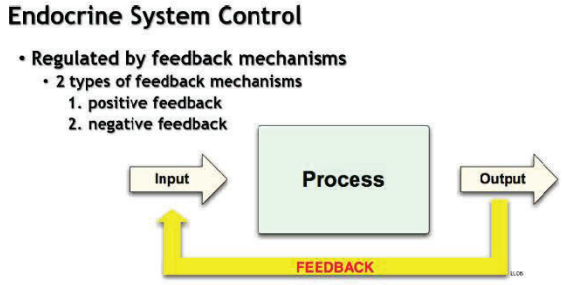


- Peptide/Protein Hormones: Such as insulin and glucagon, are water-soluble and bind to receptors on the surface of cells.
- Steroid Hormones: Such as cortisol and sex hormones, are lipid-soluble and can cross the cell membrane to bind to intracellular receptors.
- Amine Hormones: Derived from amino acids, such as thyroxine and catecholamines (epinephrine and norepinephrine).

3. Endocrine System Control

The endocrine system operates through a delicate balance of hormone secretion and feedback regulation. Feedback mechanisms ensure that hormone levels are kept within an optimal range.

3.1. Feedback Mechanisms



- Negative Feedback: This is the most common form of hormonal regulation. When hormone levels rise above or fall below the desired threshold, the endocrine system modulates its production. For example, when blood glucose levels rise, insulin is released by the pancreas to reduce glucose levels. Once blood glucose returns to normal, insulin secretion decreases.
- Positive Feedback: Positive feedback mechanisms amplify the response to a stimulus until a particular outcome is achieved. For instance, during childbirth, the release of oxytocin increases uterine contractions. These contractions lead to more oxytocin release, further intensifying the contractions until delivery is completed.

4. Hormonal Actions and Target Cells

4.1. Specificity of Hormones

Hormones exhibit specificity, meaning they affect only certain cells with the appropriate receptors. These receptors can be located either on the cell membrane or inside the cell (in the cytoplasm or nucleus). The specificity of hormone action is determined by the presence of these receptors:

- Surface receptors are typically for water-soluble hormones (e.g., peptide hormones).
- Intracellular receptors are for lipid-soluble hormones (e.g., steroid hormones).

4.2. Mechanisms of Action

- Water-soluble hormones (e.g., insulin) bind to receptors on the surface of the target cell, activating intracellular signaling pathways. This usually involves second messenger systems (e.g., cAMP) to elicit a rapid cellular response.
- Lipid-soluble hormones (e.g., cortisol) diffuse through the cell membrane and bind to intracellular receptors. These hormone-receptor complexes then enter the nucleus and alter gene transcription, resulting in longer-lasting effects.

- **Homeostasis is often maintained by two hormones who have antagonistic effects**
  - **Each hormone does the opposite of the other.**
    - **For example, if the blood pressure drops too low, the pituitary releases ADH, which causes the kidneys to reabsorb more water. If it the blood pressure increases too much, then the heart will release ANH, which will cause the kidneys to reabsorb less water.**

- **Negative Feedback mechanisms:**
  - **Act like a thermostat in a home**
  - **As the temperature cools, the thermostat detects the change and triggers the furnace to turn on and warm the house**
  - **Once the temperature reaches its thermostat setting, the furnace turns off**
    - **Example: Body sugar increases after a meal, so the pancreas secretes insulin, which tells the body's cells to take in glucose. Once blood sugar levels reach normal, the pancreas stops making insulin.**
    - **Often used to maintain homeostasis**

Positive Feedback Mechanisms

- **Positive Feedback mechanisms control events that can be out of control and do not require continuous adjustment**
- **Rarely used to maintain homeostasis**
- **Example of positive feedback found in childbirth**
  - **Oxytocin stimulates and enhances labor contractions**
  - **As labor continues, more oxytocin is produced**
  - **Intensifies contractions until the baby is outside birth canal**
  - **Oxytocin production stops and labor contractions stop**

Endocrine vs. Nervous System



Nervous system

- **exerts point-to-point control through nerves,**
  - **similar to sending messages by conventional telephone.**
- **electrical in nature and fast.**

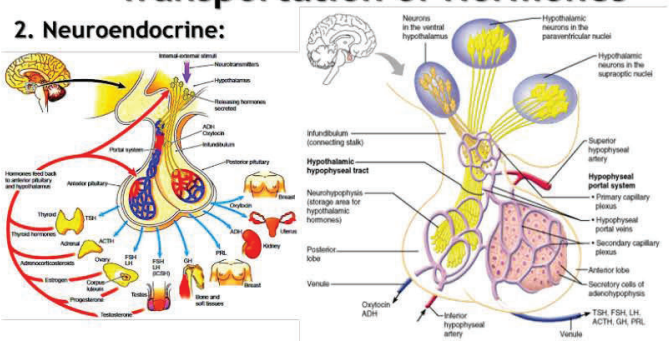
Hormones travel via the bloodstream to target cells

- **broadcasts its hormonal messages to essentially all cells**
  - **by secretion into blood and extracellular fluid.**
- **requires a receiver to get the message -**
  - **cells bear a *receptor***



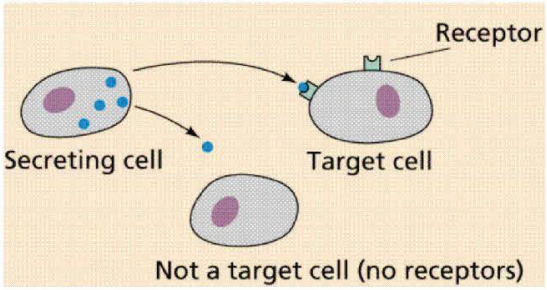
Transportation of Hormones

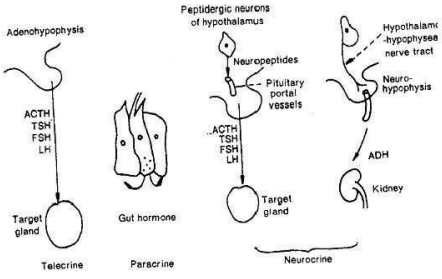
2. Neuroendocrine:

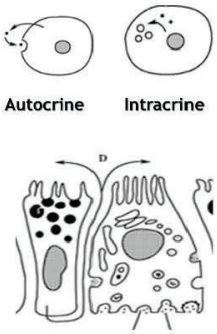


Transportation of Hormones

3. Paracrine

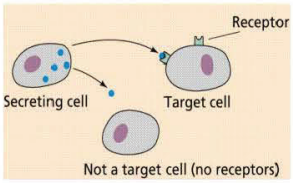






Properties of the hormone effect

1. Specificity



The receptors may be present

- **on the plasma membrane**
- **in the cytoplasm**
- **in the nucleus**

are protein in nature

may contain carbohydrate or phospholipid moieties

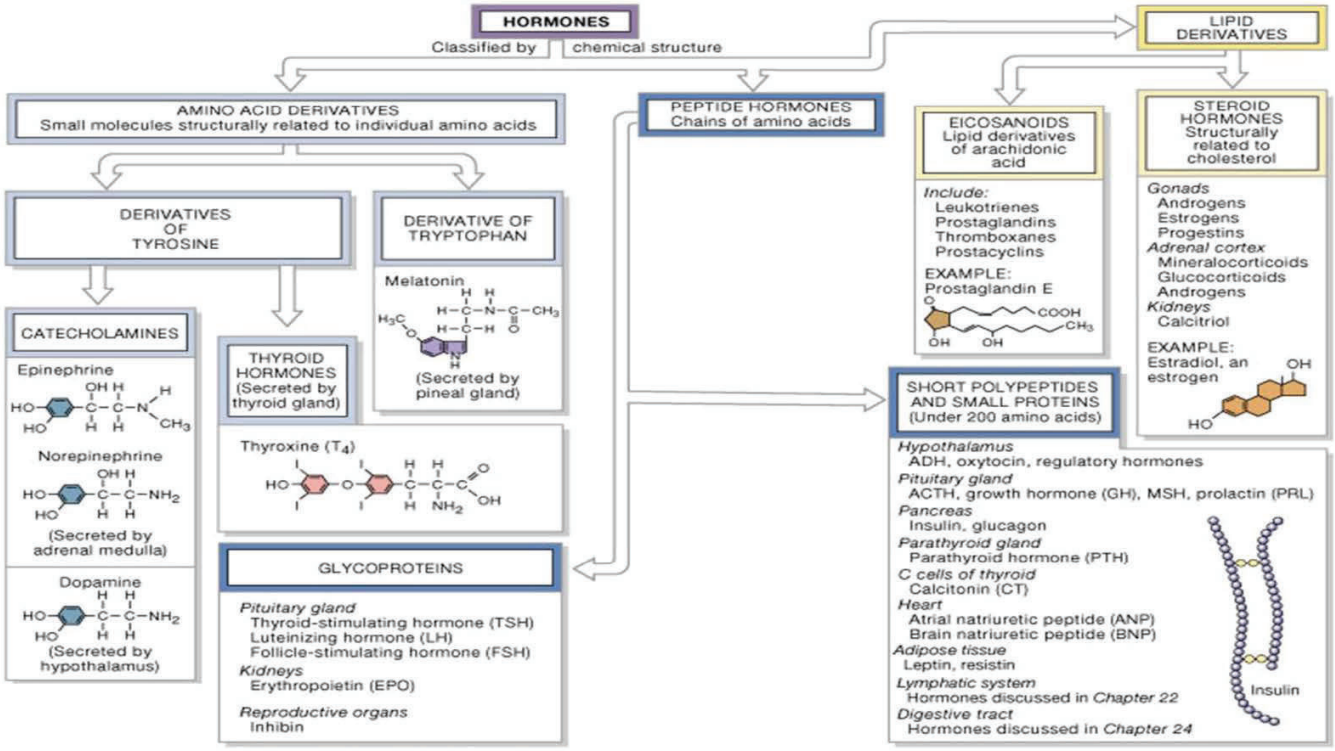
2. Signal Transmission

The role of the hormones is to transit the regulatory signals from the control (endocrine) system to the target cells (organs or glands).

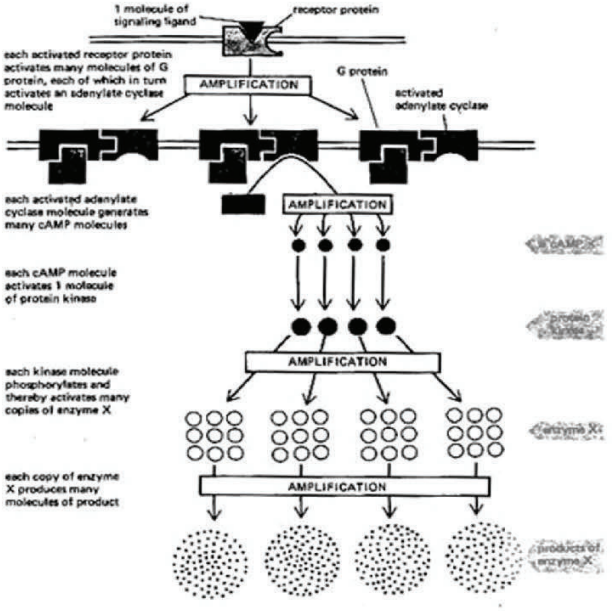
enhance or inhibit some function of the target.

3. High Biological Efficiency

Low plasma concentration (nmol - pmol/L) ⟶ great regulatory function



Signal amplification during the transmembrane and intracellular transmission



VI. Mechanisms of Hormonal Action

first step: to bind to specific receptors at the target cell.

Locations for the different types of hormones:

1) On the surface of the cell membrane.
   protein, peptide, and catecholamine hormones
2) In the cell cytoplasm.
   steroid hormones
3) In the cell nucleus.
   thyroid hormones (T_3 and T_4)

4. Interaction Between the Hormones

(1) Synergistic effects.

Additive:

Same effect of the hormones on one target organ, for example, epinephrine and norepinephrine on the heart rate

Complementary: Work on different stages of a physiological procedure, FSH (initiation) and testosterone (maintenance) on spermatogenesis

(2) Permissive effect.

A hormone

enhances the responsiveness of a target organ to the second hormone

increases the activity of the second hormone.

Estrogen - Expression of progesterone receptors on uterus - progesterone effect on the uterus.

Glucocorticoids - effects of catecholamines on cardiovascular system

(3) Antagonist Effects.

one hormone antagonize the effects of another.

1. Second Messenger Mechanisms for Mediating Intracellular Hormonal Functions

Hydrophilic hormones (proteins, peptides and catecholamine)

--bind the receptors on the membrane,

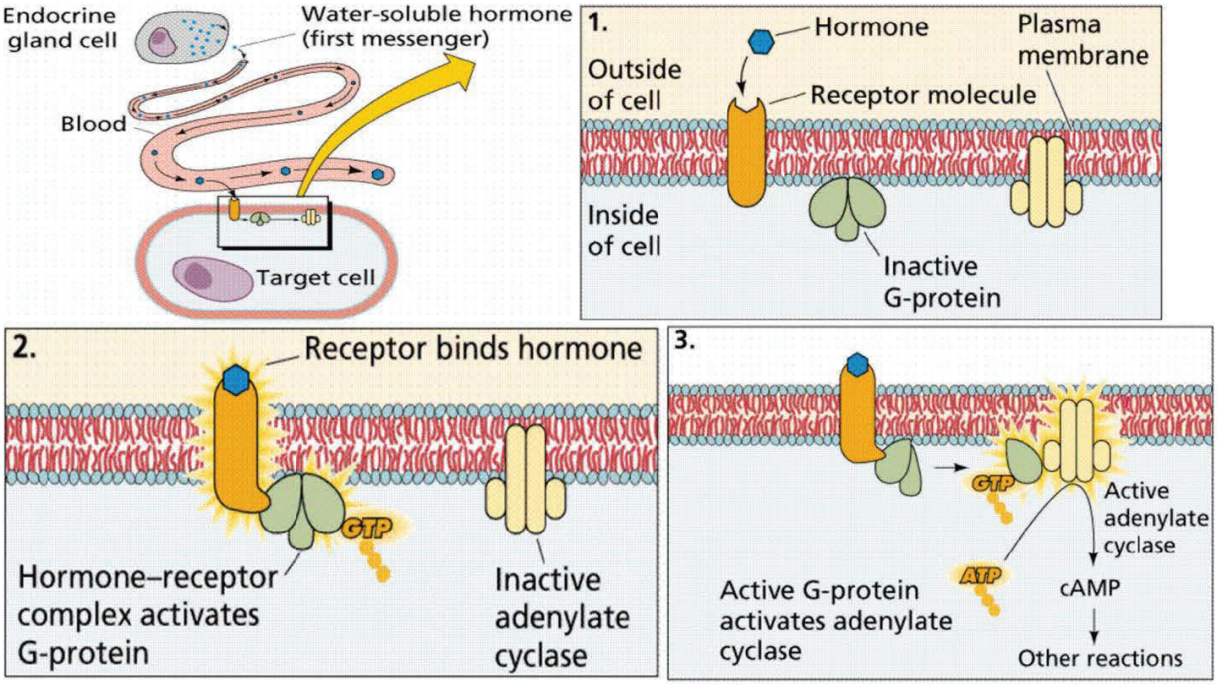
--activate some enzyme on the membrane,

-- regulate the concentration of some messengers (second messengers) in the cytoplasm. .

5. Hormonal Signaling and Second Messenger Systems

Hormonal signals are transmitted through intricate biochemical pathways, and the process often involves the use of second messengers.

- Second Messengers:
  - Second messengers like cyclic AMP (cAMP), calcium ions (Ca^{2+}), and inositol triphosphate (IP_3) mediate the effects of hormones by amplifying the signal within the cell. For example, when epinephrine binds to a receptor on the cell surface, it activates adenylate cyclase, which converts ATP to cAMP. cAMP then activates protein kinases, leading to physiological responses such as glycogen breakdown in the liver.
- Signal Amplification:
  - Hormonal binding to a receptor can trigger a cascade of events, resulting in the activation of multiple second messengers. This amplification ensures that even a small amount of hormone can produce a large biological effect. For instance, a single molecule of epinephrine can lead to the activation of thousands of enzyme molecules in the target cell.



7. Practical Experiments and Demonstrations

7.1. Measuring Hormone Levels

Students will learn techniques to measure hormone levels in blood or urine, such as ELISA (Enzyme-Linked Immunosorbent Assay) or radioimmunoassay. These techniques allow for the quantification of hormones like cortisol, insulin, or thyroid hormones, helping in the diagnosis of endocrine disorders.

7.2. Feedback Mechanism Simulation

This experiment simulates negative feedback control. Students will model how hormone levels are regulated by feedback loops, showing how the secretion of hormones like insulin and glucagon are adjusted based on blood glucose levels.

7.3. Hormone Receptor Interaction

Using cellular models, students will observe how hormones bind to their receptors and activate intracellular pathways. This demonstration will highlight the interaction between hormones like epinephrine and their receptors, leading to a cascade of second messengers and physiological changes in target cells.

Examination and Assessment

1	Pituitary gland	
a.	round organ about the size of a pea, located behind the bridge of the nose at the base of the brain	True
b.	secretes 9 different hormones	True
c.	Affect Sex organ functions in both men and women	True
d.	Affect Thyroid gland function	True
e.	Affect Metabolism	True
f.	Affect the mechanism of nuclear fusion	False
g.	Affect electricity transport and distribution	False
h.	Affect psychological aspects of life	False
i.	Affect theory and practice of human life	False
j.	Affect the mechanism of spatial integration	False

2	The endocrine system	
a.	is consisting of ductless glands	True
b.	distinct clusters of cells and diffuse neuroendocrine cells, regulates metabolic activities	True
c.	Is helping to bring about homeostasis	True
d.	Involve chemical substances called hormones	True
e.	Hormones are released into the bloodstream to influence target cells at remote sites	True
f.	is consisting of external glands	False
g.	distinct clusters of cells and diffuse neuroendocrine cells that regulates voluntarily activities	False
h.	Is helping to bring about dysterss	False
i.	Involve chemical substances called neurotransmitters	False
j.	Hormones are released into the bloodstream to influence mechanic activities	False

3	Releasing or inhibitory hormones of Hypothalamus are:	
a.	Thyroid-stimulating hormone–releasing hormone (TRH)	True
b.	Corticotropin-releasing hormone (CRH)	True
c.	Somatotropin-releasing hormone (SRH)	True
d.	Gonadotropin-releasing hormone (GnRH)	True
e.	Prolactin-releasing hormone (PRH) and Prolactin inhibitory factor (PIF)	True
f.	TSH, Thyroid stimulating hormone	False
g.	ACTH, Adrenocorticotropin hormone	False
h.	GH, Growth Hormone	False
i.	FSH, Follicle-stimulating hormone, LH, Luteinizing hormone and PRL, Prolactin	False
j.	MSH, Melanophore-stimulating hormone	False

4	Blood Supply of the Pituitary Gland	
a.	The arterial supply is provided from two pairs of vessels that arise from the internal carotid artery	True
b.	The superior hypophyseal arteries supply the pars tuberalis and the infundibulum	True
c.	The superior hypophyseal arteries also form an extensive capillary network	True
d.	Inferior hypophyseal arteries primarily supply the posterior lobe	True
e.	Inferior hypophyseal arteries primarily also send a few branches to the anterior lobe	True
f.	The arterial supply is provided from vessels that arise from the pulmonary arteries	False
g.	The superior hypophyseal arteries supply the hypothalamus	False
h.	The superior hypophyseal arteries supply the liver	False
i.	Inferior hypophyseal arteries primarily supply the thalamus	False
j.	Inferior hypophyseal arteries primarily also send a few branches to meninges	False

5	Hypothalamic neurosecretory hormones:	
a.	Are manufactured in the hypothalamus	True
b.	Are stored in the median eminence, enter the primary capillary plexus and are drained by the hypophyseal portal veins	True
c.	Portal veins connect to the secondary capillary plexus in the anterior lobe of the pituitary gland	True
d.	The neurosecretory hormones leave the blood to stimulate or inhibit the parenchymal cells	True
e.	The hypophyseal portal system is used for regulation of the pars distalis by the hypothalamus.	True
f.	Are manufactured in the thalamus	False
g.	Are stored in the hepatic portal veins	False
h.	Portal veins connect to cerebellum	False
i.	The neurosecretory hormones leave the blood to stimulate or inhibit the nervous system	False
j.	The hypophyseal portal system is used for regulation of cerebral activity	False

6	Axons of neurons that originate in various portions of the hypothalamus:	
a.	Terminate around the capillary plexuses	True
b.	The endings of these axons differ from other axons of the body	True
c.	Instead of delivering a signal to another cell, they liberate either releasing or inhibiting hormones	True
d.	Hormones are taken by the hypophyseal portal system and delivered to the secondary capillary bed	True
e.	Hormones regulate secretion of various anterior pituitary hormones.	True
f.	Terminate around the thalamus	False
g.	The endings of these axons are similar to sympathetic axons	False
h.	Instead of delivering a signal to another cell, they liberate either releasing or inhibiting waste products	False
i.	Hormones are secreted by the hypophyseal portal system	False
j.	Hormones stimulate secretion of various posterior pituitary waste products	False

7	Anterior pituitary, also known as the adenohypophysis secrets:	
a.	TSH, Thyroid stimulating hormone	True
b.	ACTH, Adrenocorticotropin hormone	True
c.	GH, Growth Hormone	True
d.	FSH, Follicle-stimulating hormone, LH, Luteinizing hormone and PRL, Prolactin	True
e.	MSH, Melanophore-stimulating hormone	True
f.	Thyroid-stimulating hormone–releasing hormone (TRH)	False
g.	Corticotropin-releasing hormone (CRH)	False
h.	Somatotropin-releasing hormone (SRH)	False
i.	Gonadotropin-releasing hormone (GnRH)	False
j.	Prolactin-releasing hormone (PRH) and Prolactin inhibitory factor (PIF)	False

8	Growth Hormone - somatotropin	
a.	Oversecretion of growth hormone: Gigantism in childhood and acromegaly in adults	True
b.	Undersecretion of growth hormone: Dwarfism in childhood	True
c.	Stimulates cell division, especially in muscle and epiphyseal cartilage of long bones	True
d.	Stimulates growth in skeletal muscle, heart, skin, connective tissue, liver, kidney	True
e.	Stimulates growth in pancreas, intestines, adrenals and parathyroids	True
f.	Undersecretion of growth hormone: Gigantism in childhood and acromegaly in adults	False

g.	Oversecretion of growth hormone: Dwarfism in childhood	False
h.	Inhibites cell division, especially in muscle and epiphyseal cartilage of long bones	False
i.	Inhibites growth in skeletal muscle, heart, skin, connective tissue, liver, kidney	False
j.	Inhibites growth in pancreas, intestines, adrenals and parathyroids	False

9	Cells of the Pituitary Gland	
a.	Pars distalis possesses three types of cells, acidophils and basophils (chromophils) and chromophobes	True
b.	There are two types of acidophils:, somatotrophs and mammotrophs	True
c.	Somatotrophs secrete somatotropin (growth hormone);	True
d.	Mammotrophs release the hormone prolactin, which promotes mammary gland development during pregnancy	True
e.	Mammotrophs release the hormone prolactin, which promotes lactation after birth.	True
f.	Pars distalis possesses two types of cells, acidophils and chromophobes	False
g.	There are two types of basophils:, somatotrophs and mammotrophs	False
h.	Somatotrophs secrete corticotrophs;	False
i.	Mammotrophs release the lipotropic hormone	False
j.	Mammotrophs release gonadotrophs	False

10	Basophils cells of the Pituitary Gland	
a.	Basophils house granules that stain blue with basic dyes	True
b.	Are three types of basophils, corticotrophs, thyrotrophs, and gonadotrophs.	True
c.	Corticotrophs secrete adrenocorticotropic hormone (ACTH) and lipotropic hormone (LPH)	True
d.	Thyrotrophs can be distinguished by their small secretory granules which contain TSH	True
e.	Gonadotrophs secrete FSH and LH	True
f.	Pars distalis possesses two types of cells, acidophils and chromophobes	False
g.	There are two types of basophils:, somatotrophs and mammotrophs	False
h.	Somatotrophs secrete corticotrophs;	False
i.	Mammotrophs release the lipotropic hormone	False
j.	Mammotrophs release gonadotrophs	False

11	Thyroid:	
a.	Located in the neck	True
b.	Releases hormone thyroxin	True
c.	The function is to regulate rates of metabolism in the body	True
d.	Essential for normal physical and mental development	True
e.	Oversecretion of thyroxin results in nervousness and weight loss	True
f.	Located in the thorax	False
g.	Releases hormone prolactin	False
h.	The function is to regulate rates of anxiety in the body	False
i.	Essential for exaggerated physical and mental development	False
j.	Oversecretion of thyroxin results in over-happiness	False

12	Biological Actions of Thyroid Hormones	
a.	T3 and T4 bind with nuclear receptor,	True
b.	activate and initiate genetic transcription	True
c.	regulate protein synthesis in cytoplasmic ribosomes	True
d.	general increase in functional activity throughout the body.	True

e.	increase O2 consumption of most tissues in the body	True
f.	T3 and T4 bind with extracelular receptors	False
g.	activate and initiate glucolitic mechanisms	False
h.	Stimulate protein degradation in cytoplasmic ribosomes	False
i.	general decrease de metabolism	False
j.	decrease O2 and increase CO2 consumption of most tissues in the body	False

13	Regulation of Thyroid Hormone Secretion	
a.	Hypothalamic Pituitary Thyroid Axis	True
b.	Feedback Mechanisms	True
c.	Autoregulation	True
d.	Effect of Autonomic Nervous System	True
e.	Thyroid-stimulating hormone–releasing hormone (TRH)	True
f.	Hypothalamic Adrenal Axis	False
g.	Energetic Mechanisms	False
h.	Corticotropin-releasing hormone (CRH)	False
i.	Effect of Somatic Nervous System	False
j.	Prolactin	False

14	Parathyroid:	
a.	Function is to control metabolism of calcium	True
b.	Necessary for normal nerve and muscle function, blood clotting, healthy bones and teeth	True
c.	Located in back of thyroid gland (in neck)	True
d.	Hormone released is parathormone	True
e.	Under secretion of parathormone results in nerve disorders, brittle bones and clotting issues	True
f.	Function is to control metabolism of sodium	False
g.	Necessary for normal digestive function	False
h.	Located in back of adrenal glands	False
i.	Hormone released is Prolactin	False
j.	Undersecretion of Prolactin results in nerve disorders, brittle bones and clotting problems	False

15	Adrenal Glands (Kidney Hats) - Suprarenal Glands	
a.	Located at the top of each kidney	True
b.	Hormones released are cortisone and adrenaline	True
c.	Function of cortisone is to regulate carbohydrate, protein and fat metabolism	True
d.	promotes conversion of fats and proteins to glucose	True
e.	The function of adrenaline is to raise blood sugar levels and increase heartbeat and breathing rates	True
f.	Located back of thyroid gland (in neck)	False
g.	Necessary for normal nerve and muscle function, blood clotting, healthy bones and teeth	False
h.	Located in back of thyroid gland (in neck)	False
i.	Hormone released is parathormone	False
j.	Under secretion of parathormone results in nerve disorders, brittle bones and clotting issues	False

16	The suprarenal gland is divided into:	
a.	two histologically regions	True
b.	functionally different regions	True
c.	an outer yellowish portion, called the suprarenal cortex	True

d.	and a small, dark, inner portion called the suprarenal medulla	True
e.	Yellowish and dark portions are endocrine in function, each develops from a different embryological origin	True
f.	Basophils house granules that stain blue with basic dyes	False
g.	Are three types of basophils, corticotrophs, thyrotrophs, and gonadotrophs.	False
h.	secrete adrenocorticotropic hormone (ACTH) and lipotropic hormone (LPH)	False
i.	Thyrotrophs can be distinguished by their small secretory granules which contain TSH	False
j.	Gonadotrophs and Corticotrophs	False

17	The zona glomerulosa of the suprarenal gland:	
a.	stimulated by angiotensin II	True
b.	stimulated by ACTH	True
c.	synthesize aldosterone and deoxycorticosterone	True
d.	release aldosterone and deoxycorticosterone	True
e.	synthesize and release deoxycorticosterone	True
f.	Cells are referred to as spongiocytes	False
g.	stimulated by ACTH	False
h.	synthesize the hormones cortisol and corticosterone.	False
i.	release cortisol	False
j.	release corticosterone	False

18	The zona fasciculata of the suprarenal gland:	
a.	Cells are referred to as spongiocytes	True
b.	stimulated by ACTH	True
c.	synthesize the hormones cortisol and corticosterone.	True
d.	release cortisol	True
e.	release corticosterone	True
f.	stimulated by angiotensin II	False
g.	stimulated by ACTH	False
h.	synthesize aldosterone and deoxycorticosterone	False
i.	release aldosterone and deoxycorticosterone	False
j.	synthesize and release deoxycorticosterone	False

19	The zona reticularis of the suprarenal gland:	
a.	stimulated by ACTH,	True
b.	synthesize dehydroepiandrosterone, androstenedione, and some glucocorticoids	True
c.	release dehydroepiandrosterone.	True
d.	release androstenedione	True
e.	release some glucocorticoids	True
f.	is functionally related to and regulated by the sympathetic nervous system.	False
g.	Its parenchymal cells are known as chromaffin cells	False
h.	chromaffin cells are considered to be modified postganglionic sympathetic cell bodies.	False
i.	chromaffin cells manufacture and release the neurotransmitter epinephrine	False
j.	chromaffin cells manufacture and release the neurotransmitter norepinephrine	False

20	The suprarenal medulla	
a.	is functionally related to and regulated by the sympathetic nervous system.	True
b.	Its parenchymal cells are known as chromaffin cells	True

c.	chromaffin cells are considered to be modified postganglionic sympathetic cell bodies.	True
d.	chromaffin cells manufacture and release the neurotransmitter epinephrine	True
e.	chromaffin cells manufacture and release the neurotransmitter norepinephrine	True
f.	Function is to control metabolism of calcium	False
g.	Necessary for normal nerve and muscle function, blood clotting, healthy bones and teeth	False
h.	Located in back of thyroid gland (in neck)	False
i.	Hormone released is parathormone	False
j.	Undersecretion of parathormone results in nerve disorders, brittle bones and clotting problems	False

21	Biological Effects of Adrenocortical Hormones on carbohydrate metabolism:	
a.	Stimulation of gluconeogenesis by the liver cell	True
b.	Activates DNA transcription in the liver cell nuclei and increase the enzymes required for gluconeogenesis.	True
c.	Causes mobilization of amino acids from extrahepatic tissues, mainly from muscle.	True
d.	Result in a marked increase in glycogen storage in the liver cells.	True
e.	Reduction of glucose utilization by cells, by inhibition of response of cells to insulin, elevate blood glucose levels	True
f.	Stimulation of gluconeogenesis by the nervous cell	False
g.	Activates DNA fosforilation in the brain cell nuclei and increase the enzymes required for glucolisis.	False
h.	Causes mobilization of DNA from extrahepatic tissues, mainly from muscle.	False
i.	Resul in a marked increase in glycogen degradation	False
j.	Increase glucose utilization by cells	False

22	Biological Effects of Adrenocortical Hormones on protein metabolism:	
a.	mobilizes amino acids from the nonhepatic tissues	True
b.	diminishes the tissue stores of protein	True
c.	decreases protein synthesis	True
d.	increases catabolism	True
e.	increases catabolism of protein in many extrahepatic tissues	True
f.	mobilizes carbohidrates from the nonhepatic tissues	False
g.	increases the tissue stores of protein	False
h.	increases protein synthesis	False
i.	decreases catabolism	False
j.	decreases catabolism of protein in many extrahepatic tissues	False

23	Excess cortisol secretion individuals:	
a.	may have Cushing's Syndrome	True
b.	develop a peculiar type of obesity	True
c.	excess deposition of fat in the chest and head regions of the body	True
d.	have a buffalo-like torso	True
e.	have a rounded "moon-face"	True
f.	Oversecretion of growth hormone: Gigantism in childhood and acromegaly in adults	False
g.	Undersecretion of growth hormone: Dwarfism in childhood	False
h.	Stimulates cell division, especially in muscle and epiphyseal cartilage of long bones	False
i.	Stimulates growth in skeletal muscle, heart, skin, connective tissue, liver, kidney	False
j.	Stimulates growth in pancreas, intestines, adrenals and parathyroids	False

24	Biological Effects of Adrenocortical Hormones on water and electrolytes :	
a.	slight enhancement of sodium reabsorption	True
b.	enhancement of potassium excretion by distal tubules and colleting ducts in kidney	True
c.	increases the rate of renal blood flow	True
d.	increases the glomerular filtration rates	True
e.	facilitates water excretion	True
f.	slight enhancement of erytrocytes reabsorption	False
g.	enhancement of zinc and iron excretion by distal tubules and colleting ducts in kidney	False
h.	decreases the rate of renal blood flow	False
i.	decreases the glomerular filtration rates	False
j.	inhibites water excretion	False

25	Biological Effects of Adrenocortical Hormones on cardiovascular system and blood cells:	
a.	increase the production of red cells and platelets by stimulating bone marrow	True
b.	decrease the number of lymphocytes and eosinocytes	True
c.	causes atrophy of the all lymphoid tissues and promotion of destruction of lymphocytes and eosinocytes.	True
d.	inhibit synthesis of prostaglandins that have vasodilator effect.	True
e.	causes permissive action, enhancing the response of vascular muscle to catecholamines.	True
f.	decrease the production of red cells and platelets	False
g.	deplete the number of endothelial cells	False
h.	causes atrophy of the all lymphoid tissues and promotion of destruction of lymphocytes and eosinocytes.	False
i.	increase synthesis of prostaglandins that have vasodilator effect.	False
j.	Blocks the response of vascular muscle to catecholamines.	False

26	Biological Effects of Adrenocortical Hormones on stress:	
a.	Almost any type of stress cause increase in ACTH secretion, and consequent cortisol secretion.	True
b.	essential for survival.	True
c.	increase production of HCl and pepsin,	True
d.	promotion of synthesis of fetal surfactant	True
e.	pharmacological effects including anti-inflammatory, antiallergic and antishock	True
f.	Almost any type of stress cause decrease in ACTH and cortisol secretion	False
g.	essential for movement	False
h.	increase production of amino acids	False
i.	promotion of synthesis of proteins	False
j.	pharmacological effects including pro-inflammatory and pro-algic	False

27	Regulation of Secretion of Adrenocortical Hormone	
a.	Hypothalamus – Anterior Pituitary – Adrenocortical Axis - Action of ACTH (adrenocorticotropin hormone)	True
b.	CRH (corticotropin releasing hormone) -promote synthesis and release of ACTH	True
c.	Cortisol has direct negative feedbacks on the hypothalamus to decrease formation of CRH	True
d.	High circulating levels of cortisol inhibit secretion and formation of ACTH	True
e.	High levels of ACTH inhibit CRH secretion by a negative feedback mechanism.	True
f.	Thalamus – Posterior Pituitary – Parathiroid Axis - Action of ACTH (adrenocorticotropin hormone)	False

g.	CRH (corticotropin releasing hormone) -promote inhibition of insulin	False
h.	Cortisol has direct negative feedbacks on the thalamus to increase formation of CRH	False
i.	High circulating levels of Cushing's protein stimulate secretion and formation of Glucagon	False
j.	High levels of thyroxin inhibit CRH secretion by a negative feedback mechanism.	False

28	Islet of Langerhans	
a.	Located on the pancreas	True
b.	Islet of Langerhans secrete insulin	True
c.	Islet of Langerhans secrete glucagon	True
d.	Insulin stimulates the glucose uptake by cells	True
e.	Glucagon promotes conversion of glycogen (animal-based carbohydrate) to glucose	True
f.	Located on the liver	False
g.	Islet of Langerhans secrete adrenocorticotropin hormone	False
h.	Islet of Langerhans secrete corticotropin releasing hormone	False
i.	Insulin inhibites the glucose uptake by cells	False
j.	Glucagon promotes conversion of amino acids to glycogen	False

29	Type 1 Diabetes symptoms:	
a.	Frequent urination	True
b.	Unusual thirst	True
c.	Extreme hunger	True
d.	Unusual weight loss	True
e.	Extreme fatigue and Irritability	True
f.	Giantism in childhood	False
g.	Acromegaly in adults	False
h.	Dwarfism in childhood	False
i.	Cretinism (mental retardation, small size) in children	False
j.	Paranoia and muscle tremor	False

30	Type 2 Diabetes symptoms:	
a.	Any of the type 1 symptoms	True
b.	Frequent infections, Recurring skin, gum, or bladder infections	True
c.	Blurred vision	True
d.	Cuts/bruises that are slow to heal	True
e.	Tingling/numbness in the hands/feet	True
f.	Giantism in childhood	False
g.	Acromegaly in adults	False
h.	Dwarfism in childhood	False
i.	Cretinism (mental retardation, small size) in children	False
j.	Paranoia and muscle tremor	False

Course 8: The Physiology of the Digestive System
Sub-topic: Structure, Function, and Nutrition

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1. Overview of the Digestive System

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2. Anatomy of the Gastrointestinal (GI) Tract
2.1. Structure of the GI Tract
2.2. Accessory Glandular Organs

---

3. Functions of the Digestive System
3.1. Gastrointestinal Motility
3.2. Secretion
3.3. Digestion and Absorption
3.4. Control of Digestive Functions

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4. Digestive Phases
4.1. Cephalic Phase
4.2. Gastric Phase
4.3. Intestinal Phase

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5. Secretory Functions of the GI Tract
5.1. Enzyme Secretion
5.2. Mucus Secretion
5.3. Bile Production

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6. Nutrient Absorption
6.1. Carbohydrate Absorption
6.2. Protein Absorption
6.3. Fat Absorption

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7. Gastrointestinal Reflexes and Control
7.1. Enterogastric Reflex
7.2. Gastrocolic Reflex

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8. Nutrition
8.1. Macronutrient Needs
8.2. Micronutrients
8.3. Caloric Intake

Examination and Assessment

Practical Session 8: Gastrointestinal Secretions. Pancreas and Liver

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1. Introduction to Gastrointestinal Secretions
   - Role of GI Secretions
   - Functions of GI Secretions

---

2. Salivary Secretion
2.1. Composition and Function
   - Saliva Components:
     - Water, ions, mucus, enzymes (e.g., amylase, lysozyme), and electrolytes.
   - Functions of Saliva

---

3. Gastric Secretion
3.1. Gastric Gland Cells
   - Oxyntic Glands
   - Pyloric and Cardiac Glands

3.2. Composition and Function of Gastric Secretions
   - Hydrochloric Acid (HCl)
   - Pepsinogen
   - Mucus
   - Intrinsic Factor

---

4. Regulation of Gastric Secretions
4.1. Phases of Gastric Secretion
   - Cephalic Phase (Before Food Enters Stomach)
   - Gastric Phase (During Food Presence in the Stomach)
   - Intestinal Phase (After Food Moves into the Intestine)

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5. Pancreatic Secretion
5.1. Composition and Function
5.2. Regulation

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6. Bile Secretion
6.1. Composition and Function
6.2. Regulation

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7. Intestinal Secretion
7.1. Composition and Function

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8. Practical Experiments and Demonstrations
8.1. Measurement of pH in Gastric Secretions
8.2. Enzyme Activity in Digestive Fluids
8.3. Regulation of Secretions

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9. Clinical Relevance
   - Peptic Ulcer Disease:
   - Pancreatitis
   - Biliary Obstruction

Course 8: The Physiology of the Digestive System
Sub-topic: Structure, Function, and Nutrition

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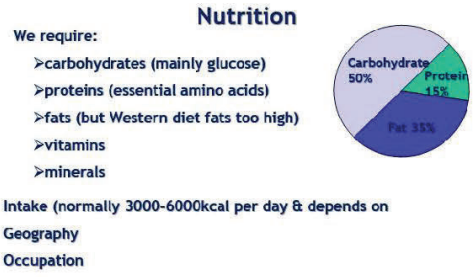
1. Overview of the Digestive System

The digestive system is responsible for breaking down food into smaller, absorbable molecules, absorbing nutrients, and eliminating waste. It includes the gastrointestinal (GI) tract and accessory organs that assist in digestion and nutrient absorption. Its major functions are motility, secretion, digestion, and absorption, which are regulated by neural and hormonal control mechanisms.



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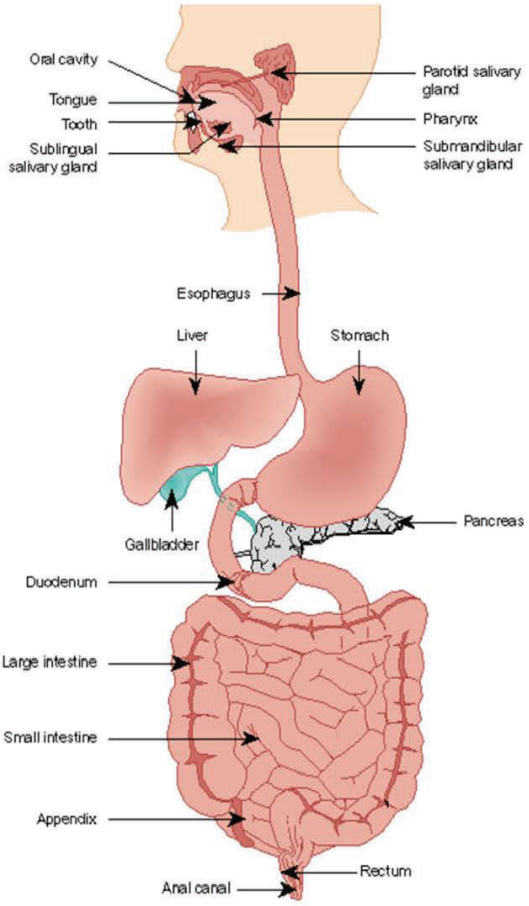
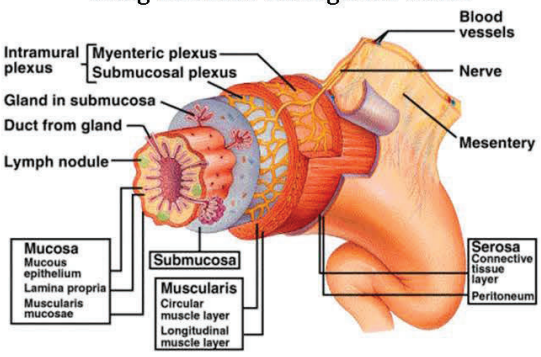
2. Anatomy of the Gastrointestinal (GI) Tract

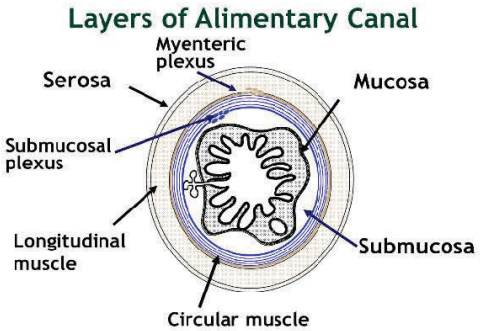
The gastrointestinal tract consists of several distinct organs that work in unison to facilitate digestion and nutrient absorption.

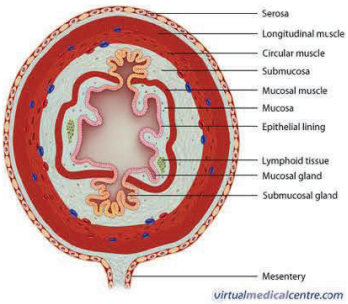
2.1. Structure of the GI Tract

- Mouth: The starting point of digestion, where food is broken down mechanically by chewing and mixed with saliva containing digestive enzymes.
- Esophagus: A muscular tube that transports food from the mouth to the stomach via peristalsis.
- Stomach: Secretes hydrochloric acid and digestive enzymes to begin protein digestion and break food into chyme.
- Small Intestine: The primary site for digestion and absorption. It consists of three segments: the duodenum, jejunum, and ileum.
- Large Intestine: Absorbs water and electrolytes, forming solid waste (feces), which is stored in the rectum before being excreted through the anus.









(1)the serosa
(2)longitudinal smooth muscle layer
(3)circular smooth muscle layer
(4)the submucosa
(5)the mucosa

The motor functions of the gut are performed by the different layers of smooth muscle.

2.2. Accessory Glandular Organs

- Salivary Glands: Secrete saliva, which contains the enzyme amylase to start carbohydrate digestion.
- Liver: Produces bile, which is essential for fat emulsification.
- Gallbladder: Stores bile and releases it into the small intestine.
- Pancreas: Secretes digestive enzymes and bicarbonate into the duodenum to neutralize stomach acid and continue digestion.

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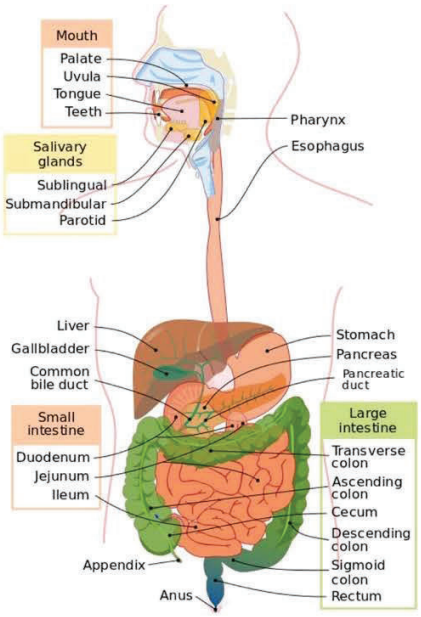
3. Functions of the Digestive System

The digestive system has four major functions: motility, secretion, digestion, and absorption.



3.1. Gastrointestinal Motility

Motility refers to the contraction of smooth muscles in the GI tract, which moves food through the digestive system.

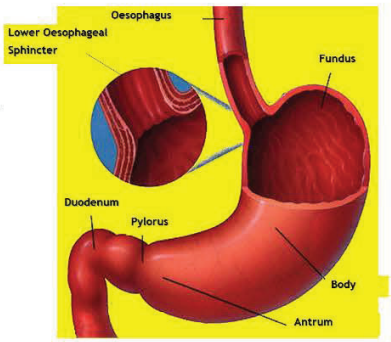
- Peristalsis: Wave-like contractions that push food through the esophagus, stomach, and intestines.
- Segmentation: Rhythmic contractions in the small intestine that mix food with digestive enzymes to enhance absorption.

3.2. Secretion

Various glands secrete enzymes, acid, mucus, and bile to aid in digestion.

- Salivary secretion in the mouth, gastric juice in the stomach, pancreatic juice and bile in the small intestine all play crucial roles in breaking down food.

3.3. Digestion and Absorption



- Digestion involves breaking down macromolecules (carbohydrates, proteins, fats) into their smaller components.
- Absorption occurs primarily in the small intestine, where nutrients pass through the intestinal walls into the bloodstream or lymphatic system.

3.4. Control of Digestive Functions

The autonomic nervous system (ANS) and hormones regulate digestive functions:

- Parasympathetic stimulation promotes digestion (rest-and-digest), while sympathetic stimulation inhibits it.
- Hormones such as gastrin, secretin, and cholecystokinin (CCK) regulate secretion and motility.

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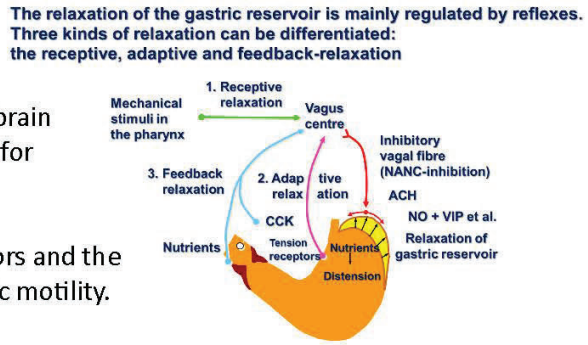
4. Digestive Phases

The digestive process is divided into three phases:



4.1. Cephalic Phase

- Triggered by the sight, smell, or thought of food. The brain stimulates saliva and gastric secretions in preparation for digestion.

4.2. Gastric Phase

- Begins when food enters the stomach. Stretch receptors and the release of gastrin stimulate acid production and gastric motility.

4.3. Intestinal Phase

- Starts when chyme enters the small intestine. Secretions from the pancreas and gallbladder aid digestion, while hormones like secretin and CCK regulate the release of bile and pancreatic enzymes.

Gastric Motility

Peristaltic waves: Body → Antrum

Body

Thin muscle → weak contraction

→ No mixing

Antrum

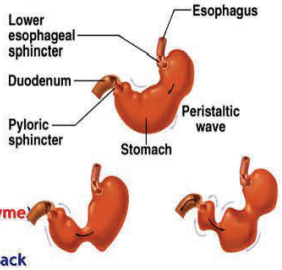
Thick muscle → powerful contraction

A Mixing

B Contraction of pyloric sphincter →

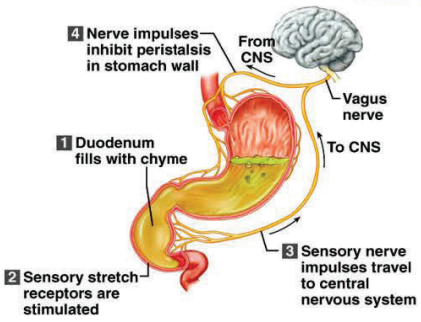
1 Only small quantity of gastric content (chyme) entering duodenum

2 Further mixing as antral contents forced back towards body



Enterogastric Reflex

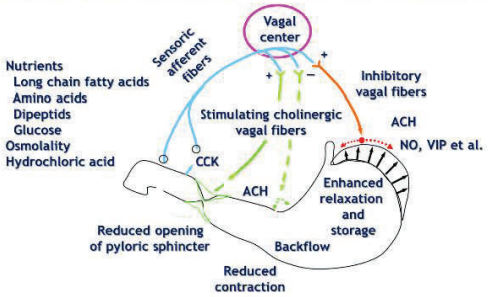
regulates the rate at which chyme leaves the stomach



What produces gastric peristaltic waves?

- Peristaltic rhythm (~3/min) generated by pacemaker cells (longitudinal muscle layer)
- Slow waves - spontaneous depolarisation/ repolarisation
- Slow wave rhythm = basic electrical rhythm (BER)
- Slow waves conducted through gap junctions along longitudinal muscle layer
- Slow wave depolarisation sub-threshold - require further depolarisation to induce action potentials → contraction
- Number of APs/wave determines strength of contraction

The feedback regulation of gastric emptying is performed by entero-gastric reflexes and release of intestinal hormones



It causes enhanced relaxation of the gastric reservoir, inhibition of the antral pump, and reduced opening of the pyloric sphincter.

Gastrointestinal Smooth Muscle Functions as a Syncytium

- In the longitudinal muscle layer, the bundles extend *longitudinally* down the intestinal tract;
- In the circular muscle layer, they extend *around* the gut.
  - electrical signals that initiate muscle contractions can travel readily from one fiber to the next within each bundle but more rapidly along the length of the bundle than sideways
- The enteric nervous system is composed mainly of two plexuses:

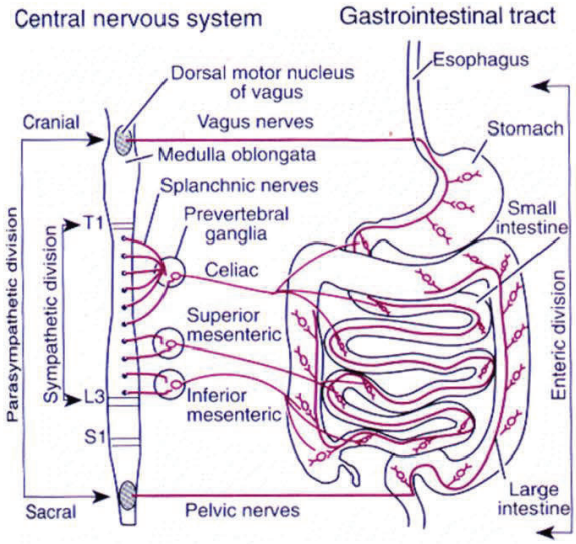
(1) an *outer plexus* lying between the longitudinal and circular muscle layers, called the myenteric plexus or Auerbach's plexus

(2) an inner plexus, called the submucosal plexus or Meissner's plexus, that lies in the submucosa.

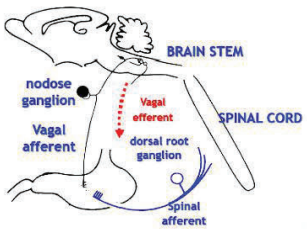
- The myenteric plexus controls mainly the gastrointestinal movements, and the submucosal plexus controls mainly gastrointestinal secretion and local blood flow.

Neural Control of Gastrointestinal Function—Enteric Nervous System

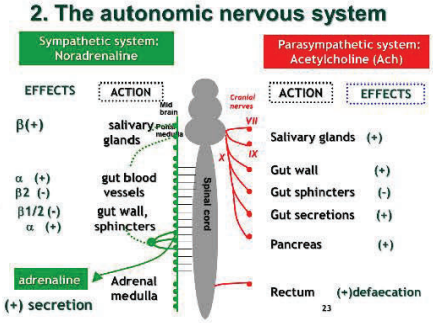
- The gastrointestinal tract has a nervous system all its own called the enteric nervous system. It lies entirely in the wall of the gut, beginning in the esophagus and extending all the way to the anus.
- This highly developed enteric nervous system is especially important in controlling gastrointestinal movements and secretion.



CNS to gut connections



2. The autonomic nervous system



Innervation of the GI tract

3. Intrinsic (enteric) nerve plexuses

Located

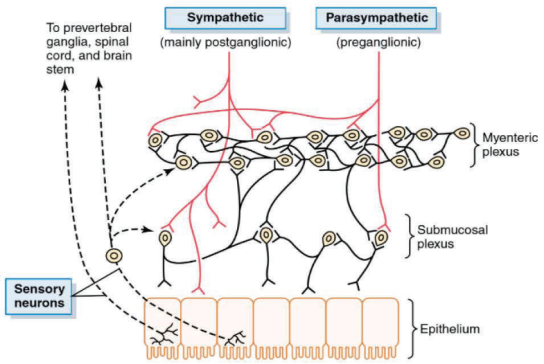
in the submucosa (submucosal or Meissner's plexus) and between circular and longitudinal muscle layers (myenteric or Auerbach's plexus)

Control

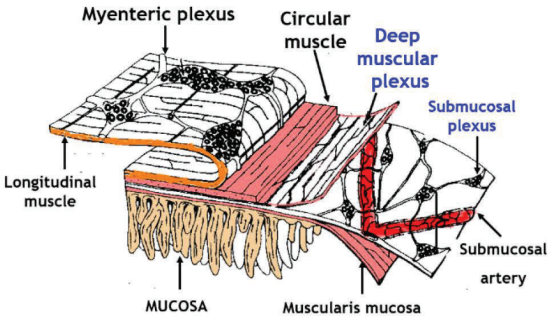
Motility - Myenteric plexus → Excitatory - Acetylcholine, Substance P; Inhibitory - VIP, nitric oxide

Secretion - Submucosal plexus → Excitatory - Acetylcholine

through release of neurotransmitters

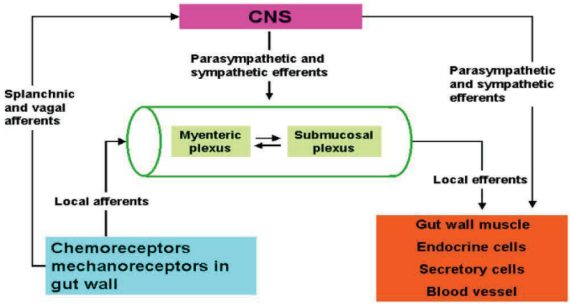


The enteric nervous system



Gastrointestinal reflex

Reflex control of gut activity



Hormonal Control of Gastrointestinal Motility

- The gastrointestinal hormones are released into the portal circulation and exert physiological actions on target cells with specific receptors for the hormone.
- The effects of the hormones persist even after all nervous connections between the site of release and the site of action have been severed.

Functional Types of Movements in the Gastrointestinal Tract

- Two types of movements occur in the gastrointestinal tract:

(1) ***propulsive movements***, which cause food to move forward along the tract at an appropriate rate to accommodate digestion and absorption

(2) ***mixing movements***, which keep the intestinal contents thoroughly mixed at all times.

Hormone	Stimuli for Secretion	Site of Secretion	Actions
Gastrin	Protein Distention Nerve *(Acid inhibits release)*	G cells of the antrum, duodenum, and jejunum	Stimulates Gastric acid secretion Mucosal growth
Cholecystokinin	Protein Fat Acid	I cells of the duodenum, jejunum, and ileum	Stimulates Pancreatic enzyme secretion Pancreatic bicarbonate secretion Gallbladder contraction Growth of exocrine pancreas Inhibits Gastric emptying
Secretin	Acid Fat	S cells of the duodenum, jejunum, and ileum	Stimulates Pepsin secretion Pancreatic bicarbonate secretion Biliary bicarbonate secretion Growth of exocrine pancreas Inhibits Gastric acid secretion
Gastric inhibitory peptide	Protein Fat Carbohydrate	K cells of the duodenum and jejunum	Stimulates Insulin release Inhibits Gastric acid secretion
Motilin	Fat Acid Nerve	M cells of the duodenum and jejunum	Stimulates Gastric motility Intestinal motility

Gastrointestinal Blood Flow—"Splanchnic Circulation" - The blood vessels of the gastrointestinal system are part of a more extensive system called the splanchnic circulation. It includes the blood flow through the gut itself plus blood flows through the spleen, pancreas, and liver. The design of this system is such that all the blood that courses through the gut, spleen, and pancreas flows immediately into the liver through the portal vein.

In the liver, the blood passes through millions of minute liver sinusoids. Finally, it leaves the liver through hepatic veins that empty into the vena cava of the general circulation. This flow of blood through the liver, before it empties into the vena cava, allows the reticuloendothelial cells that line the liver sinusoids to remove bacteria and other particulate matter that might enter the blood from the gastrointestinal tract, thus preventing direct transport of potentially harmful agents into the remainder of the body.

Propulsion and Mixing of Food in the Alimentary Tract - The time that food remains in each part of the alimentary tract is critical for optimal processing and absorption of nutrients. Also, appropriate mixing must be provided. Because the requirements for mixing and propulsion are quite different at each stage of processing, multiple automatic nervous and hormonal mechanisms control the timing of each so that they will occur optimally, not too rapidly and not too slowly.

Ingestion of Food. The amount of food that a person ingests is determined principally by intrinsic desire for food called hunger. The type of food that a person preferentially seeks is determined by appetite. These mechanisms are extremely important for maintaining an adequate nutritional supply for the body. The current discussion of food ingestion is confined to the mechanics of ingestion, especially mastication and swallowing.

Mastication (Chewing). The teeth are admirably designed for chewing. The anterior teeth (incisors) provide a strong cutting action, and the posterior teeth (molars) a grinding action. All the jaw muscles working together can close the teeth with a force as great as 55 pounds on the incisors and 200 pounds on the molars. Chewing is vital for the digestion of all foods but essential for most fruits and raw vegetables because these have indigestible cellulose membranes around their nutrient portions that must be broken before the food can be digested. Also, chewing aids the digestion of food for still another simple reason: Digestive enzymes act only on the surfaces of food particles.

Swallowing (Deglutition). Swallowing is a complicated mechanism because the pharynx subserves respiration and swallowing. The pharynx is converted for only a few seconds at a time into a tract for the propulsion of food. It is especially important that respiration not be compromised because of swallowing.

In general, swallowing can be divided into:

(1) a voluntary stage, which initiates the swallowing process
(2) a pharyngeal stage, which is involuntary and constitutes the passage of food through the pharynx into the esophagus
(3) an esophageal stage, another involuntary phase that transports food from the pharynx to the stomach.

The motor functions of the stomach are:

(1) storage of large quantities of food until the food can be processed in the stomach, duodenum, and lower intestinal tract

(2) mixing of this food with gastric secretions until it forms a semifluid mixture called chyme

(3) slow emptying of the chyme from the stomach into the small intestine at a rate suitable for proper digestion and absorption by the small intestine.

Movements of the Small Intestine. The movements of the small intestine, like those elsewhere in the gastrointestinal tract, can be divided into mixing and propulsive contractions. To a great extent, this separation is artificial because essentially all movements of the small intestine cause at least some degree of mixing and propulsion.

Movements of the Colon. The principal functions of the colon are the absorption of water and electrolytes from the chyme to form solid feces and the storage of fecal matter until it can be expelled. The proximal half of the colon is concerned principally with absorption and the distal half with storage. Because intense colon wall movements are not required for these functions, the movements of the colon are normally sluggish.

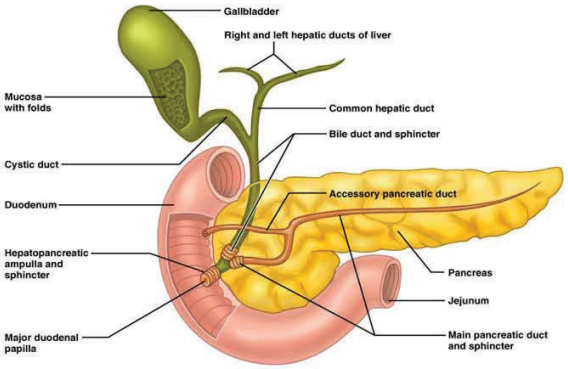
5. Secretory Functions of the GI Tract

5.1. Enzyme Secretion

- Salivary Amylase: Begins starch digestion in the mouth.
- Pepsin: Initiates protein digestion in the stomach.
- Pancreatic Enzymes: Trypsin, amylase, and lipase continue the digestion of proteins, carbohydrates, and fats, respectively, in the small intestine.

5.2. Mucus Secretion

- Mucus protects the lining of the GI tract from digestive acids and enzymes, preventing auto-digestion and facilitating the movement of food through the digestive tract.



5.3. Bile Production

- Bile is produced in the liver and stored in the gallbladder. It emulsifies fats, breaking them into smaller droplets, making them more accessible for enzyme action.

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6. Nutrient Absorption

6.1. Carbohydrate Absorption - Simple sugars like glucose are absorbed in the small intestine via active transport and enter the bloodstream for energy production or storage.

6.2. Protein Absorption - Proteins are broken down into amino acids, which are absorbed via active transport into the bloodstream and used for protein synthesis or energy.

6.3. Fat Absorption - Fats are emulsified by bile and broken down into fatty acids and monoglycerides. These are absorbed into the lymphatic system via micelles and transported as chylomicrons before entering the bloodstream.

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7. Gastrointestinal Reflexes and Control

GI reflexes regulate motility and secretion, ensuring coordinated and efficient digestion.

7.1. Enterogastric Reflex: Inhibits gastric motility and secretion when chyme enters the small intestine, allowing time for digestion and absorption.

7.2. Gastrocolic Reflex: Stimulates colonic motility in response to food entering the stomach, promoting the urge to defecate after a meal.

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8. Nutrition

8.1. Macronutrient Needs

- The body requires carbohydrates, proteins, and fats for energy, growth, and repair.
    - Carbohydrates provide quick energy.
    - Proteins are essential for tissue repair and enzyme production.
    - Fats serve as long-term energy storage and support cell membrane structure.

8.2. Micronutrients

- Vitamins (e.g., A, D, E, K, B-complex, C) and minerals (e.g., calcium, potassium, magnesium) are needed in smaller amounts but are essential for metabolic functions and maintaining cellular health.

8.3. Caloric Intake

- The total energy intake must meet the body's energy expenditure, which includes basal metabolic rate (BMR), physical activity, and the thermic effect of food. Macronutrient balance and calorie intake must be optimized for proper body function.

Practical Session 8: Gastrointestinal Secretions, Pancreas and Liver

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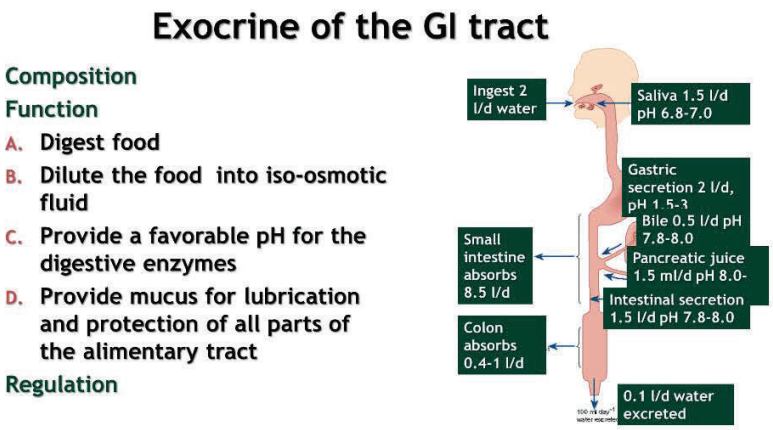
1. Introduction to Gastrointestinal Secretions

The gastrointestinal (GI) tract secretes various fluids essential for digestion and absorption of nutrients. These secretions are produced by specialized glands and cells throughout the digestive system, including the salivary glands, stomach, pancreas, liver, and intestines.

Role of GI Secretions:

- Saliva, gastric juice, bile, pancreatic secretions, and intestinal fluids work together to facilitate digestion by breaking down food into smaller molecules, neutralizing stomach acid, and emulsifying fats.
- GI secretions also contain protective components, such as mucus, which shields the lining of the GI tract from mechanical damage and acidic environments.



Functions of GI Secretions:

- Digestion: Enzymes in these secretions help break down carbohydrates, proteins, and fats.
- Absorption: Secretion of water and electrolytes ensures proper hydration and ion balance in the intestines, which facilitates nutrient absorption.
- Protection: Mucus and bicarbonate neutralize acidic chyme and protect the mucosa.
- Excretion: Some secretions, such as bile, carry waste products, including bilirubin and excess cholesterol, out of the body.

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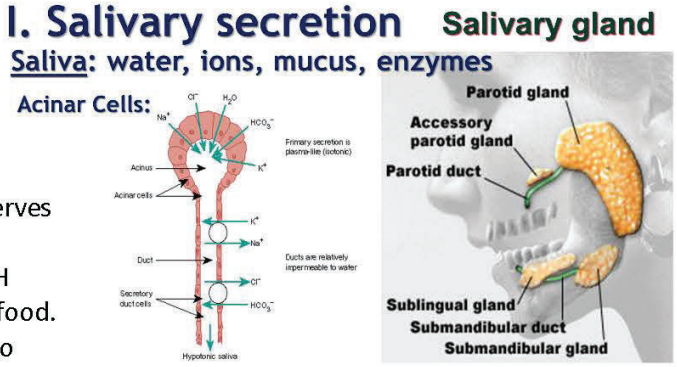
2. Salivary Secretion

2.1. Composition and Function

Saliva is produced by the salivary glands (parotid, submandibular, and sublingual glands) and plays an essential role in the initial phase of digestion.



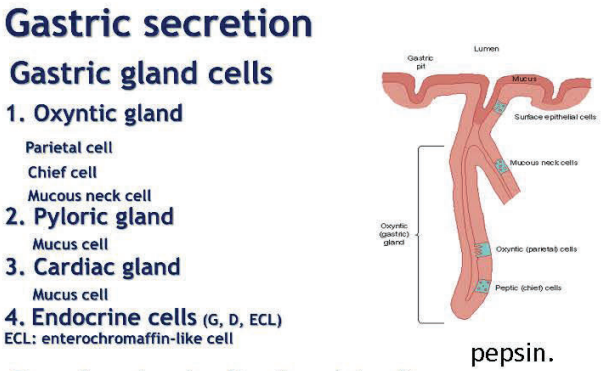
- Saliva Components:
  - Water: Makes up 99% of saliva and serves as a solvent for taste and digestion.
  - Ions (Na^+, K^+, Cl^-, HCO_3^-): Maintain pH balance and aid in the breakdown of food.
  - Mucus: Lubricates the bolus of food to facilitate swallowing.
  - Enzymes:
    - Amylase: Initiates the breakdown of starch into maltose and glucose.
    - Lysozyme: An enzyme with antibacterial properties that protects the oral cavity from pathogens.
  - Electrolytes: Contribute to the osmolarity and pH of saliva, optimizing conditions for enzyme activity.
- Functions of Saliva:
  - Lubrication: Mucus moistens food and aids in its passage through the esophagus.
  - Digestion: Amylase begins the chemical breakdown of carbohydrates in the mouth.
  - Protection: Lysozyme and immunoglobulins in saliva inhibit microbial growth, protecting the teeth and gums from infection.

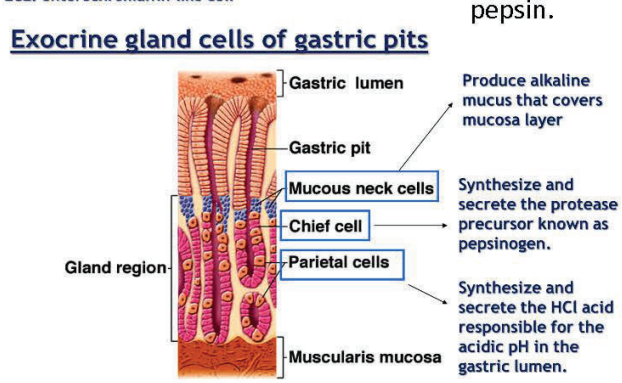
3. Gastric Secretion

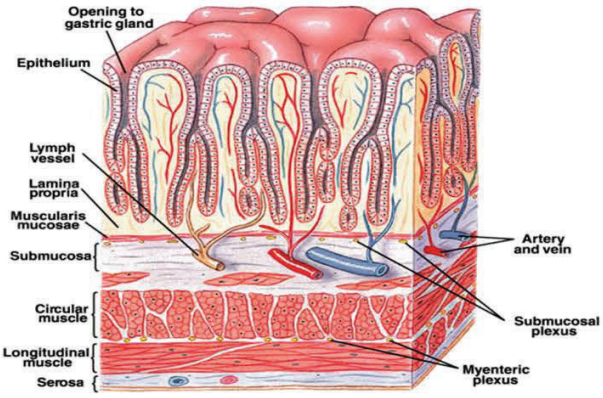
3.1. Gastric Gland Cells

The stomach lining contains specialized cells organized into gastric glands that produce different components of gastric juice.

- Oxyntic Glands (located in the body and fundus of the stomach):
  - Parietal cells: Secrete hydrochloric acid (HCl) and intrinsic factor.
  - Chief cells: Produce pepsinogen, the precursor to the proteolytic enzyme pepsin.
  - Mucous neck cells: Produce mucus to protect the stomach lining from acidic damage.
- Pyloric and Cardiac Glands (located in the antrum and cardiac regions):
  - Produce primarily mucus and some pepsinogen, providing protection to the gastric mucosa near the esophagus and duodenum.



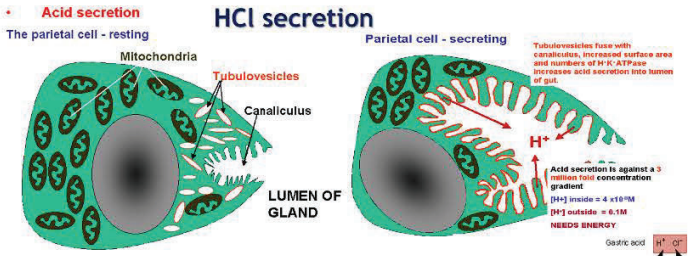


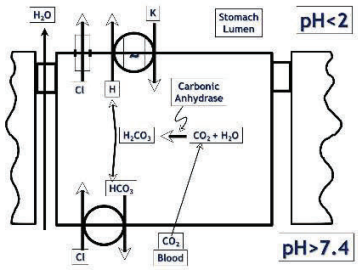


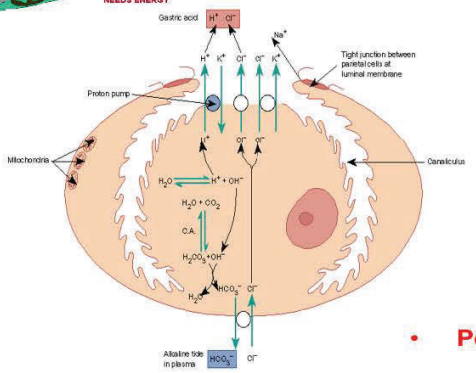
3.2. Composition and Function of Gastric Secretions

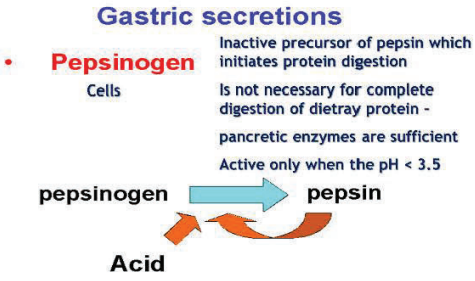
Hydrochloric Acid (HCl):

- Secreted by parietal cells, HCl lowers the stomach's pH to around 1-2, which is necessary for activating pepsinogen into pepsin and helps kill ingested bacteria.



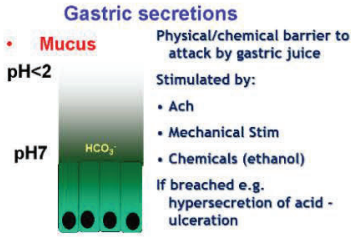


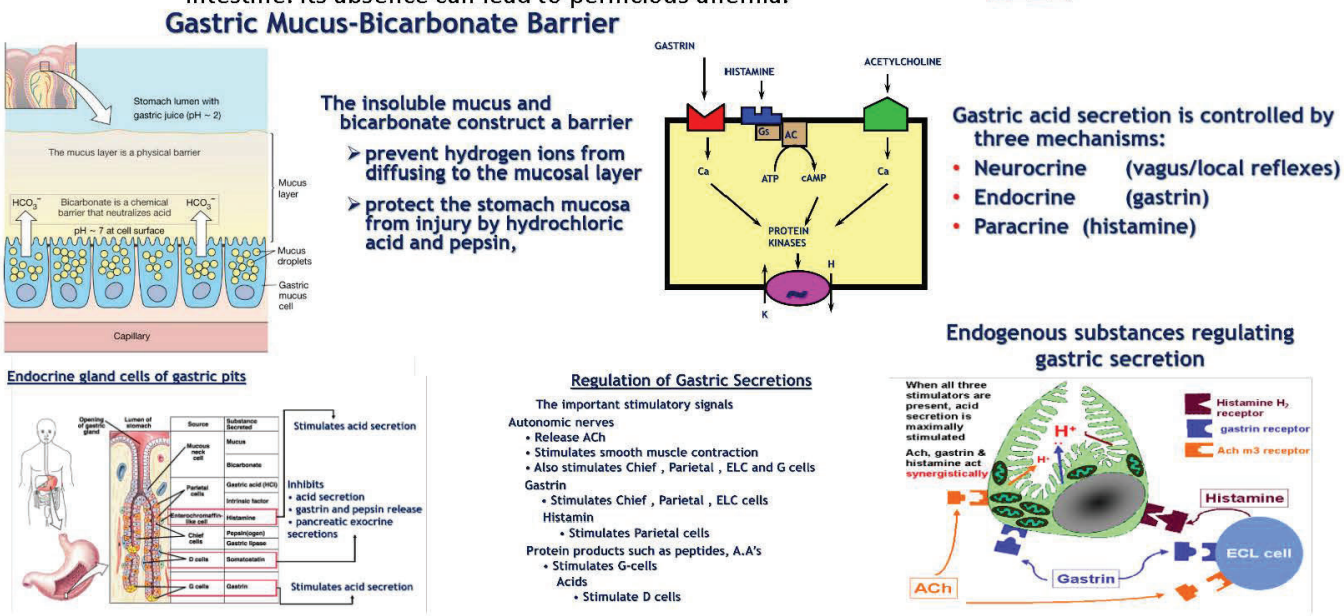




- Pepsinogen:
  - An inactive precursor secreted by chief cells that is converted into pepsin by the acidic environment. Pepsin breaks down proteins into smaller peptides.

- Mucus:
  - Mucus is produced by mucous neck cells and coats the stomach lining, preventing damage from stomach acid and mechanical stress.
- Intrinsic Factor:
  - Essential for the absorption of vitamin B12 in the small intestine. Its absence can lead to pernicious anemia.



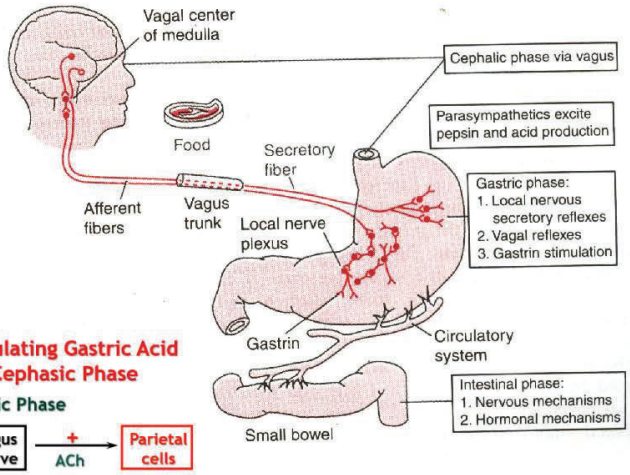


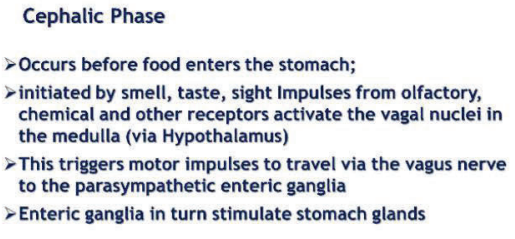
4. Regulation of Gastric Secretions

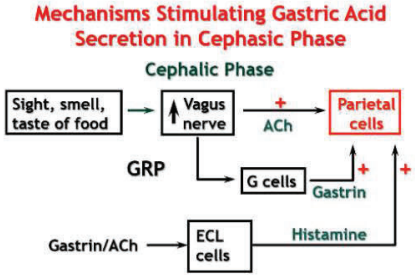
Gastric secretion is regulated through three overlapping phases, controlled by neural and hormonal signals.

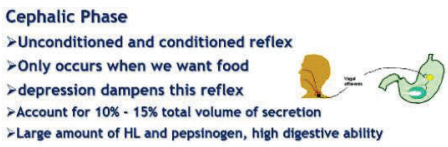
4.1. Phases of Gastric Secretion

- Cephalic Phase (Before Food Enters the Stomach):
  - Triggered by the sight, smell, taste, or thought of food. The vagus nerve stimulates gastric secretion even before food reaches the stomach.









- Gastric Phase (During Food Presence in the Stomach):
  - Initiated by food stretching the stomach and the presence of proteins. Gastrin is secreted, which further stimulates HCl and pepsinogen production. It starts when food reaches the stomach. Provides 2/3 of the juice released

There are two parts (neural and chemical) to this phase

- Neural part, activated by stretch receptors - Initiates both local neural reflexes and the longer vago-vagal reflex. Both reflexes release ACh at stomach synapses which stimulates secretory cells. This branch is inhibited by Sympathetic action (emotional upset).
- Chemical part, increased pH (thus, 'less' acidity), peptides, and caffeine activate the G-cells. This results in Gastrin being released. Gastrin acts on Parietal cells that start secreting HCl. Gastrin also stimulates Histamine release, which in turn stimulates Parietal cells. The increase in HCl promotes pepsin production and protein degradation. The release of Gastrin is partly regulated by acidity. Increased acidity inhibits the G-cells. The increased presence of proteins in a meal tends to buffer the protons. This in turn keeps the pH from becoming too acidic and allows more gastrin to be released.

- Intestinal Phase (After Food Moves into the Intestine):
  - As chyme enters the duodenum, the secretion of enterogastrones (e.g., secretin and cholecystokinin) inhibits further gastric acid secretion and slows gastric emptying. Account for about 5% of secretion. Primarily hormonal – the denervated stomach will be stimulated to secrete acid by protein in the duodenum. A very small number of G-cells in the duodenum also release gastrin in response to amino acids.

Regulation of Gastric Secretions occurs via 3 phases

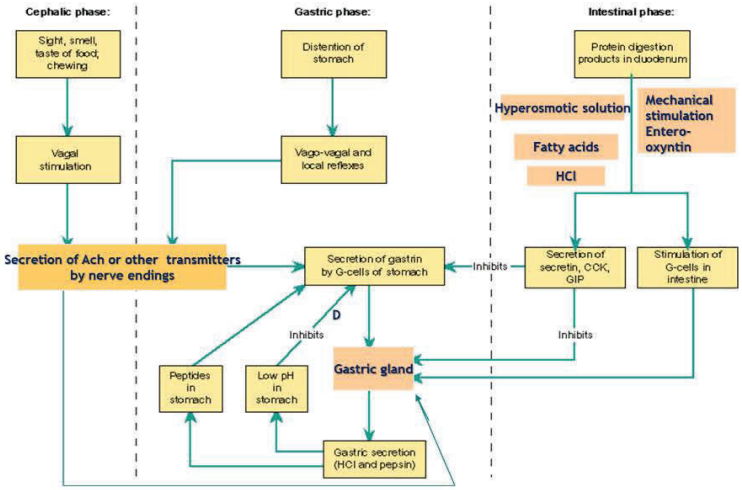
TABLE 15–5 Control of HCL Secretion during a Meal

STIMULI	PATHWAYS	RESULT
Cephalic phase Sight Smell Taste Chewing	Parasympathetic nerves to enteric nervous system	↑HCl secretion
Gastric contents (gastric phase) Distension ↑Peptides ↓H^+ concentration	Long and short neural reflexes, and direct stimulation of gastrin secretion	↑HCl secretion
Intestinal contents (intestinal phase) Distension ↑H^+ concentration ↑Osmolarity ↑Nutrient concentrations	Long and short neural reflexes; secretin, CCK, and other duodenal hormones	↓HCl secretion

Mechanisms Inhibiting Gastric Acid Secretion

Cephalic Phase
Stopping eating → ↓ Vagal activity
Gastric Phase
↓pH (↑[HCl]) → ↓Gastrin
Intestinal Phase
Acid in duodenum → Enterogastric (splanchnic) reflex → Gastrin secrⁿ; Gastrin stimⁿ of parietal cells
Acid in duodenum → Secretin release → Gastrin secrⁿ; Gastrin stimⁿ of parietal cells
Fat in duodenum → GIP release → Gastrin secrⁿ; Parietal HCl secrⁿ

Regulation of gastric secretion



Enterogastrones

- Hormones released from gland cells in duodenal mucosa - secretin, cholecystokinin (CCK), GIP
- Released in response to acid, hypertonic solutions, fatty acids or monoglycerides in duodenum
- Act collectively to prevent further acid build up in duodenum
- Two strategies:
  - inhibit gastric acid secretion
  - reduce gastric emptying (inhibit motility/contract pyloric sphincter)

5. Pancreas and Liver

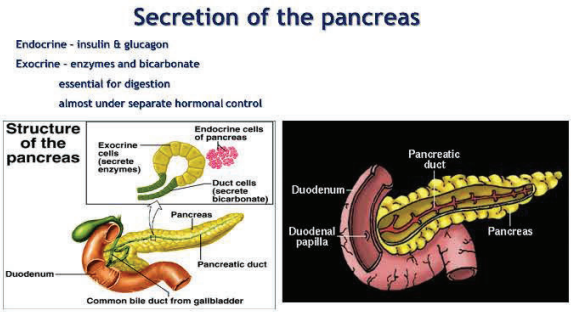
The pancreas and liver are essential in digestion, metabolism, and homeostasis. The pancreas functions both as an exocrine gland, secreting digestive enzymes, and as an endocrine gland, regulating blood glucose through insulin and glucagon secretion. The liver is the largest internal organ and plays a vital role in nutrient metabolism, detoxification, bile production, and the synthesis of crucial plasma proteins.

1. Pancreas: Structure and Secretions

1.1. Anatomy of the Pancreas

The pancreas is located in the upper abdomen, posterior to the stomach. It consists of:

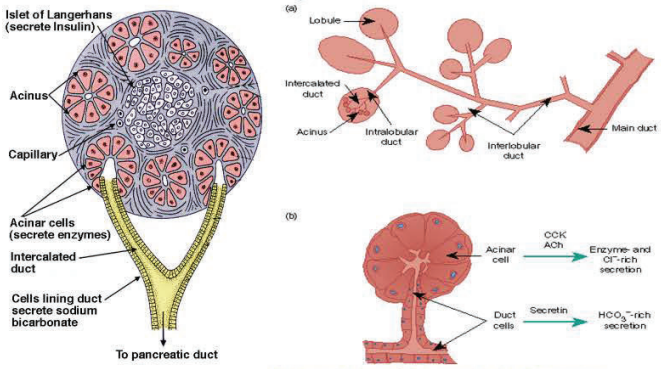
- Exocrine Portion: Comprising acinar cells, which secrete digestive enzymes into the duodenum via the pancreatic duct.
- Endocrine Portion: Made up of the islets of Langerhans, which secrete hormones such as insulin and glucagon into the bloodstream to regulate blood glucose levels.

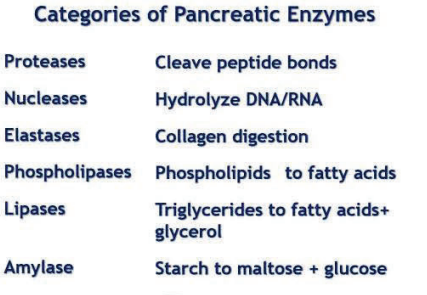


1.2. Pancreatic Enzymes and Their Functions

The pancreas produces a variety of digestive enzymes crucial for breaking down macromolecules into absorbable units:

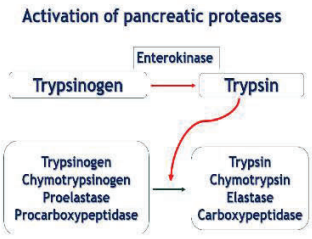
- Proteases (e.g., Trypsin, Chymotrypsin): These enzymes break down proteins into smaller peptides, which are further digested into amino acids in the small intestine.
- Lipase: Lipase hydrolyzes triglycerides (fats) into fatty acids and glycerol, which the intestinal mucosa can then absorb.
- Amylase: Amylase breaks down carbohydrates, specifically starches, into simpler sugars such as maltose and glucose, which are absorbed in the small intestine.
- Nucleases: Nucleases hydrolyze nucleic acids (DNA and RNA) into their constituent nucleotides, which are absorbed and used for cellular functions.



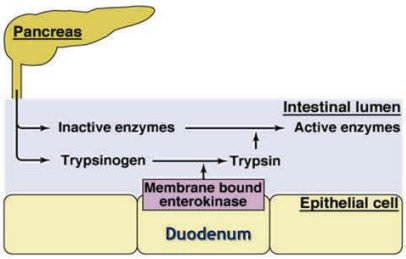


1.3. Zymogens and Enzyme Activation

Digestive enzymes produced by the pancreas are secreted in an inactive form
known as zymogens to prevent pancreatic tissue autodigestion. For example:



- Trypsinogen is secreted by the pancreas and activated to trypsin by enterokinase, an enzyme present in the small intestine. Trypsin then activates other proteases, such as chymotrypsinogen, into chymotrypsin.



- This activation cascade ensures that digestion occurs only in the small intestine, where it is required, protecting the pancreas from enzyme activity.

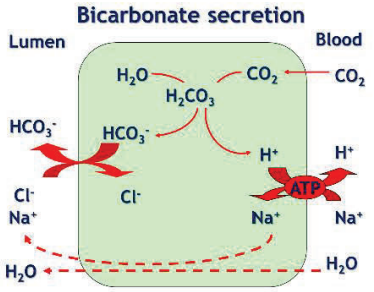
1.4. Regulation of Pancreatic Secretion

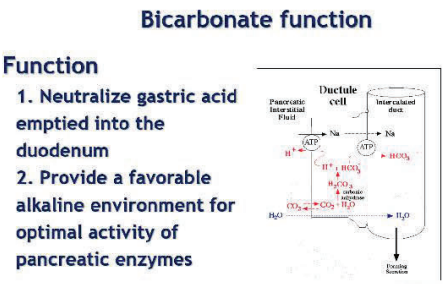
Pancreatic secretions are tightly regulated by both neural and hormonal mechanisms:

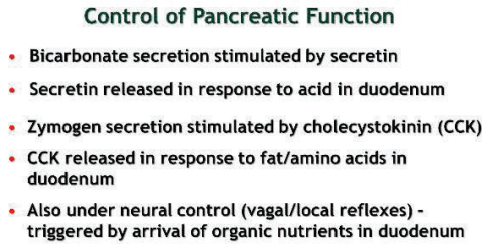
- Hormonal Regulation:

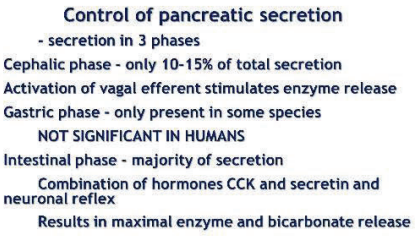
- Cholecystokinin (CCK): Released in response to fats and proteins in the duodenum, CCK stimulates acinar cells in the pancreas to secrete digestive enzymes.
- Secretin: Released in response to acidic chyme entering the duodenum, secretin stimulates the ductal cells of the pancreas to release bicarbonate, neutralizing stomach acid.

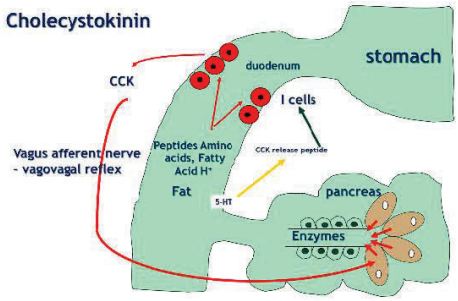
- Neural Regulation:
  - The vagus nerve stimulates pancreatic secretions in response to the sight, smell, or taste of food, priming the digestive system for incoming nutrients.

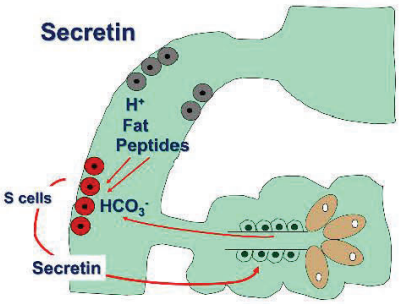




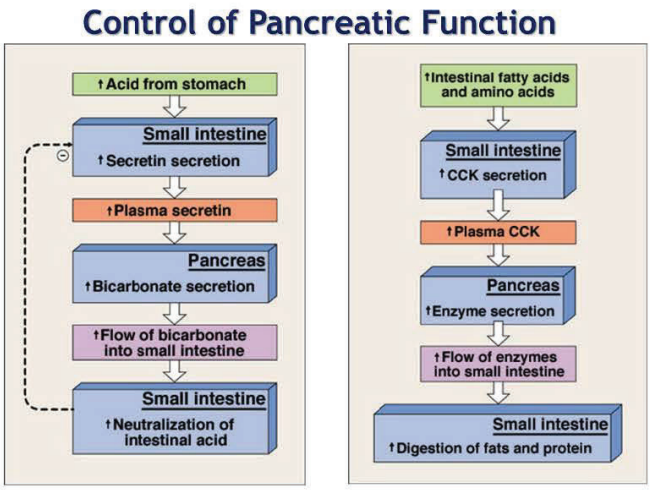


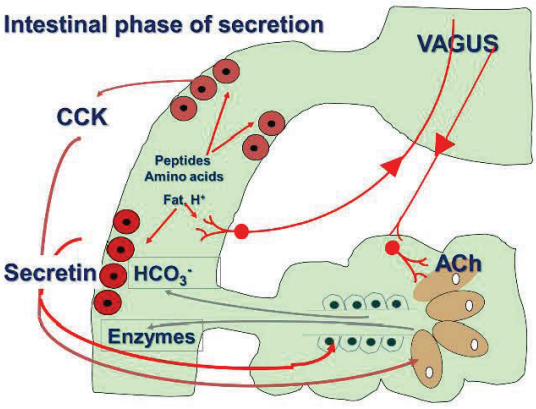






Cholecystokinin (CCK) and Secretin (released by small intestine) - key hormones that stimulate secretion. Inhibiting factors: SS, PP, glucagon.



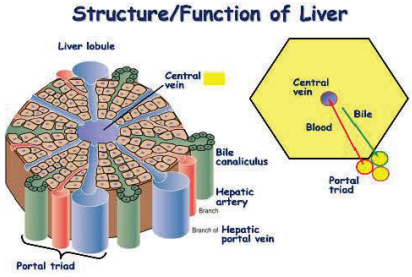


2. Liver: Structure and Secretions

2.1. Anatomy of the Liver

The liver is located in the upper right quadrant of the abdomen and is composed of hexagonally shaped functional units called liver lobules. Each lobule consists of hepatocytes arranged around a central vein, with blood entering the lobule via branches of the portal triad:

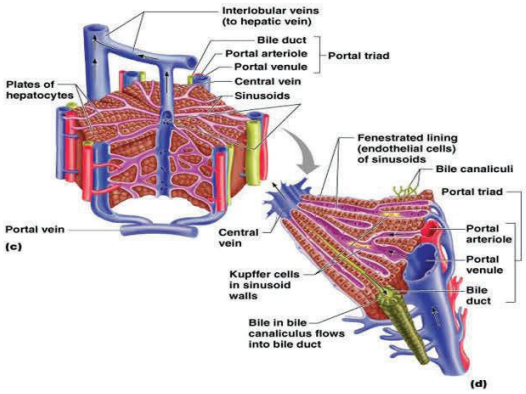
- Hepatic artery: Supplies oxygenated blood to the liver.



- Portal vein: Brings nutrient-rich but deoxygenated blood from the intestines.
- Bile duct: Collects bile produced by hepatocytes and transports it to the gallbladder for storage.

2.2. Functions of the Liver

The liver performs several essential functions that are critical for digestion, metabolism, and detoxification:



- Bile Production:
  Hepatocytes produce bile, which is stored in the gallbladder and released into the duodenum during digestion. Bile emulsifies fats, breaking them into smaller droplets, which increases the surface area for lipase action, aiding fat digestion.
- Metabolism:
  The liver processes nutrients absorbed from the digestive tract. It stores glycogen (a storage form of glucose), synthesizes plasma proteins (e.g., albumin, clotting factors), and produces cholesterol and lipoproteins for lipid transport.
- Detoxification:
  The liver detoxifies harmful substances such as alcohol, drugs, and metabolic waste products. Hepatocytes metabolize these substances, making them more water-soluble for excretion by the kidneys or into bile.
- Excretion:
  The liver excretes waste products such as bilirubin, a byproduct of red blood cell breakdown, which is secreted into bile for elimination in the feces.

Secretion and storage of bile

Constituents of bile	Liver	Gallbladder
Water	98%	92%
Bile salts	1%	6%
Bilirubin	0.04%	0.3%
Cholesterol	0.1%	0.3-0.9%
Fatty acids	0.12%	0.3-1.2%
Lecithin	0.04%	0.3%
Na, K, Ca, Cl, HCO3		

Functions of bile

- Emulsification of fats
- Increased absorption of lipids into enterocytes (include vitamin A, D, E, K)
- Increased synthesis and secretion of bile
- Cholesterol excretion (only route)
- Excretion of breakdown products of haemoglobin (bilirubin)

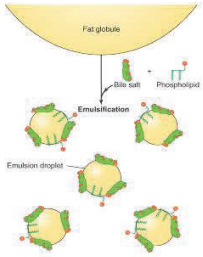
2.3. Bile Composition and Function

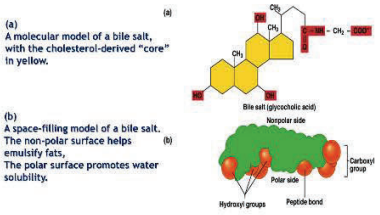
- Components:
  - Bile salts: Derived from cholesterol, they play a critical role in emulsifying fats.
  - Cholesterol: Excreted in bile as a means to eliminate excess cholesterol from the body.
  - Phospholipids and bilirubin: Help in fat digestion and the excretion of waste products.

Of the 6 components present in bile, only Bile salts and phospholipids aid in digestive processes.

Bile salts and phospholipids convert large fat globules into smaller pieces with polar surfaces that inhibit re-aggregation.

emulsification





- Functions:
  - Emulsification of Fats: Bile salts break down large fat globules into smaller droplets, allowing pancreatic lipase to digest the fats more efficiently.
  - Excretion of Waste: Bile helps excrete bilirubin and excess cholesterol, which are not readily soluble in water and are eliminated in the feces.

2.4. Regulation of Bile Secretion

Bile production and release are controlled by both hormonal and neural signals:

Regulation of bile secretion and empty of gallbladder

1. Nervous regulation: Vagus-vagus reflex

2. Humoral regulation: CCK , Gastrin, Secretin, SS

3. Bile salt: Enteroheptic circulation

- Hormonal Control:
  - Cholecystokinin (CCK): Released in response to fats in the duodenum, CCK stimulates the gallbladder to contract, releasing bile into the duodenum, and relaxes the sphincter of Oddi to allow bile flow.

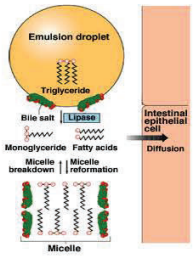
Emulsified fat globules are small enough

that lipase enzymes gain access to degrade triglycerides to monoglycerides and fatty acids,

Monoglycerides and fatty acids

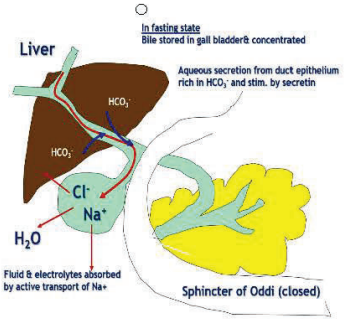
enter the absorptive cells by simple diffusion

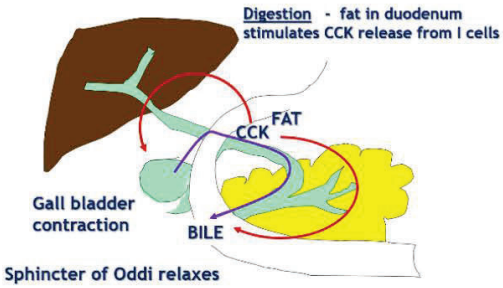
or aggregate to form loosely held micelles, which readily break down.

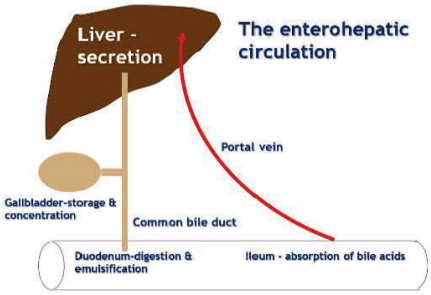


- Secretin: Stimulates hepatocytes to increase bile production, particularly the bicarbonate content, in response to acidic chyme entering the duodenum.

- Neural Control:
  - The vagus nerve provides parasympathetic input that can cause weak contractions of the gallbladder during the cephalic and gastric phases of digestion.



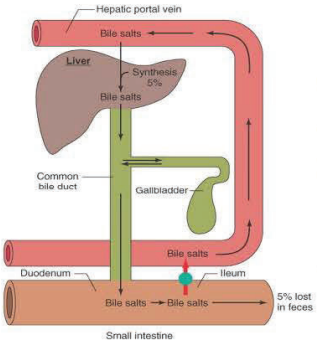




Up to 95% of the cholesterol-based bile salts are "recycled" by reabsorption along the intestine.

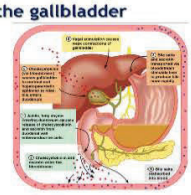
Inhibition of reabsorption results in synthesis of new bile acids and lowering of cholesterol levels.

Increasing dietary fiber could trap a greater percentage of the bile in the fibrous feces.



Regulation of Bile Release

- Acidic, fatty chyme causes the duodenum to release:
  - Cholecystokinin (CCK) and secretin into the bloodstream
- Bile salts and secretin transported in blood stimulate the liver to produce bile
- Vagal stimulation causes weak contractions of the gallbladder
- Cholecystokinin causes:
  - The gallbladder to contract
  - The sphincter of Oddi to relax
- As a result, bile enters the duodenum



2.4. Enterohepatic Circulation

Bile Recycling. Bile salts are reabsorbed in the ileum, the last part of the small intestine, and returned to the liver via the hepatic portal vein. This process, known as enterohepatic circulation, allows bile salts to be reused multiple times during digestion.

- Clinical Significance: Interruption of this recycling process, as seen with the use of bile acid sequestrants (drugs that bind bile acids in the intestine), leads to an increase in bile acid synthesis from cholesterol, which can help lower blood cholesterol levels.

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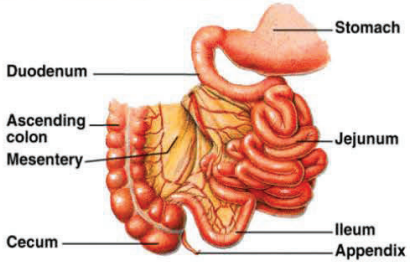
7. Intestinal Secretion

7.1. Composition and Function

The small intestine secretes intestinal juice, which contains:

- Enzymes (e.g., peptidases, sucrase, lactase): Complete the digestion of proteins and carbohydrates into absorbable units.
- Mucus: Lubricates and protects the intestinal lining.
- Water and Electrolytes: Maintain fluid balance and facilitate nutrient absorption.

Small Intestine secretion



Composition and function

Digestive enzymes not secreted from small intestine - from pancreas or found on enterocytes

except enterokinase secreted from duodenal mucosa

Mucus/alkali secretions - mucosal protection

Aqueous secretions

Function

Lubricate and protect intestinal surface (Ig A)
Dilute digestive products
Digest specific food substances
(enzymes in enterocytes: peptidase, sucrase, etc)

Regulation of small intestinal secretion

Local stimuli
The presence of chyme in the intestine
Hormonal regulation
Secretin
CCK
Neuronal regulation
Vagus nerve - excitatory
Sympathetic nerve - inhibitory

Examination and Assessment

1	Nutritional elements:	
a.	Carbohydrates (mainly glucose)	True
b.	Proteins (essential amino acids)	True
c.	Fats	True
d.	Vitamins	True
e.	Minerals	True
f.	DNA	False
g.	Drugs	False
h.	Condiments	False
i.	Cells	False
j.	Microorganisms	False

2	The alimentary tract provides supplies of water, electrolytes, vitamins, and nutrients after:	
a.	movement of food through the alimentary tract;	True
b.	secretion of digestive juices and digestion of the food;	True
c.	absorption of water, various electrolytes, vitamins, and digestive products;	True
d.	circulation of blood through the gastrointestinal organs to carry the absorbed substances;	True
e.	control of all these functions by local, nervous, and hormonal systems	True
f.	movement of food through the accessory glandular organs;	False
g.	circulation of digestive juices	False
h.	secretion of water, various electrolytes, vitamins, and digestive products;	False
i.	circulation of mucous through the gastrointestinal organs to carry the absorbed substances;	False
j.	control of all these functions by microorganisms	False

3	Gastrointestinal (GI) tract includes:	
a.	mouth	True
b.	pharynx and esophagus	True
c.	stomach	True
d.	small intestine	True
e.	large intestine, anus	True
f.	salivary glands	False
g.	accessory Glandular Organs	False
h.	liver	False
i.	gallbladder	False
j.	pancreas	False

4	Are accessory Glandular Organs	
a.	salivary glands	True
b.	accessory Glandular Organs	True
c.	liver	True
d.	gallbladder	True
e.	pancreas	True
f.	mouth	False
g.	pharynx and esophagus	False
h.	stomach	False
i.	small intestine	False
j.	large intestine	False

5	Digestive system is adapted to its specific functions	
a.	passage of food	True
b.	temporary storage of food	True
c.	digest food	True
d.	Absorb nutrients	True
e.	Secretion - glands associated with the gastrointestinal tract release water and substance	True
f.	movement of food through the accessory glandular organs;	False
g.	circulation of digestive juices	False
h.	secretion of water, various electrolytes, vitamins, and digestive products;	False
i.	circulation of mucous through the gastrointestinal organs to carry the absorbed substances;	False
j.	control of all these functions by microorganisms	False

6	Layers of Alimentary Canal	
a.	Mucosa	True
b.	Submucosa	True
c.	Circular muscle	True
d.	Longitudinal muscle	True
e.	Serosa	True
f.	Schwann	False
g.	Valves	False
h.	Blood vessels	False
i.	Myelin	False
j.	Water	False

7	Gastrointestinal Motility:	
a.	movements at the gastrointestinal level	True
b.	mix gastrointestinal contents	True
c.	circulate gastrointestinal contents	True
d.	propel gastrointestinal contents along the length of the tract	True
e.	movement of food through gastrointestinal system	True
f.	movements at the excretory level	False
g.	mix water and mucus contents	False
h.	circulate hepatic contents	False
i.	propel gastrointestinal contents along the length of the urinary tract	False
j.	movement of food through the circulatory system	False

8	Gastrointestinal secretion:	
a.	process by which the associated glands release water into the tract	True
b.	process by which the associated glands release various substances into the tract	True
c.	secretion of digestive juices for food digestion	True
d.	done by gastrointestinal glands	True
e.	necessary for digestion	True
f.	process by which the gastrointestinal tract releases water into the urinary tract	False
g.	process by which the gastrointestinal tract releases various substance into the urinary tract	False
h.	secretion of digestive vitamins for food digestion	False
i.	done by gastrointestinal muscles	False
j.	necessary for motility	False

9	Gastrointestinal digestion:	
a.	process by which food and large molecules are chemically degraded to produce smaller	True
b.	smaller molecules can be absorbed across the wall of the gastrointestinal tract.	True
c.	main function of the digestive system	True
d.	process by which nutrients are chemically degraded to produce smaller	True
e.	smaller molecules can be absorbed	True
f.	process by which the gastrointestinal tract releases water into the urinary tract	False
g.	process by which the gastrointestinal tract releases various substance into the urinary tract	False
h.	secretion of digestive vitamins for food digestion	False
i.	done by gastrointestinal muscles	False
j.	necessary for respiration	False

10	Gastrointestinal absorption:	
a.	process by which nutrient molecules are absorbed by cells that line the gastrointestinal tract	True
b.	molecules enter the bloodstream	True
c.	absorption of small molecules in the bloodstream	True
d.	nutrient molecules are absorbed	True
e.	main function of the digestive system	True
f.	process by which the gastrointestinal tract releases water into the urinary tract	False
g.	process by which the gastrointestinal tract releases various substance into the urinary tract	False
h.	secretion of digestive vitamins for food digestion	False
i.	done by gastrointestinal muscles	False
j.	necessary for intelligence	False

11	Major Function of Gastric Motility	
a.	To serve as a reservoir	True
b.	To break food into small particles	True
c.	mix food with gastric secretions	True
d.	To empty gastric contents into the duodenum	True
e.	controlled rate of digestion	True
f.	To serve as a water reservoir	False
g.	To break food into large particles	False
h.	mix food with urinary secretions	False
i.	To empty gastric contents into the blood	False
j.	controlled rate of micturition	False

12	Functional Anatomy of Stomach	
a.	Fundus - storage	True
b.	Body: Storage, Mucus, HCl, Pepsinogen, Intrinsic factor	True
c.	Antrum: Mixing/Grinding, Gastrin	True
d.	To serve as a reservoir	True
e.	To break food into small particles	True
f.	Fundus - Mixing/Grinding, Gastrin	False
g.	Body: Storage, Mucus, HCl, Pepsinogen, Intrinsic factor	False
h.	Antrum: storage	False
i.	To serve as a reservoir	False
j.	To break food into small particles	False

13	The relaxation of the gastric reservoir	
a.	is mainly regulated by reflexes	True
b.	Three kinds of relaxation can be differentiated	True
c.	Receptive reflexes	True
d.	Adaptive reflexes	True
e.	Feedback-relaxation	True
f.	is mainly regulated by mitochondria	False
g.	Four kinds of relaxation can be differentiated	False
h.	Receptive images	False
i.	Adaptive conclusions	False
j.	Language	False

14	What produces gastric peristaltic waves?	
a.	Peristaltic rhythm (~3/min) generated by pacemaker cells (longitudinal muscle layer)	True
b.	Slow waves – spontaneous depolarisation/ repolarisation	True
c.	Slow wave rhythm = basic electrical rhythm (BER)	True
d.	Slow waves conducted through gap junctions along longitudinal muscle layer	True
e.	Slow wave sub-threshold - requires further depolarization to induce action potentials	True
f.	Receptive reflexes	False
g.	Adaptive reflexes	False
h.	Feedback-relaxation	False
i.	Peristaltic rhythm generated by the Sino-Atrial Node	False
j.	Peristaltic rhythm generated by the Atrio-Ventricular Node	False

15	Enterogastric Reflex	
a.	regulates the rate at which chyme leaves the stomach	True
b.	Duodenum fills with chyme	True
c.	Sensory stretch receptors are stimulated	True
d.	Sensory nerve impulses travel to central nervous system	True
e.	Nerve impulses inhibit peristalsis in stomach wall	True
f.	regulates the rate at which chyme leaves the mouth	False
g.	Duodenum eliminate chyme	False
h.	Sensory stretch receptors are inhibited	False
i.	Sensory nerve impulses travel to frontal area centers	False
j.	Nerve impulses stimulate peristalsis in the stomach wall	False

16	The feedback regulation of gastric emptying is:	
a.	performed by entero-gastric reflexes and release of intestinal hormones	True
b.	It causes enhanced relaxation of the gastric reservoir	True
c.	inhibition of the antral pump	True
d.	reduced opening of the pyloric sphincter	True
e.	reduced contraction	True
f.	performed by mitactic reflexes	False
g.	It causes contraction of the gastric wall	False
h.	stimulate the antral pump	False
i.	stimulate opening of the pyloric sphincter	False
j.	stimulate contractions of the intestin	False

17	Neural Control of Gastrointestinal Function—Enteric Nervous System	
a.	The gastrointestinal tract has a nervous system all its own	True
b.	The enteric nervous system lies entirely in the wall of the gut, from the esophagus to the anus	True
c.	The enteric nervous system is highly developed	True
d.	is especially important in controlling gastrointestinal movements	True
e.	is especially important in controlling gastrointestinal secretion	True
f.	The gastrointestinal tract has a somatic nervous system	False
g.	The enteric nervous system lies from the stomach and to the liver	False
h.	The enteric nervous system is not important	False
i.	is especially important in controlling gastrointestinal absorption	False
j.	is especially important in controlling gastrointestinal reflux	False

18	The enteric nervous system:	
a.	the submucosal plexus controls mainly gastrointestinal secretion and local blood flow	True
b.	outer plexus lying between the longitudinal and circular muscle layers	True
c.	outer plexus is called the myenteric plexus or Auerbach's plexus	True
d.	inner plexus, called the submucosal plexus or Meissner's plexus, that lies in the submucosa	True
e.	myenteric plexus controls mainly the gastrointestinal movements	True
f.	the submucosal plexus controls mainly gastrointestinal motility	False
g.	inner plexus lying between the longitudinal and circular muscle layers	False
h.	outer plexus is called the submucosal plexus or Meissner's plexus, that lies in the submucosa	False
i.	inner plexus, called the myenteric plexus or Auerbach's plexus	False
j.	myenteric plexus controls mainly the gastrointestinal secretion and local blood flow	False

19	Hormonal Control of Gastrointestinal Motility	
a.	The gastrointestinal hormones are released into the portal circulation	True
b.	The gastrointestinal hormones exert physiological actions on target cells	True
c.	There are specific receptors for the gastrointestinal hormones	True
d.	Control exerted by Gastrin, Cholecystokinin, Secretin, Gastric inhibitory peptide, Motilin	True
e.	The effects of the hormones persist even after all nervous connections have been severed	True
f.	The gastrointestinal hormones are released into the liver	False
g.	The gastrointestinal hormones exert physiological actions on dermal cells	False
h.	There are nociceptive receptors for the gastrointestinal hormones	False
i.	Hormonal control is exerted by insulin and glucagon	False
j.	The effects of the hormones persist even after several days	False

20	Functional Types of Movements in the Gastrointestinal Tract	
a.	Two types of movements occur in the gastrointestinal tract	True
b.	propulsive movements	True
c.	mixing movements	True
d.	propulsive movements cause food to move forward along the tract at an appropriate rate	True
e.	mixing movements keep the intestinal contents thoroughly mixed at all times	True
f.	Five types of movements occur in the gastrointestinal tract	False
g.	Anti-propulsive movements	False
h.	Direct and indirect movements	False
i.	mixing movements cause food to move forward along the tract at an appropriate rate	False
j.	propulsive movements keep the intestinal contents thoroughly mixed at all times	False

21	Gastrointestinal hormones:	
a.	Gastrin	True
b.	Cholecystokinin	True
c.	Secretin	True
d.	Gastric inhibitory peptide	True
e.	Motilin	True
f.	TSH, Thyroid stimulating hormone	False
g.	ACTH, Adrenocorticotropin hormone	False
h.	GH, Growth Hormone	False
i.	FSH, Follicle-stimulating hormone, LH, Luteinizing hormone and PRL, Prolactin	False
j.	MSH, Melanophore-stimulating hormone	False

22	Gastrointestinal Blood Flow—"Splanchnic Circulation"	
a.	In the liver, the blood passes through liver sinusoids and finally leaves the liver by way of hepatic veins	True
b.	This flow of blood allows the reticuloendothelial cells that line the liver sinusoids to remove bacteria	True
c.	The blood vessels of the gastrointestinal system are part the splanchnic circulation	True
d.	Splanchnic Circulation includes the blood flow through the gut and through the spleen, pancreas, and liver	True
e.	all the blood that courses through the gut, spleen, and pancreas then flows immediately into portal vein	True
f.	In the liver, the blood passes through heart sinusoids and finally leaves the liver by way of arteries	False
g.	This flow of blood allows the nervous cells that line the liver sinusoids to remove carbohydrates	False
h.	The blood vessels of the gastrointestinal system are part the pulmonary circulation	False
i.	Splanchnic Circulation includes the blood flow through the kidneys	False
j.	all the blood that courses through the gut, spleen, and pancreas then flows immediately into aorta	False

23	Propulsion and Mixing of Food in the Alimentary Tract	
a.	The time that food remains in each part of the alimentary tract is critical for optimal processing	True
b.	Requirements for mixing and propulsion are quite different at each stage of processing	True
c.	Absorption of nutrients. Also, appropriate mixing must be provided.	True
d.	Multiple automatic nervous and hormonal mechanisms control the timing of each stage of processing	True
e.	Nervous and hormonal mechanisms are critical for optimal food processing	True
f.	The time that food remains in each part of the alimentary tract is critical for optimal processing	False
g.	Requirements for mixing and propulsion are quite different at each stage of processing	False
h.	Absorption of nutrients. Also, appropriate mixing must be provided.	False
i.	Multiple automatic nervous and hormonal mechanisms control the timing of each stage of processing	False
j.	Nervous and hormonal mechanisms are critical for optimal food processing	False

24	Ingestion of Food	
a.	The amount of food that a person ingests is determined principally by intrinsic desire for food called hunger	True
b.	The type of food that a person preferentially seeks is determined by appetite.	True
c.	These mechanisms are extremely important for maintaining an adequate nutritional supply for the body	True
d.	Food ingestion is confined to the mechanics of ingestion	True
e.	Mastication and swallowing are important for optimal food processing	True
f.	The amount of food that a person ingests is determined principally by obesity	False
g.	The type of food that a person preferentially seeks is determined by hunger	False
h.	These mechanisms are extremely important for maintaining an adequate excretional level	False
i.	Food ingestion is independent of the mechanics of ingestion	False
j.	Mastication and swallowing are important for external food preparation	False

25	Mastication (Chewing)	
a.	Chewing is important for digestion of all foods, but especially important for most fruits and raw vegetables	True
b.	Digestive enzymes act only on the surfaces of food particles.	True
c.	The teeth are admirably designed for chewing.	True
d.	The anterior teeth (incisors) provide a strong cutting action and the posterior teeth (molars) a grinding action.	True
e.	All the jaw muscles working together can close the teeth with a great force	True
f.	Chewing is important for hormonal activity	False
g.	Digestive enzymes act only on the micromolecules	False
h.	The teeth are admirably designed for absorbtion	False
i.	The anterior teeth (incisors) provide a weak cutting action	False
j.	All the jaw muscles working together can close the teeth in one minute	False

26	Swallowing (Deglutition)	
a.	A voluntary stage initiates the swallowing process	True
b.	The pharyngeal stage is involuntary and constitutes passage of food through the pharynx into the esophagus	True
c.	The esophageal stage, another involuntary phase that transports food from the pharynx to the stomach.	True
d.	The pharynx subserves respiration and swallowing.	True
e.	The pharynx is converted for only a few seconds at a time into a tract for propulsion of food	True
f.	A involuntary stage initiates the swallowing process	False
g.	The pharyngeal stage is a voluntary phase and constitutes passage of food through the pharynx into the stomach	False
h.	The esophageal stage is a involuntary phase that transports food from the pharynx to the duodenum.	False
i.	The pharynx subserves respiration and chewing	False
j.	The pharynx is converted for only two minutes per day into a tract for propulsion of food	False

27	Motor Functions of the Stomach	
a.	storage of large quantities of food until the food can be processed in the stomach, duodenum, and intestinal tract	True
b.	mixing of this food with gastric secretions until it forms a semifluid mixture called chyme	True
c.	slow emptying of the chyme from the stomach into the small intestine	True

d.	The rate emptying of the chyme is suitable for proper digestion	True
e.	The rate emptying of the chyme is suitable for proper absorption by the small intestine	True
f.	storage of small quantities of food until the food can be processed in the external tract	False
g.	mixing of this food with gastric secretions until it forms a solid mixture called microbiom	False
h.	slow emptying of the chyme from the stomach into the liver	False
i.	The rate emptying of the chyme is suitable for proper swallowing	False
j.	The rate emptying of the chyme is suitable for proper chewing	False

28	Movements of the Small Intestine	
a.	The movements of the small intestine can be divided into mixing and propulsive contractions	True
b.	To a great extent, this separation into mixing and propulsive contractions is artificial	True
c.	Essentially, all movements of the small intestine cause at some degree of both mixing and propulsion	True
d.	propulsive movements cause food to move forward along the tract at an appropriate rate	True
e.	mixing movements keep the intestinal contents thoroughly mixed at all times.	True
f.	Five types of movements occur in the small intestine	False
g.	Anti-propulsive movements	False
h.	Direct and indirect movements	False
i.	Mixing movements cause food to move forward along the small intestine at a high rate	False
j.	propulsive movements keep the intestinal contents thoroughly mixed at all times	False

29	Functions of the colon are:	
a.	absorption of water and electrolytes from the chyme	True
b.	form solid feces	True
c.	storage of fecal matter until it can be expelled	True
d.	The proximal half of the colon is concerned principally with absorption	True
e.	The distal half of the colon is concerned principally with storage	True
f.	absorption of microorganisms	False
g.	form the primary urinary product	False
h.	storage of food until it can be expelled	False
i.	The proximal half of the colon is concerned principally with storage	False
j.	The distal half of the colon is concerned principally with absorption	False

30	Secretory Functions of the Alimentary Tract:	
a.	digestive enzymes are secreted in most areas of the alimentary tract	True
b.	mucous glands provide mucus for lubrication and protection of all parts of the alimentary tract	True
c.	most digestive secretions are formed only in response to the presence of food in the tract	True
d.	the quantity secreted in each segment of the tract is usually the precise amount needed for proper digestion	True
e.	the types of enzymes and other constituents of the secretions are varied by the types of food	True
f.	digestive enzymes are secreted in most areas of the respiratory tract	False
g.	mucous glands provide mucus for lubrication and protection of all parts of the nervous system	False
h.	most digestive secretions are formed only in response to the presence of water in the tract	False
i.	the quantity secreted in each segment of the tract is usually the precise amount needed for transpiration	False
j.	the types of enzymes and other constituents of the secretions are varied by the brain size	False

Course 9: The Urinary System
Sub-topic: Structure, Function, and Regulation

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1. Overview of the Urinary System
    - Primary Function
    - Components of the Urinary System

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2. Anatomy of the Kidneys
2.1. General Organization
2.2. Internal Structure of the Kidneys

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3. The Nephron: Functional Unit of the Kidney
3.1. Types of Nephrons
3.2. Structure of the Nephron
    - Glomerulus
    - Renal Tubule

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4. Kidney Function
4.1. Filtration
4.2. Reabsorption
4.3. Secretion

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5. Urine Formation
5.1. Filtration
5.2. Reabsorption
5.3. Secretion
5.4. Excretion

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6. Regulation of Kidney Function
6.1. Renin-Angiotensin-Aldosterone System (RAAS)
6.2. Antidiuretic Hormone (ADH)
6.3. Atrial Natriuretic Peptide (ANP)

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7. Role of the Kidneys in Homeostasis
7.1. Regulation of Electrolytes
7.2. Acid-Base Balance
7.3. Erythropoiesis
7.4. Gluconeogenesis

Practical Session 9: The Urinary System – Filtration

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1. Introduction to Filtration in the Urinary System

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2. Glomerular Filtration

2.1. Process of Filtration

2.2. Glomerular Filtration Rate (GFR)

- Definition:
  - GFR is the volume of filtrate produced per minute by the kidneys, approximately 125 mL/min, which equates to 180 L/day. Only about 1% of this filtrate becomes urine, with the rest reabsorbed.
- Factors Affecting GFR:
  - Renal Blood Flow: Increased blood flow to the kidneys increases GFR.
  - Plasma Protein Concentration: Decreased plasma proteins can increase GFR, potentially leading to edema.
  - Blood Pressure: Hemorrhage or low capillary pressure decreases GFR.
  - Capsular Pressure: Increased pressure in Bowman's capsule reduces GFR.

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3. Factors Determining Glomerular Filterability

- Molecular Weight:
  - Smaller molecules such as ions, glucose, and urea are filtered freely. Larger molecules like proteins are not filtered.
- Charge of the Molecule:
  - Negatively charged molecules are less likely to be filtered due to the negatively charged filtration barrier, which repels them.

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4. Regulation of Glomerular Filtration Rate (GFR)

4.1. Renal Autoregulation

- Mechanism:
  - The kidneys can adjust the diameter of the afferent arteriole to maintain a stable GFR despite fluctuations in systemic blood pressure.

4.2. Neural Regulation

- Sympathetic Nervous System:
  - Sympathetic stimulation typically causes constriction of both afferent and efferent arterioles. During extreme conditions like hemorrhage, increased sympathetic activity reduces GFR to conserve fluids.

4.3. Hormonal Regulation

- Angiotensin II
- Atrial Natriuretic Peptide (ANP)
- Endothelin and Prostaglandins

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5. Measurement of GFR

- Plasma Clearance:
  - GFR is often measured by the clearance of specific substances that are filtered but neither reabsorbed nor secreted by the kidneys (e.g., inulin).
- Calculation Example:
  - If the plasma concentration of a substance is 3 mg/L and the GFR is 180 L/day, the excreted amount would be 540 mg/day.

Course 9: The Urinary System
Sub-topic: Structure, Function, and Regulation

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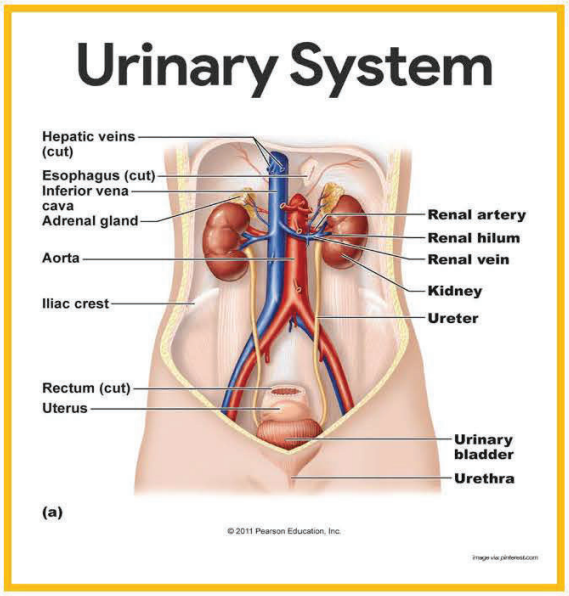
1. Overview of the Urinary System

The urinary system plays a critical role in maintaining the body's internal environment by regulating fluid and electrolyte balance, removing waste products, and contributing to homeostasis.

- Primary Function:
  - Filtration of blood to remove metabolic wastes.
  - Regulation of fluid and electrolyte balance.
  - Maintenance of acid-base balance.
  - Regulation of blood pressure through fluid volume control.
  - Hormonal regulation (erythropoietin and renin secretion).
- Components of the Urinary System:
  - Kidneys: Primary organs responsible for filtering blood and producing urine.
  - Ureters: Tubes that carry urine from the kidneys to the bladder.
  - Bladder: A muscular organ that stores urine before excretion.
  - Urethra: The tube through which urine is excreted from the body.



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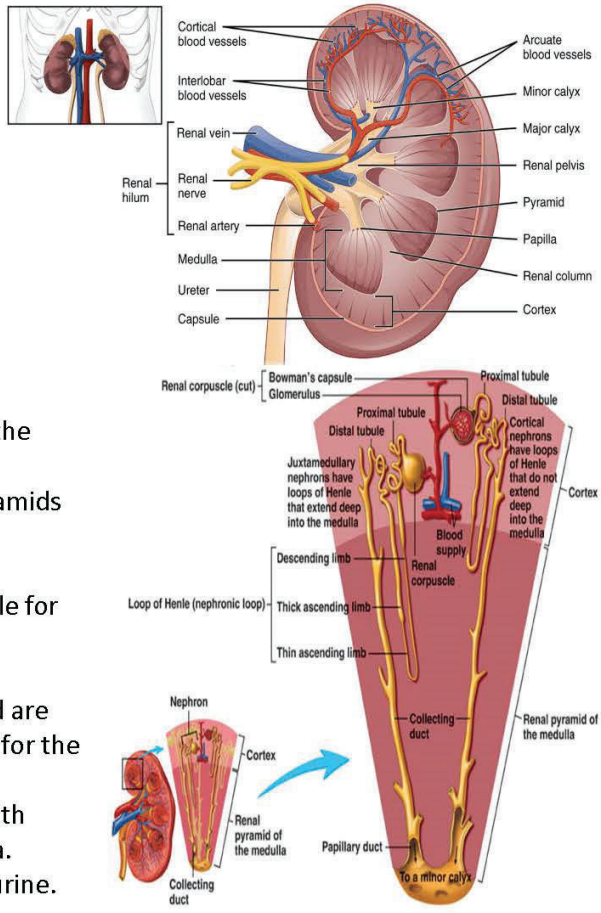
2. Anatomy of the Kidneys

2.1. General Organization

- The kidneys are located retroperitoneally on either side of the vertebral column at the level of the T12-L3 vertebrae. They are bean-shaped and receive about 25% of the cardiac output to filter the blood.

2.2. Internal Structure of the Kidneys

- Cortex: The outer layer, containing most of the nephrons where filtration occurs.
- Medulla: The inner layer, organized into renal pyramids, where reabsorption and secretion take place.
- Renal Pelvis: The central cavity that collects urine from the nephrons and funnels it into the ureter.
- Calyces: Structures that funnel urine from the renal pyramids into the renal pelvis.



3. The Nephron: Functional Unit of the Kidney

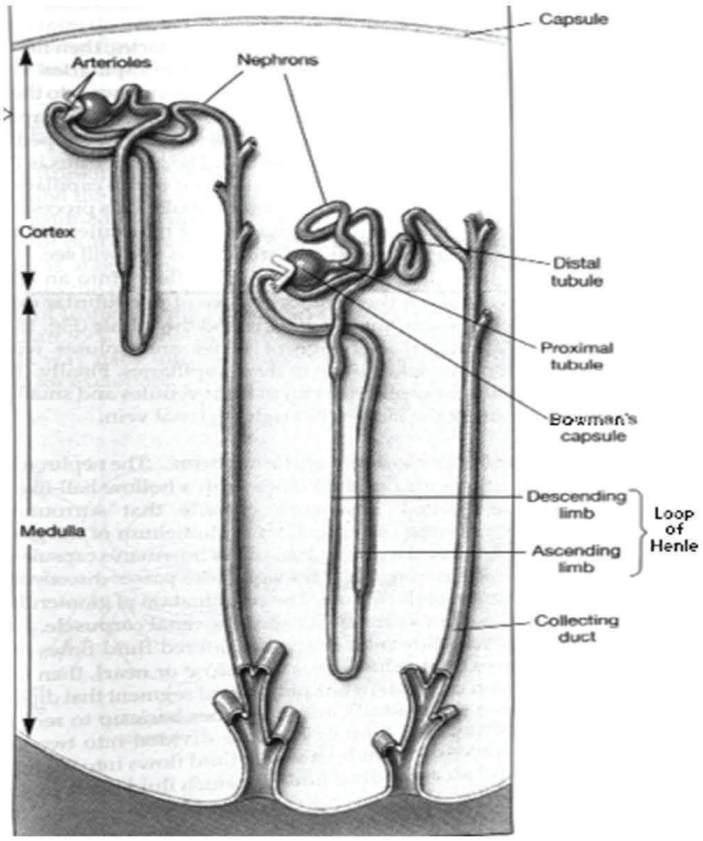
The nephron is the basic functional unit of the kidney responsible for filtering blood and forming urine.

3.1. Types of Nephrons

- Cortical Nephrons: Make up about 85% of nephrons and are located mainly in the renal cortex. They are responsible for the majority of filtration.
- Juxtamedullary Nephrons: Located near the medulla, with longer loops of Henle that extend deep into the medulla. These nephrons play a key role in the concentration of urine.

3.2. Structure of the Nephron

- Glomerulus: A network of capillaries where blood filtration begins. Hydrostatic and osmotic pressures across the glomerular capillaries determine the glomerular filtration rate (GFR).
- Renal Tubule:
  - Proximal Convoluted Tubule (PCT): Responsible for the majority of reabsorption (water, electrolytes, glucose, and amino acids).
  - Loop of Henle: Functions in the creation of a concentration gradient in the medulla, allowing the kidney to produce urine of varying concentrations.
  - Distal Convoluted Tubule (DCT): Involved in further reabsorption and secretion, especially under hormonal control (e.g., aldosterone).
  - Collecting Duct: Final adjustment of urine concentration and volume, influenced by ADH and aldosterone.



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4. Kidney Function

4.1. Filtration

- Blood is filtered in the glomerulus, where water, electrolytes, and small molecules pass into Bowman's capsule, forming the filtrate. Large molecules (e.g., proteins and blood cells) are retained in the blood.

4.2. Reabsorption

- Selective reabsorption occurs mainly in the proximal tubule, where essential substances (e.g., glucose, amino acids, water, and electrolytes) are reabsorbed back into the bloodstream.

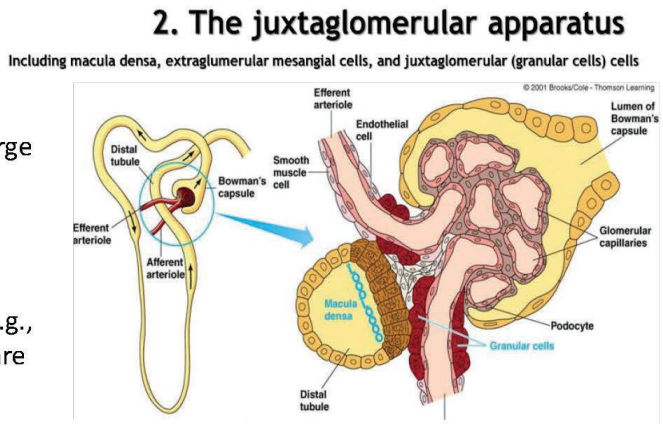
4.3. Secretion

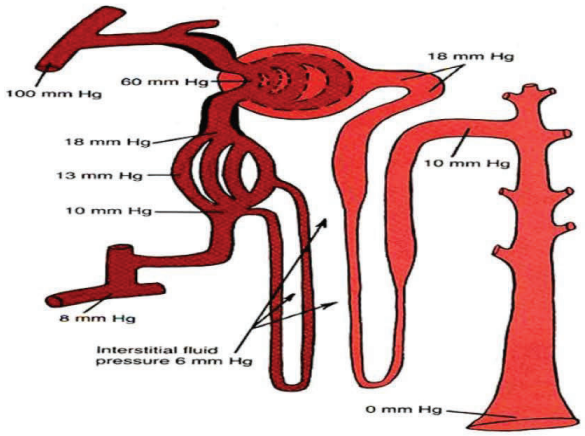
- Waste products and excess ions (e.g., hydrogen, potassium) are secreted from the blood into the renal tubule, mainly in the distal convoluted tubule and collecting ducts.

5. Urine Formation

5.1. Filtration

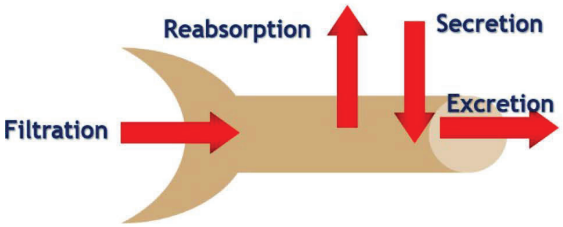
- The glomerulus filters blood, producing a filtrate that enters Bowman's capsule. Filtration is driven by the pressure gradient between the glomerulus and Bowman's space.





5.2. Reabsorption

- Most water, electrolytes, and nutrients are reabsorbed from the renal tubules into the peritubular capillaries. This process is regulated to maintain electrolyte balance and proper hydration. Process of returning filtered material to the bloodstream
  99% of what is filtered
  It may involve transport proteins.
  Usually, glucose is totally reabsorbed



5.3. Secretion

- Additional waste products, excess ions, and certain drugs are actively secreted into the filtrate to be eliminated in the urine. Active transport (usually) of toxins and foreign substances: Saccharine, Penicillin

5.4. Excretion

- The final urine, composed of waste products and excess substances, is transported to the bladder for storage and ultimately excreted from the body through the urethra.

- Loss of fluid from body in form of urine

$$\left[\begin{array}{l}\text{Amount}\\ \text{of Solute}\\ \text{Excreted}\end{array}\right] = \left[\begin{array}{l}\text{Amount}\\ \text{Filtered}\end{array}\right] + \left[\begin{array}{l}\text{Amount}\\ \text{Secreted}\end{array}\right] - \left[\begin{array}{l}\text{Amount}\\ \text{Reabsorbed}\end{array}\right]$$

---

6. Regulation of Kidney Function

6.1. Renin-Angiotensin-Aldosterone System (RAAS)

- Renin is secreted in response to low blood pressure or low sodium levels. Renin converts angiotensinogen into angiotensin I, which is then converted to angiotensin II by ACE. Angiotensin II constricts blood vessels and stimulates aldosterone release, increasing sodium and water reabsorption to raise blood pressure.

6.2. Antidiuretic Hormone (ADH)

- ADH, released from the posterior pituitary, acts on the collecting ducts to increase water reabsorption, concentrating the urine and reducing water loss.

6.3. Atrial Natriuretic Peptide (ANP)

- ANP is released by the atria in response to high blood pressure. It inhibits sodium reabsorption, leading to increased excretion of sodium and water, thereby reducing blood volume and pressure.

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7. Role of the Kidneys in Homeostasis

7.1. Regulation of Electrolytes

- The kidneys regulate the balance of electrolytes such as sodium, potassium, calcium, and phosphate, essential for maintaining cellular functions and osmotic balance.

7.2. Acid-Base Balance

- The kidneys contribute to maintaining acid-base balance by reabsorbing bicarbonate (HCO_3^-) and secreting hydrogen ions (H^+), ensuring the blood's pH remains within a narrow range (7.35-7.45).

7.3. Erythropoiesis

- The kidneys secrete erythropoietin, a hormone that stimulates red blood cell production in the bone marrow in response to hypoxia (low oxygen levels).

7.4. Gluconeogenesis

- During prolonged fasting or starvation, the kidneys can produce glucose from non-carbohydrate sources, a process called gluconeogenesis, to help maintain blood glucose levels.

Practical Session 9: The Urinary System – Filtration

1. Introduction to Filtration in the Urinary System

Filtration is the first essential step in the formation of urine, where blood plasma is filtered across the glomerular capillaries into the Bowman's capsule. The process occurs in the renal corpuscle, which includes the glomerulus and Bowman's capsule. Filtration ensures the removal of waste products, excess ions, and other molecules from the blood while retaining cells and larger molecules like proteins. This filtrate is processed along the nephron, where important substances are reabsorbed and waste is excreted as urine.

2. Glomerular Filtration

2.1. Process of Filtration

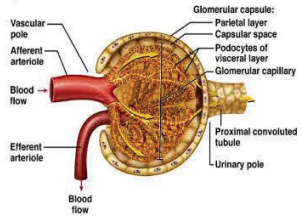
The filtration process occurs in the glomerulus, where blood enters through the afferent arteriole and exits via the efferent arteriole. The capillary walls of the glomerulus act as a selective barrier, allowing water and small solutes to pass through while preventing the passage of large molecules such as proteins and blood cells.

Glomerular filtration

- blood enters glomerular capillary
- filters out of renal corpuscle
  - large proteins and cells stay behind
  - everything else is filtered into nephron
  - glomerular filtrate
    - plasma like fluid

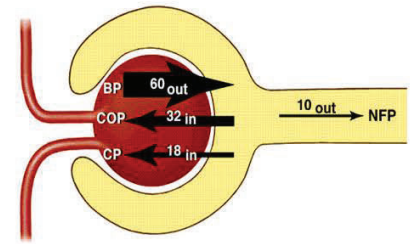
Factors that determining the glumerular filterability

- Molecular weight
- Charges of the molecule



- Filtration Membrane: The filtration membrane consists of three layers:
  1. Endothelial cells of the glomerular capillaries (fenestrated to allow passage of small molecules).
  2. Basement membrane (negatively charged, repelling larger molecules).
  3. Podocytes of Bowman's capsule, which have filtration slits.

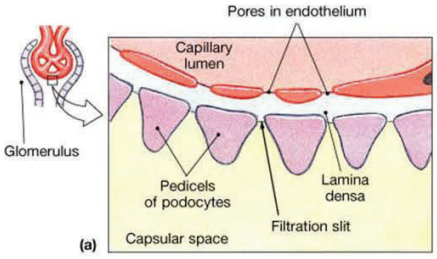
The pressure difference between the glomerular capillaries and Bowman's capsule drives the filtration process, with hydrostatic pressure being the primary force pushing fluid through the membrane.

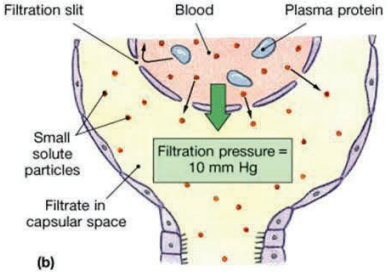


Capillary blood pressure (BP)	60 mmHg out
Colloid osmotic pressure (COP)	−32 mmHg in
Capsular pressure (CP)	−18 mmHg in
Net filtration pressure (NFP)	10 mmHg out

2.2. Glomerular Filtration Rate (GFR)

- Definition: GFR is the volume of filtrate produced by both kidneys per minute. In healthy adults, the GFR is approximately 125 mL/min, which equates to 180 L/day. Only about 1% of the filtrate becomes urine, while the remaining 99% is reabsorbed along the nephron.
- Factors Affecting GFR:
  - Renal Blood Flow: Increased blood flow to the glomerulus raises the hydrostatic pressure in the glomerular capillaries, enhancing GFR. Conversely, decreased blood flow reduces GFR.
  - Plasma Protein Concentration:
    Plasma proteins, particularly albumin, exert colloid osmotic pressure, opposing filtration. A reduction in plasma proteins (as seen in liver disease or nephrotic syndrome) decreases this pressure, increasing GFR. This can lead to an excessive loss of fluid from the capillaries, causing edema.
  - Blood Pressure: GFR is closely linked to systemic blood pressure. Low capillary pressure, such as during hemorrhage or dehydration, reduces GFR, while high pressure can increase it, sometimes damaging the filtration barrier.
  - Capsular Pressure: Pressure within Bowman's capsule opposes glomerular hydrostatic pressure. Increased capsular pressure (due to conditions like kidney stones or swelling) reduces GFR by impeding the flow of filtrate out of the glomerulus.





3. Factors Determining Glomerular Filterability

- Molecular Weight:
  The filtration membrane selectively allows smaller molecules to pass through based on size. Molecules like ions, glucose, amino acids, and urea are filtered freely because of their small molecular size. Larger molecules like proteins and blood cells are too large to pass through the filtration slits, preventing their entry into the filtrate.
- Charge of the Molecule:
  The glomerular basement membrane is negatively charged, which repels similarly charged molecules, especially large negatively charged proteins such as albumin. Positively charged molecules are filtered more readily than negatively charged ones, even if they are of similar size.

---

4. Regulation of Glomerular Filtration Rate (GFR)

4.1. Renal Autoregulation

- Mechanism:
  The kidneys possess an intrinsic ability to maintain a stable GFR despite fluctuations in systemic blood pressure. This is achieved through the myogenic mechanism and tubuloglomerular feedback.
  - Myogenic Mechanism:
    The afferent arteriole constricts or dilates in response to changes in blood pressure. When blood pressure rises, the arteriole constricts to reduce blood flow into the glomerulus, maintaining a stable GFR. Conversely, when blood pressure falls, the arteriole dilates.
  - Tubuloglomerular Feedback:
    The macula densa cells in the distal tubule sense the sodium concentration in the filtrate. If GFR increases, there is less time for sodium reabsorption, and the macula densa releases signals that constrict the afferent arteriole, reducing GFR.

4.2. Neural Regulation

- Sympathetic Nervous System:
  Sympathetic activation, particularly during stress or hemorrhage, leads to vasoconstriction of both the afferent and efferent arterioles. This decreases renal blood flow and GFR, conserving fluids and maintaining blood pressure in critical situations. Severe vasoconstriction can, however, lead to acute kidney injury.

4.3. Hormonal Regulation

- Angiotensin II:
  Angiotensin II is a potent vasoconstrictor that primarily constricts the efferent arteriole. This increases glomerular hydrostatic pressure and maintains GFR during low blood pressure states, such as dehydration or hemorrhage. However, prolonged angiotensin II activity can damage the kidneys.
- Atrial Natriuretic Peptide (ANP):
  ANP is released by the heart in response to increased blood volume. It causes vasodilation of the afferent arteriole and vasoconstriction of the efferent arteriole, increasing GFR and promoting the excretion of sodium and water to reduce blood volume and pressure.
- Endothelin and Prostaglandins:
  These local mediators influence the tone of renal arterioles. Endothelin is a vasoconstrictor that can reduce GFR, while prostaglandins (especially prostaglandin E_2) dilate arterioles, counteracting excessive vasoconstriction and preserving renal blood flow.

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5. Measurement of GFR

GFR is an important clinical indicator of kidney function, and it is measured using the clearance of substances that are freely filtered by the kidneys and neither reabsorbed nor secreted by the nephron.

- Plasma Clearance:
  GFR can be estimated by measuring the clearance of certain substances from the plasma. One commonly used substance is inulin, which is ideal because it is filtered but neither reabsorbed nor

secreted. However, in clinical practice, creatinine clearance is often used, even though a small amount of creatinine is secreted by the renal tubules.

The clearance of a substance is calculated using the formula:

$$\text{Clearance}(C) = \frac{U \times V}{P}$$

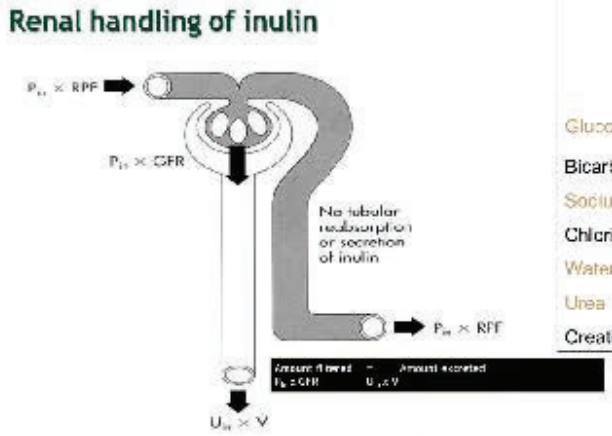
Where:

- UUU is the concentration of the substance in urine.
- VVV is the urine flow rate.
- PPP is the plasma concentration of the substance.

- Calculation Example:
  If the plasma concentration of a substance is 3 mg/L and the GFR is 180 L/day, the amount excreted per day can be calculated as:

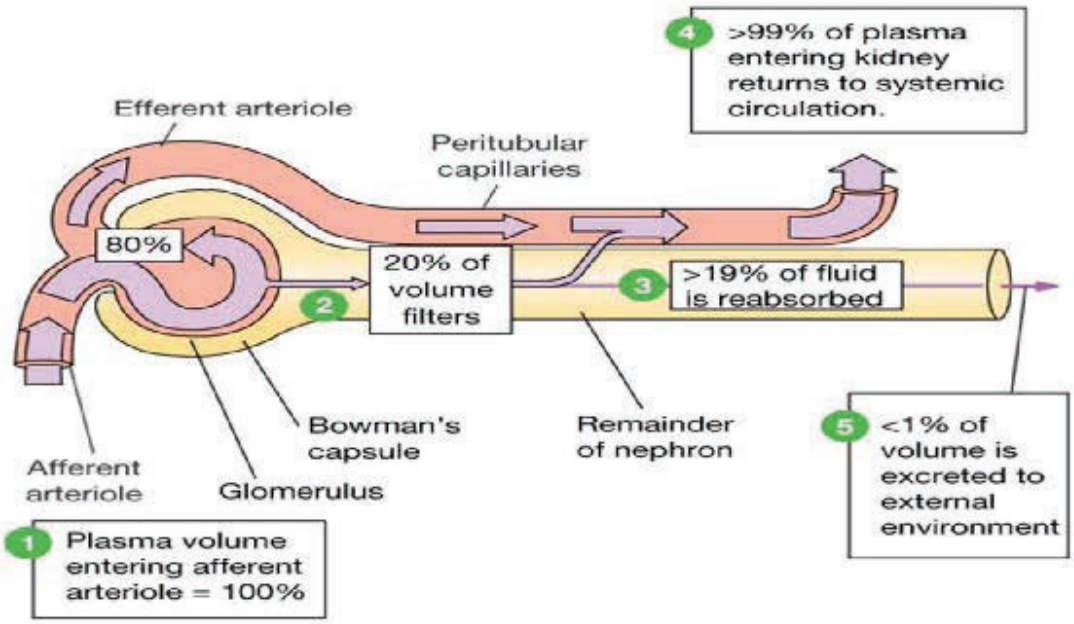
$$\text{Excreted Amount} = 3\,\text{mg/L} \times 180\,\text{L/day} = 540\,\text{mg/day}.$$

This value indicates the amount of the substance removed from the blood by the kidneys daily.



Filtration, reabsoption, and excretion rates of substances by the kidneys

		Filtered (meq/24h)	Reabsorbed (meq/24h)	Excreted (meq/24h)	Reabsorbed (%)
Glucose	(g/day)	180	180	0	100
Bicarbonate	(meq/day)	4,320	4,318	2	> 99.9
Sodium	(meq/day)	25,560	25,410	150	99.4
Chloride	(meq/day)	19,440	19,260	180	99.1
Water	(l/day)	169	167.5	1.5	99.1
Urea	(g/day)	48	24	24	50
Creatinine	(g/day)	1.8	0	1.8	0



Course 10: The Urinary System
Sub-topic: Fluid and Electrolyte Balance
Course Structure

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1. Overview of the Urinary System

- **Primary Functions**
- **Main Components of the Urinary System:**

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2. Mechanisms of Urine Formation
2.1. Filtration
2.2. Reabsorption
2.3. Secretion
2.4. Excretion

---

3. Regulation of Kidney Function
3.1. Renin-Angiotensin-Aldosterone System (RAAS)
3.2. Antidiuretic Hormone (ADH)
3.3. Atrial Natriuretic Peptide (ANP)

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4. Fluid and Electrolyte Balance
4.1. Sodium and Water Reabsorption
4.2. Potassium Balance

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5. Urine Concentration and Dilution
5.1. Mechanism of Urine Concentration
5.2. Obligatory vs. Facultative Water Reabsorption

---

6. Micturition (Urination)
6.1. Bladder Filling and Stretch Receptors
6.2. Micturition Reflex

---

7. Practical Applications and Clinical Implications
7.1. Common Disorders of the Urinary System

- **Kidney Stones (Nephrolithiasis): Hard deposits of minerals that can obstruct urine flow.**
- **Urinary Tract Infections (UTIs): Infections that affect the bladder, urethra, or kidneys.**
- **Chronic Kidney Disease (CKD): Gradual loss of kidney function, leading to waste accumulation in the blood and fluid imbalance.**

7.2. Diagnostic Tools

- **Urinalysis: Examination of urine to detect diseases such as diabetes, infections, or kidney disorders.**
- **Blood Tests: Measurement of waste products (e.g., creatinine, urea) to assess kidney function.**

Examination and Assessment

Course 10: The Urinary System
Sub-topic: Fluid and Electrolyte Balance

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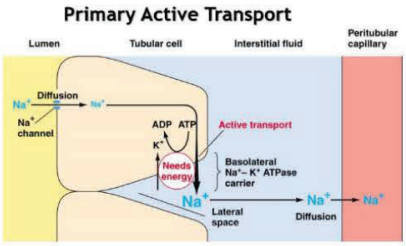
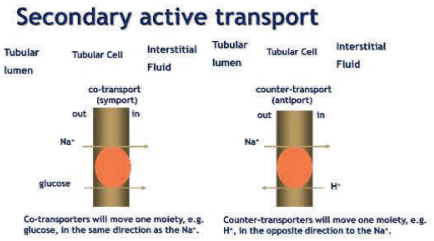
1. Mechanism of Transport
    - Primary Active Transport
    - Secondary Active Transport
    - Pinocytosis
    - Passive Transport





2. Mechanisms of Urine Formation

The kidneys produce urine through a series of processes that involve filtering the blood, reabsorbing essential substances, and secreting waste products.

2.1. Filtration

- Occurs in the glomeruli of the nephrons.
- Blood pressure forces water and solutes out of the blood and into Bowman's capsule, forming the filtrate.
- The filtration barrier consists of fenestrated capillaries, a basement membrane, and podocytes, allowing selective filtration based on size and charge.

2.2. Reabsorption

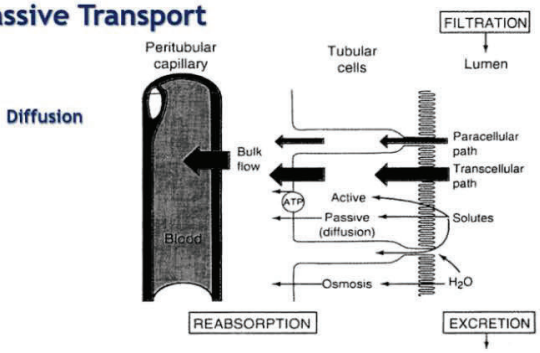
- Reabsorption takes place in the renal tubules (proximal tubule, loop of Henle, distal tubule, and collecting duct).
- Most water, electrolytes, and nutrients (e.g., glucose, amino acids) are reabsorbed into the bloodstream from the filtrate.
- This process is highly regulated to maintain electrolyte balance and hydration.

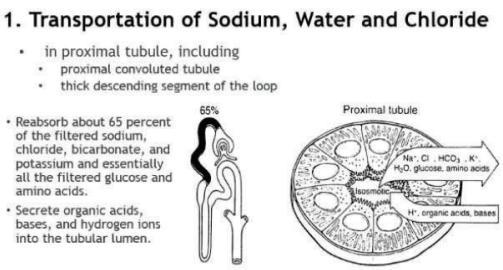
2.3. Secretion

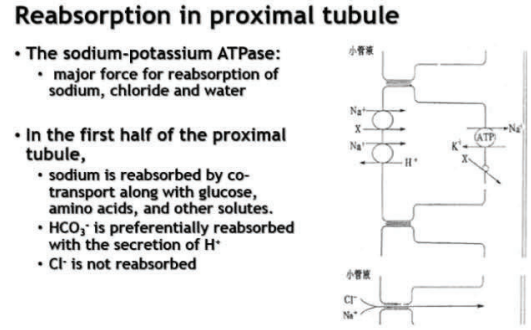
- Active process in which waste products (e.g., hydrogen ions, potassium, and drugs) are secreted from the blood into the filtrate in the distal tubule and collecting ducts.
- Secretion helps regulate pH and electrolyte composition of blood.

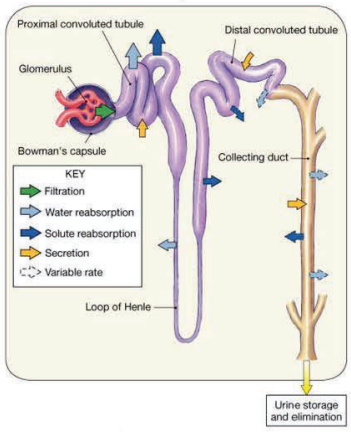
2.4. Excretion

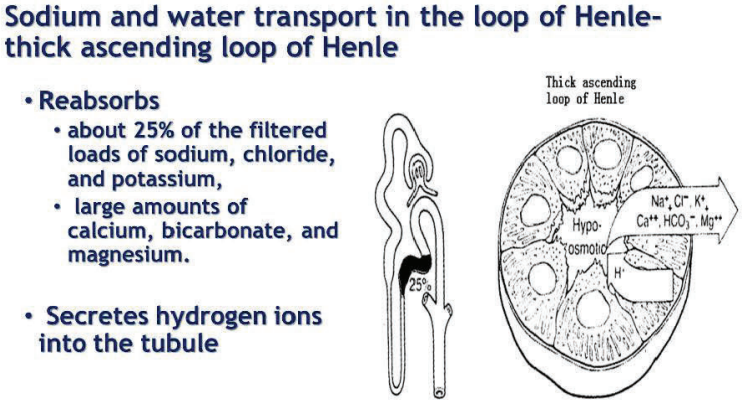
- The final urine, containing unabsorbed substances and waste products, is excreted through the ureters, stored in the bladder, and released via the urethra during micturition.



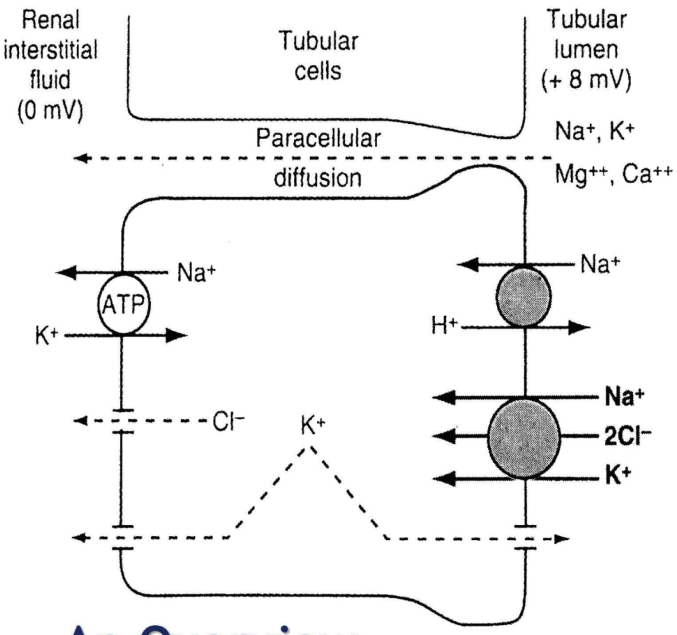








Mechanism of sodium, chloride, and potassium transport in the thick ascending loop of Henle



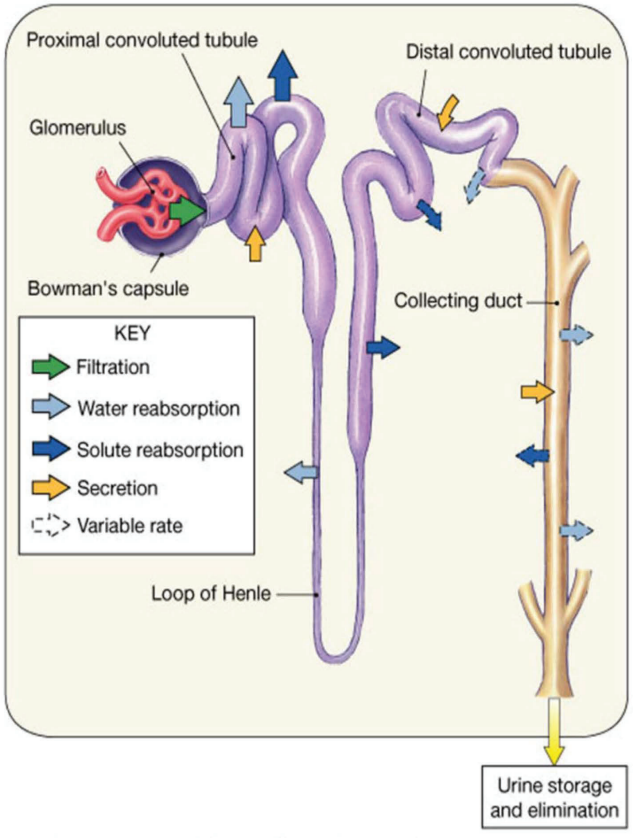
2. Glucose Reabsorption

- Reabsorbed along with Na^+ in the early portion of the proximal tubule.
  - by secondary active transport.
- Essentially all of the glucose is reabsorbed
  - and no more than a few milligrams appear in the urine per 24 hours.
- The amount reabsorbed is proportionate to the amount filtered
  - When the transport maximum of glucose (TmG) is exceed, the amount of glucose in the urine rises
  - The TmG is about 375 mg/min in men and 300 mg/min in women.

Urine Concentration and Dilution

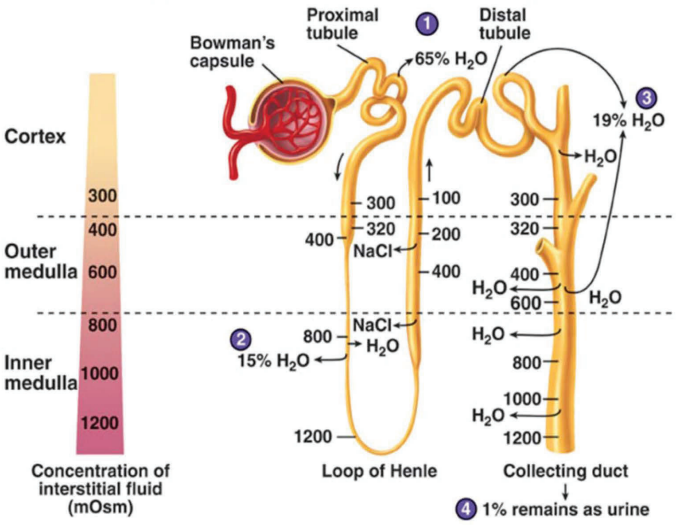
- **Importance: maintaince of the water balance in the body**
  - **When there is excess water in the body**
    - the kidney can excrete urine with an osmolarity as low as 50 mOsm/liter
  - **When there is a deficient of water**
    - the kidney can excrete urine with a concentration of about 1200 to 1400 mOsm/liter

An Overview of Urine Formation

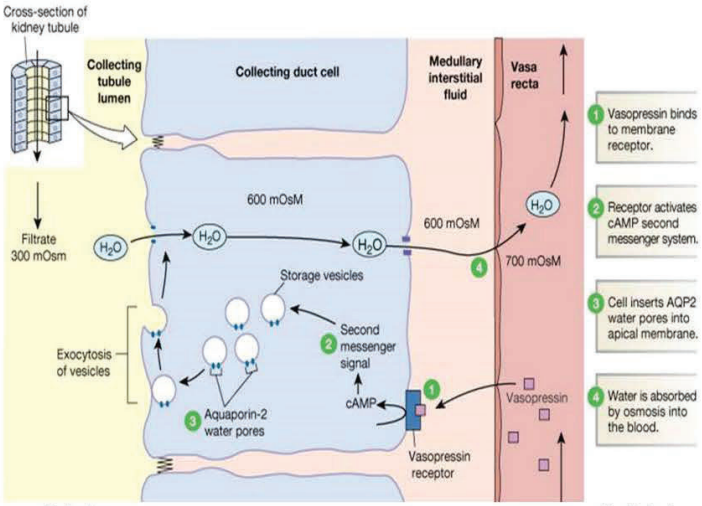


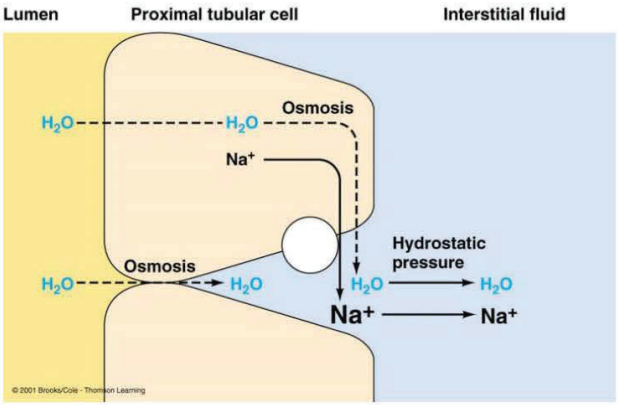
The basic requirements for forming a concentrated or diluted urine

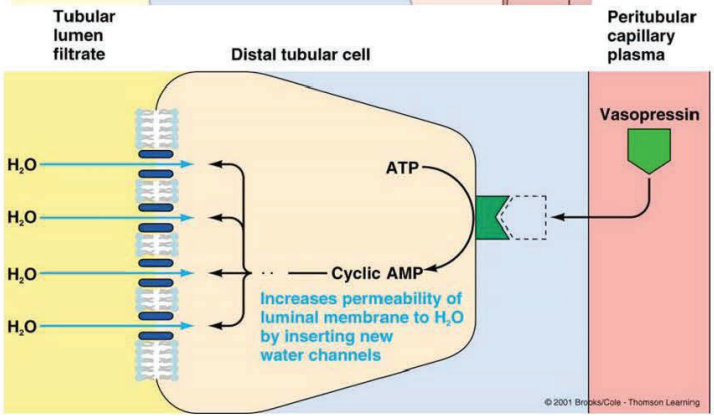
- the controlled secretion of antidiuretic hormone (ADH)
  - regulates the permeability of the distal tubules and collecting ducts to water
- a high osmolarity of the renal medullary interstitial fluid
  - provides the osmotic gradient necessary for water reabsorption to occur in the presence of high level of ADH



Water reabsorption



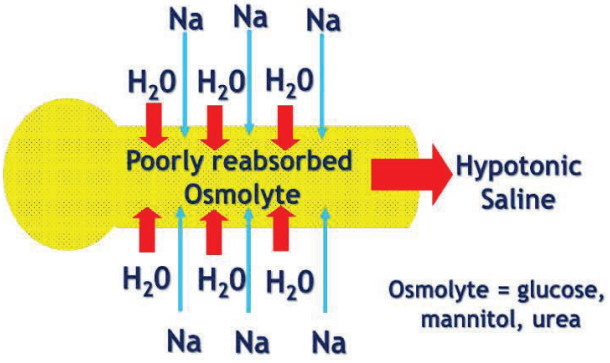


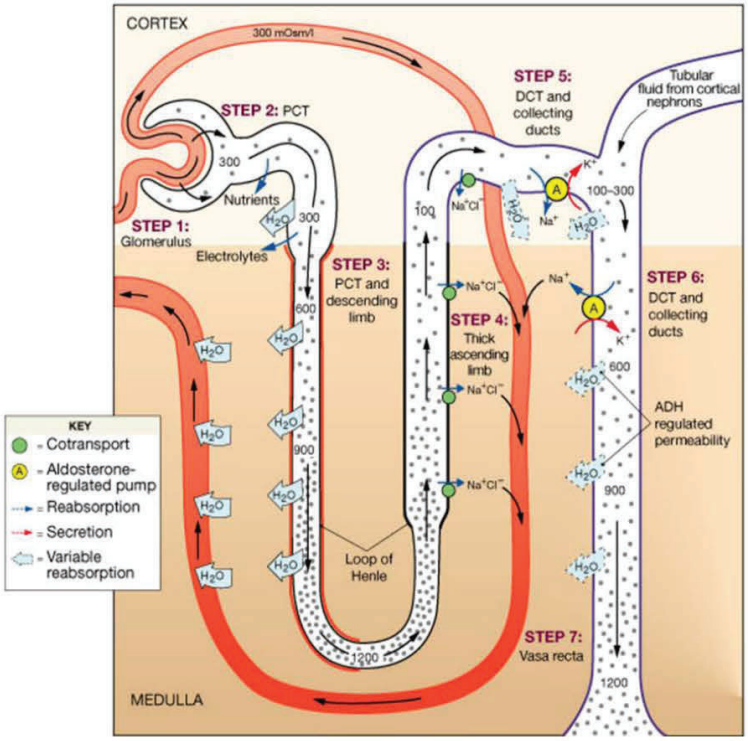


Facultative water reabsorption:

- Occurs mostly in collecting ducts
- Through the water poles (channel)
- Regulated by the ADH

Osmotic Diuresis





A Summary of Renal Function

INNERVATION OF THE KIDNEY

Nerves from the renal plexus (sympathetic nerve) enter kidney at the hilus→innervate smooth muscle of afferent & efferent arterioles→regulates blood pressure & distribution throughout kidney

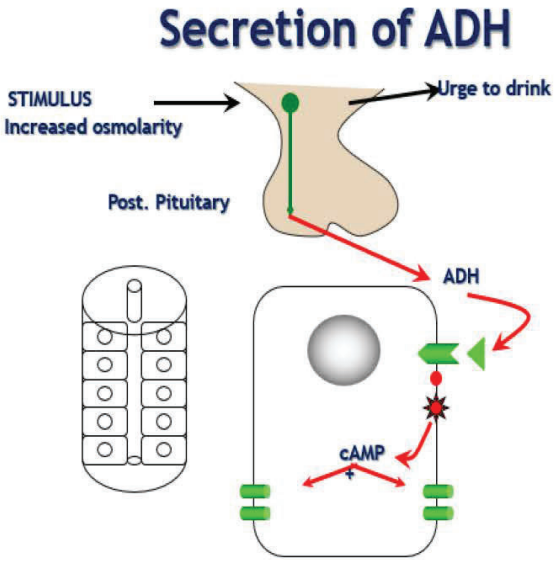
Effect: (1) Reduce the GPF and GFR through contracting the afferent and efferent artery (α receptor)

(2) Increase the Na^+ reabsorption in the proximal tubules (β receptor)

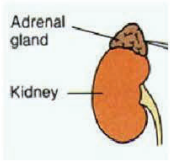
(3) Increase the release of renin (β receptor)

- **Retention of Water is controlled by ADH (Anti Diuretic Hormone)**
  - **ADH Release is Controlled by:**
    - Decrease in Blood Volume
    - Decrease in Blood Pressure
    - Increase in extracellular fluid (ECF) osmolarity

2. Aldosterone



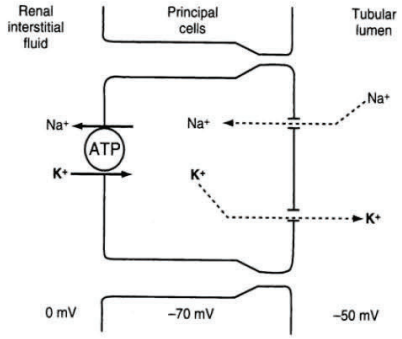
- Sodium Balance Is Controlled By Aldosterone

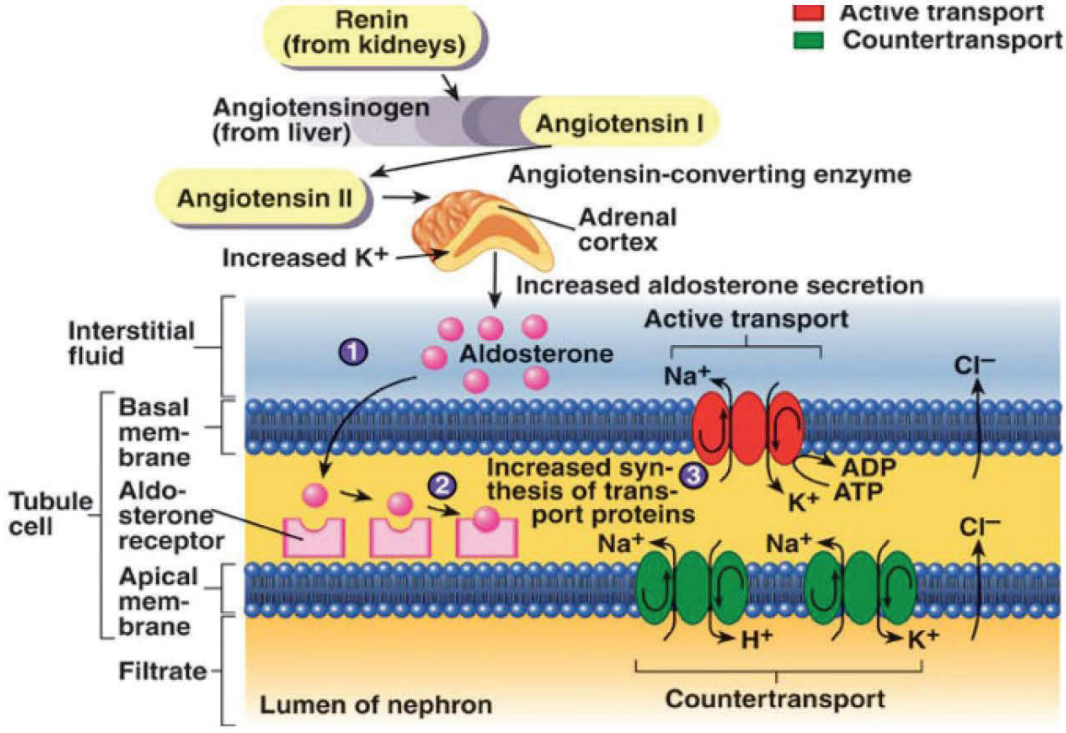


- Aldosterone:
  - Steroid hormone
  - Synthesized in Adrenal Cortex
  - Causes reabsorbtion of Na^+ and H_2O in DCT & CD
    - Also, K^+ secretion

Effect of Aldeosterone

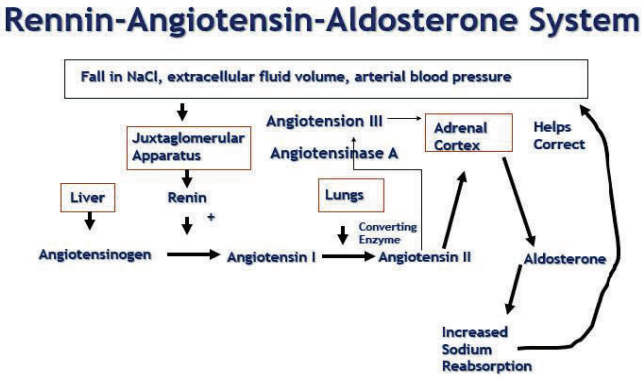
- to make the kidneys retain Na^+ and water reabsorption and K^+ secretion.
  - Acting on the principal cells of the cortical collecting duct.
  - stimulating the Na^+ - K^+ ATPase pump
  - increases the Na^+ permeability of the luminal side of the membrane.





3. Regulation of Kidney Function

The regulation of kidney function is essential for maintaining fluid and electrolyte balance, blood pressure, and overall homeostasis.



3.1. Renin-Angiotensin-Aldosterone System (RAAS)

- Renin is secreted by the juxtaglomerular cells of the kidney in response to low blood pressure or low sodium levels.
- Renin converts angiotensinogen (produced by the liver) to angiotensin I, which is converted to angiotensin II by ACE (Angiotensin-Converting Enzyme).
- Angiotensin II constricts blood vessels, increases aldosterone secretion from the adrenal cortex, and promotes sodium and water reabsorption in the kidneys, thus raising blood pressure.

3.2. Antidiuretic Hormone (ADH)

- Also called vasopressin, ADH is released by the posterior pituitary in response to high plasma osmolarity or low blood volume.
- ADH increases water reabsorption in the distal tubules and collecting ducts by inserting aquaporin channels, thus concentrating urine and conserving water.

3.3. Atrial Natriuretic Peptide (ANP)

- ANP is released by the atria of the heart in response to increased blood volume and pressure.
- It inhibits sodium reabsorption in the kidneys, promoting natriuresis (sodium excretion), which reduces blood volume and pressure.

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4. Fluid and Electrolyte Balance

The kidneys are essential in maintaining the balance of fluids and electrolytes, primarily sodium, potassium, and water.

4.1. Sodium and Water Reabsorption

- Sodium is actively reabsorbed in the proximal tubules, loop of Henle, distal tubules, and collecting ducts.
- Water follows sodium passively by osmosis in response to the osmotic gradient.
- Aldosterone and ADH play key roles in regulating sodium and water reabsorption, respectively.

4.2. Potassium Balance

- Potassium is filtered, reabsorbed, and secreted in the renal tubules.
- Aldosterone promotes the secretion of potassium in exchange for sodium in the distal tubule and collecting ducts.
- Potassium balance is crucial for normal nerve and muscle function, and imbalances can lead to serious cardiovascular complications.

---

5. Urine Concentration and Dilution

The kidneys adjust urine concentration and volume in response to the body's hydration status.

5.1. Mechanism of Urine Concentration

- Occurs in the loop of Henle and the collecting ducts through a counter-current mechanism.
- In the presence of ADH, the collecting ducts become permeable to water, concentrating the urine.

5.2. Obligatory vs. Facultative Water Reabsorption

- Obligatory reabsorption occurs in the proximal tubule and descending loop of Henle, where water is reabsorbed regardless of the body's hydration status.
- Facultative reabsorption occurs in the distal tubule and collecting ducts, regulated by ADH according to the body's need to conserve water.

6. Micturition (Urination)

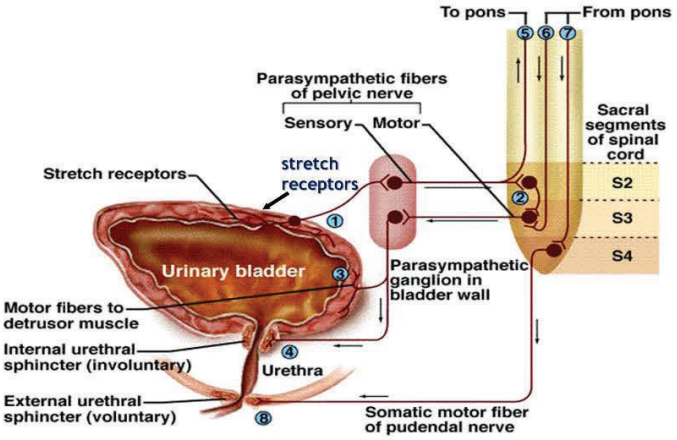
Micturition is the process of expelling urine from the bladder.

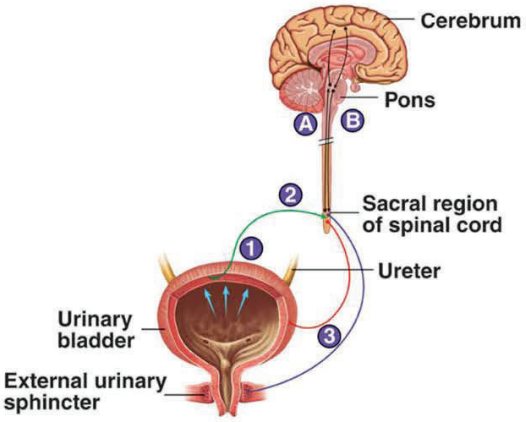
6.1. Bladder Filling and Stretch Receptors

- As the bladder fills, stretch receptors in the bladder wall are activated, sending signals to the brain and initiating the urge to urinate.

6.2. Micturition Reflex

- Controlled by both voluntary and involuntary mechanisms.
- The parasympathetic nervous system causes the detrusor muscle to contract and the internal urethral sphincter to relax, facilitating urination.
- The external urethral sphincter is under voluntary control.





- 1) APs generated by stretch receptors
- 2) reflex arc generates APs that
- 3) stimulate smooth muscle lining bladder
- 4) relax internal urethral sphincter (IUS)
- 5) stretch receptors also send APs to Pons
- 6) if it is o.k. to urinate
  - -APs from Pons excite smooth muscle of bladder and relax IUS
  - -relax external urethral sphincter
- 7) if not o.k.
- -APs from Pons keep EUS contracted

Changes with aging include:

- Decline in the number of functional nephrons
- Reduction of GFR
- Reduced sensitivity to ADH
- Problems with the micturition reflex

7. Practical Applications and Clinical Implications

7.1. Common Disorders of the Urinary System

- Kidney Stones (Nephrolithiasis): Hard deposits of minerals, often calcium oxalate, that can obstruct urine flow, causing severe pain.
- Urinary Tract Infections (UTIs): Bacterial infections of the urinary tract, commonly affecting the bladder (cystitis) or kidneys (pyelonephritis).
- Chronic Kidney Disease (CKD): Progressive loss of kidney function, leading to electrolyte imbalances, fluid retention, and the need for dialysis in end-stage kidney failure.

7.2. Diagnostic Tools

- Urinalysis: Evaluates physical and chemical properties of urine, detecting abnormalities such as blood, proteins, glucose, or bacteria.
- Blood Tests: Measure serum levels of waste products like creatinine and urea to assess kidney function and diagnose kidney disease.

Examination and Assessment

1	Functions of the Kidneys:	
a.	Excretion of metabolic waste products and foreign chemicals	True
b.	Regulation of water and electrolyte balances	True
c.	Regulation of body fluid osmolality and electrolyte concentrations	True
d.	Regulation of arterial pressure	True
e.	Regulation of acid-base balance	True
f.	Excretion of carbohydrates	False
g.	Excretion of amino acids	False
h.	Excretion of hormones	False
i.	Regulation of brain size	False
j.	Regulation of body activity	False

2	General Organization of the Kidneys and Urinary Tract	
a.	The two kidneys lie on the posterior wall of the abdomen, outside the peritoneal cavity.	True
b.	Each kidney of the adult human weighs about 150 grams and is about the size of a clenched fist.	True
c.	The medial side of each kidney contains an indented region called the hilum	True
d.	through hilum pass the renal artery and vein, lymphatics, nerve supply, and ureter	True
e.	The kidney is surrounded by a tough, fibrous capsule that protects its delicate inner structures.	True
f.	The two kidneys lie on the anterior wall of the abdomen, inside the peritoneal cavity.	False
g.	Each kidney of the adult human weighs about 750 grams and is about the size of a leg.	False
h.	The medial side of each kidney contains an striated region called the medula oblongata	False
i.	through hilum pass the aorta and nerve plexus	False
j.	The kidney is surrounded by a protective bone	False

3	The Nephron Is the Functional Unit of the Kidney	
a.	Each kidney in the human contains about 800,000 to 1,000,000 nephrons	True
b.	The kidney cannot regenerate new nephrons.	True
c.	Renal injury, disease, or normal aging, there is a gradual decrease in nephron number.	True
d.	After 40, the number of functioning nephrons usually decreases about 10 percent every 10 years	True
e.	Adaptive changes in nephrons allow to excrete water, electrolytes, waste products	True
f.	Each kidney in the human contains about 10,000 nephrons	False
g.	The kidney produce daly 10,000 new nephrons.	False
h.	Renal injury, disease, or normal aging, there is a gradual increase in nephron number.	False
i.	After 40, the number of nephrons usually increases with about 10 percent every 10 years	False
j.	Adaptive changes in the nephrons allow them to excrete the proper amounts of nutrients	False

4	Major Functions of the Kidneys	
a.	Regulation of osmolarity and volume, electrolyte balance, acid-base balance, blood pressure	True
b.	Excretion of metabolic products	True
c.	Excretion of foreign substances (pesticides, chemicals etc.)	True
d.	Excretion of excess substance (water, etc)	True
e.	Secretion of erythropoitin, 1,25-dihydroxy vitamin D3, renin, prostaglandin	True
f.	Regulation of body mass	False
g.	Excretion of nutrients	False
h.	Absorption of foreign substances (pesticides, chemicals etc.)	False
i.	Retention of excess substance (water, etc)	False
j.	Secretion of insulin and glucagon	False

5	Kidneys regulate body fluid:	
a.	osmolarity	True
b.	volume	True

c.	electrolyte balance	True
d.	acid-base balance	True
e.	blood pressure	True
f.	polarity	False
g.	nutritional content	False
h.	electrons	False
i.	divisions	False
j.	blood cellular composition	False

6	Kidneys regulate excretion of	
a.	metabolic products	True
b.	foreign substances (chemicals)	True
c.	excess substance (, etc)	True
d.	water	True
e.	pesticides	True
f.	nutrients	False
g.	carbohydrates	False
h.	amino acids	False
i.	vitamins	False
j.	DNA	False

7	Nephron:	
a.	is the functional unit of the kidney	True
b.	Each kidney is made up of about 1 million nephrons	True
c.	Each nephrons has two major components	True
d.	Each nephrons has a glomerulus	True
e.	Each nephrons has a long tube	True
f.	is the functional unit of the liver	False
g.	Each kidney is made up of about 10,000 nephrons	False
h.	Each nephrons has five major components	False
i.	Each nephrons has two glomeruli	False
j.	Each nephrons has a kidney	False

8	Cortical nephrons:	
a.	80%-90%	True
b.	glomeruli in outer cortex	True
c.	short loops of Henle extend only short distance into medulla	True
d.	blood flow through cortex is rapid	True
e.	cortical interstitial fluid 300 mOsmolar	True
f.	10%-20%	False
g.	glomeruli connected with uretra	False
h.	long loops of Henle extend untill the end of urinary tract	False
i.	blood flow through cortex is very slow	False
j.	cortical interstitial fluid -20 mOsmolar	False

9	Juxtamedullary nephrons:	
a.	glomeruli in inner part of cortex	True
b.	long loops of Henle extend deeply into medulla	True
c.	blood flow through vasa recta in medulla is slow	True
d.	medullary interstitial fluid is hyperosmotic	True
e.	maintains osmolality, filtering blood and maintaining acid-base balance	True
f.	80%-90%	False
g.	glomeruli in outer cortex	False

h.	short loops of Henle extend only short distance into medulla	False
i.	blood flow through cortex is rapid	False
j.	cortical interstitial fluid 300 mOsmolar	False

10	The juxtaglomerular apparatus include:	
a.	macula densa	True
b.	extraglumerular cells	True
c.	juxtaglomerular cells	True
d.	mesangial cells	True
e.	granular cells	True
f.	glomeruli	False
g.	cortex	False
h.	capsula	False
i.	ectoderm	False
j.	subepiderm	False

11	Characteristics of the renal blood flow:	
a.	high blood flow - 1200 ml/min, or 21 percent of the cardiac output	True
b.	94% to the cortex	True
c.	two capillary beds	True
d.	high hydrostatic pressure in glomerular capillary (about 60 mmHg)	True
e.	low hydrostatic pressure in peritubular capillaries (about 13 mmHg)	True
f.	low blood flow – 120 ml/min	False
g.	14% to the cortex	False
h.	five capillary beds	False
i.	low hydrostatic pressure in glomerular capillary (about 60 mmHg)	False
j.	high hydrostatic pressure in peritubular capillaries (about 13 mmHg)	False

12	Functions of the Nephron	
a.	Filtration	True
b.	Reabsorption	True
c.	Secretion	True
d.	Excretion	True
e.	Homeostasis	True
f.	Respiration	False
g.	Digestion	False
h.	Division	False
i.	Mutation	False
j.	Sweating	False

13	Nephron filtration function:	
a.	First step in urine formation	True
b.	Bulk transport of fluid from blood to kidney tubule	True
c.	Blood cells and proteins don't filter	True
d.	Result of hydraulic pressure	True
e.	GFR = 180 L/day	True
f.	Second step in urine formation	False
g.	Anti-transport of fluid from blood to kidney tubule	False
h.	Blood cells and proteins are directly filtered	False
i.	Result of sweating	False
j.	GFR = 13 L/day	False

14	Reabsorption	
a.	Process of returning filtered material to bloodstream	True
b.	99% of what is filtered	True
c.	May involve transport proteins	True
d.	Normally glucose is totally reabsorbed	True
e.	More than 19% of fluid is reabsorbed	True
f.	Process of returning unfiltered material to internal cells	False
g.	2% of what is filtered	False
h.	May involve receptor proteins	False
i.	Normally glucose is totally eliminated	False
j.	More than 99% of fluid is reabsorbed	False

15	Secretion	
a.	Material added to lumen of kidney from blood	True
b.	Active transport	True
c.	(usually) of toxins and foreign substances	True
d.	Saccharine	True
e.	Penicillin	True
f.	Material added to glomeruli of kidney from blood	False
g.	Pasive transport	False
h.	(usually) of glucose	False
i.	Sodium	False
j.	Potassium	False

16	Filtration, reabsorption and excretion rates of substances by the kidneys	
a.	Glucose is totally (100%) reabsorbed	True
b.	Bicarbonate is over 99% reabsorbed	True
c.	Ureea is half reabsorbed	True
d.	Creatinine is totally excreted (100%)	True
e.	sodium and chloride are over 99% reabsorbed	True
f.	Glucose is totally (100%) excreted	False
g.	Bicarbonate is over 10% reabsorbed	False
h.	Ureea is totally excreted (100%)	False
i.	Creatinine is totally reabsorbed (100%)	False
j.	sodium and chloride are over 2% reabsorbed	False

17	Mechanism of Transport at the nephron level	
a.	Active Transport	True
b.	Primary Active Transport	True
c.	Secondary Active Transport	True
d.	Pinocytosis	True
e.	Passive Transport	True
f.	Complex Diffusion	False
g.	Oxmosis	False
h.	Separation	False
i.	Oriented diffusion	False
j.	Lipid channels	False

18	Transportation of Sodium, Water and Chloride	
a.	in proximal tubule 65 percent of the filtered sodium is reabsorbed	True
b.	in proximal tubule 65 percent of the filtered chloride is reabsorbed	True
c.	in proximal tubule 65 percent of the filtered bicarbonate is reabsorbed	True
d.	in proximal tubule 65 percent of the filtered potassium is reabsorbed	True

e.	in proximal tubule essentially all the filtered glucose and amino acids are reabsorbed	True
f.	in anterior tubule 90 percent of the filtered sodium is excreted	False
g.	in posterior tubule 90 percent of the filtered chloride is excreted	False
h.	in distal tubule 95 percent of the filtered bicarbonate is excreted	False
i.	in anterior tubule 95 percent of the filtered potassium is excreted	False
j.	in anterior tubule essentially all the filtered glucose and amino acids are excreted	False

19	Reabsorption in proximal tubule	
a.	The sodium-potassium ATPase: major force for reabsorption of sodium	True
b.	The sodium-potassium ATPase: major force for reabsorption of chloride and water	True
c.	In first half of proximal tubule, sodium is reabsorbed by co-transport with glucose, amino acids	True
d.	In the first half of proximal tubule, HCO3- is preferentially reabsorbed with the secretion of H+	True
e.	In the first half of the proximal tubule, Cl- is not reabsorbed	True
f.	The sodium-potassium ATPase: major force for reabsorption of ethanol	False
g.	The sodium-potassium ATPase: major force for reabsorption of magnesium	False
h.	In the first half of the proximal tubule, sodium is reabsorbed by co-transport along with DNA	False
i.	In the first half of proximal tubule, HCO3- is preferentially excreted with the reabsorption of Ca2+	False
j.	In the first half of the proximal tubule, Cl- is reabsorbed with calcium	False

20	Sodium and water transport in the loop of Henle	
a.	Henle-thick ascending loop of Henle reabsorbs about 25% of the filtered loads of sodium	True
b.	Henle-thick ascending loop of Henle reabsorbs about 25% of the filtered loads of chloride	True
c.	Henle-thick ascending loop of Henle reabsorbs about 25% of the filtered loads of potassium,	True
d.	Henle-thick ascending loop of Henle reabsorbs large amounts of Ca, bicarbonate, and Mg.	True
e.	Henle-thick ascending loop of Henle secretes hydrogen ions into the tubule	True
f.	Henle-thick ascending loop of Henle secretes about 99% of the filtered loads of sodium	False
g.	Henle-thick ascending loop of Henle secretes about 99% of the filtered loads of chloride	False
h.	Henle-thick ascending loop of Henle secretes about 95% of the filtered loads of potassium,	False
i.	Henle-thick ascending loop of Henle reabsorbs large amounts of creatinin	False
j.	Henle-thick ascending loop of Henle reabsorbs hydrogen ions into the tubule	False

21	Glucose Reabsorption	
a.	Reabsorbed along with Na+ in the early portion of the proximal tubule.	True
b.	Reabsorbed by secondary active transport.	True
c.	Essentially all of the glucose is reabsorbed	True
d.	No more than a few milligrams appear in the urine per 24 hours.	True
e.	The amount reabsorbed is proportionate to the amount filtered	True
f.	Reabsorbed along with creatinin in the early portion of the proximal tubule.	False
g.	Reabsorbed by secondary pasive transport.	False
h.	Essentially all of the glucose is excreted	False
i.	More than a few grams appear in the urine per 24 hours.	False
j.	The amount reabsorbed is proportionate to the body mass	False

22	Urine Concentration and Dilution	
a.	Importance: maintaince of the water balance in the body	True
b.	When there is excess water in the body, kidney excrete low level osmolarity urine	True
c.	the kidney can excrete urine with an osmolarity as low as 50 mOsm/liter	True
d.	When there is a deficient of water kidney excrete high level osmolarity urine	True
e.	the kidney can excrete urine with a concentration of about 1200 to 1400 mOsm/liter	True
f.	Importance: maintaince of the body wight	False

g.	When there is excess water in the body	False
h.	the kidney can excrete urine with no osmolarity	False
i.	When there is a deficient of water kidney excrete low level osmolarity urine	False
j.	the kidney can excrete urine with a concentration of about 10000 Osm/liter	False

23	The basic requirements for forming a concentrated or diluted urine	
a.	the controlled secretion of antidiuretic hormone (ADH)	True
b.	regulates the permeability of the distal tubules to water	True
c.	regulates the permeability of the collecting ducts to water	True
d.	a high osmolarity of the renal medullary interstitial fluid	True
e.	provides the osmotic gradient necessary for water reabsorption, in the presence of ADH	True
f.	the controlled secretion of insulin	False
g.	regulates the permeability of the pancreas to water	False
h.	regulates the permeability of the liver to water	False
i.	a high osmolarity of the renal glomerular fluid	False
j.	provides the osmotic gradient necessary for water reabsorption in the presence of creatinin	False

24	INNERVATION OF THE KIDNEY	
a.	Nerves from the renal plexus (sympathetic nerve) enter kidney at the hilus	True
b.	innervate smooth muscle of afferent & efferent arterioles, regulates blood pressure	True
c.	Reduce the GPF and GFR through contracting the afferent and efferent artery (α receptor)	True
d.	Increase the Na+ reabsorption in the proximal tubules (β receptor)	True
e.	Increase the release of renin (β receptor)	True
f.	Nerves from the spinal cord enter kidney at the capsula level	False
g.	innervate smooth muscle of afferent & efferent veins	False
h.	Reduce the urinary frequency through contracting the afferent and efferent artery (α receptor)	False
i.	Increase the zinc reabsorption in the proximal tubules (β receptor)	False
j.	Increase the release of insulin (β receptor)	False

25	Retention of Water	
a.	is controlled by ADH (Anti Diuretic Hormone)	True
b.	ADH Released by Posterior Pituitary Gland	True
c.	ADH Release is Controlled by Decrease in Blood Volume	True
d.	ADH Release is Controlled by Decrease in Blood Pressure	True
e.	ADH Release is Controlled by increase in extracellular fluid (ECF) osmolarity	True
f.	is controlled by tyroxine	False
g.	Insulin Released by Posterior Pituitary Gland	False
h.	Insulin Release is Controlled by Decrease in Blood Volume	False
i.	Insulin Release is Controlled by Decrease in Blood Pressure	False
j.	Insulin Release is Controlled by increase in extracellular fluid (ECF) osmolarity	False

26	Aldosterone	
a.	Sodium Balance Is Controlled by Aldosterone	True
b.	Aldosterone is a Steroid hormone	True
c.	Aldosterone is synthesized in Adrenal Cortex	True
d.	Aldosterone causes reabsorbtion of Na+	True
e.	Aldosterone causes reabsorbtion of H2O	True
f.	Sodium Balance Is Controlled by prolactine	False
g.	Aldosterone is a nuclear hormone	False
h.	Aldosterone is synthesized in pthe pituitary gland	False
i.	Aldosterone causes reabsorbtion of cromofores	False
j.	Aldosterone causes reabsorbtion of creatinine	False

27	Effects of Aldeosterone	
a.	to make the kidneys retain Na+ and water reabsorption	True
b.	to make the kidneys K+ secretion	True
c.	Acting on the principal cells of the cortical collecting duct	True
d.	stimulating the Na+ - K+ ATPase pump	True
e.	increases the Na+ permeability of the luminal side of the membrane	True
f.	to make the kidneys excrete Na+ and water	False
g.	to make the kidneys K+ absorbtion	False
h.	Acting on the principal cells of the liver	False
i.	inhibites the Na+ - K+ ATPase pump	False
j.	decreases the Na+ permeability of the external side of the membrane	False

28	Micturition	
a.	Once urine enters the renal pelvis, it flows through the ureters and enters the bladder and stored	True
b.	Micturition is the process of emptying the urinary bladder	True
c.	The bladder fills progressively until the tension in its wall rises above a threshold level	True
d.	A nervous reflex called the micturition reflex occurs that empties the bladder	True
e.	The micturition reflex is an automatic spinal cord reflex	True
f.	Once urine enters the renal pelvis, it flows through the ureters and enters the stomach	False
g.	Micturition is the process of emptying the duodenum	False
h.	The bladder fills progressively until the tension in its wall decreases	False
i.	A nervous reflex called the micturition reflex occurs that fill the bladder	False
j.	The micturition reflex is an voluntarly spinal cord reflex	False

29	Urine Micturition	
a.	Action potentials generated by stretch receptors - reflex arc	True
b.	Action potentials stimulate smooth muscle lining bladder	True
c.	relax internal urethral sphincter, stretch receptors also send APs to Pons	True
d.	if it is ok to urinate, will be excited bladder smooth muscle, relax internal and external urethral sphincter	True
e.	if not ok to urinate, Action potentials from Pons keep external urethral sphincter contracted	True
f.	Action potentials generated by cortex - reflex arc	False
g.	Action potentials stimulate somatic muscle	False
h.	relax internal urethral sphincter, relax receptors also send APs to Cerebral cortex	False
i.	if it is ok to urinate, will be excited bladder somatic muscle, keep external urethral sphincter contracted	False
j.	if not ok to urinate, Action potentials from Pons relax internal and external urethral sphincter	False

30	Changes with aging include:	
a.	Decline in the number of functional nephrons	True
b.	Reduction of GFR	True
c.	Reduced sensitivity to ADH	True
d.	Problems with the micturition reflex	True
e.	Urinary problems	True
f.	Increase in the number of functional nephrons	False
g.	Accelerated of GFR	False
h.	Increased sensitivity to insulin	False
i.	Problems with action potentials	False
j.	mass problems	False

Course 11: The Respiratory System
Sub-topic: Respiration and Gas Exchange

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1. Overview of the Respiratory System

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2. Anatomy of the Respiratory System
2.1. Upper Respiratory Tract
2.2. Lower Respiratory Tract

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3. The Process of Respiration
3.1. Pulmonary Ventilation
- Inspiration
- Expiration

3.2. Respiratory Volumes and Capacities

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4. Gas Exchange and Transport
4.1. Pulmonary Diffusion
- Gas Exchange at the Alveoli

4.2. Oxygen and Carbon Dioxide Transport in the Blood
- Oxygen Transport
- Carbon Dioxide Transport

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5. Regulation of Respiration
5.1. Neural Control of Breathing
- Respiratory Centers
- Chemoreceptors

5.2. Voluntary and Involuntary Control

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6. Pulmonary Circulation and Perfusion
6.1. Pulmonary Circulation
6.2. Perfusion of the Lungs

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7. Non-Respiratory Functions of the Lungs
- Regulation of Blood pH
- Filtering of Blood
- Metabolism of Compounds

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8. Practical Applications and Clinical Implications
8.1. Respiratory Disorders
8.2. Diagnostic Tools
- Spirometry: Measures lung volumes and capacities, helping to diagnose obstructive and restrictive lung diseases.
- Pulse Oximetry: Non-invasive measurement of oxygen saturation in the blood.

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9. Review and Case Studies
- Case studies on respiratory disorders and their effect on gas exchange and overall health.
- Clinical examples involving the diagnosis and management of obstructive and restrictive lung diseases.

Examination and Assessment

Practical Session 11: The Respiratory System – Respiration

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1. Introduction to the Respiratory System

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2. Pulmonary Volumes and Capacities

2.1. Pulmonary Volumes

- Tidal Volume (TV):
  The amount of air that enters and exits the lungs during a normal, quiet breath. Average value: 500 mL.
- Inspiratory Reserve Volume (IRV):
  The maximum volume of air that can be inhaled after a normal inspiration. Value: 1,500 mL.
- Expiratory Reserve Volume (ERV):
  The maximum volume of air that can be exhaled after a normal expiration. Value: 1,500 mL.
- Residual Volume (RV):
  The volume of air remaining in the lungs after a maximal expiration. Value: 1,300-1,500 mL.

2.2. Pulmonary Capacities

- Vital Capacity (VC): The total amount of air that can be exhaled after a maximal inhalation (TV + IRV + ERV). Value: 3,500-4,000 mL.
- Total Lung Capacity (TLC):
  The sum of vital capacity and residual volume, representing the total amount of air the lungs can hold. Value: 5,000-6,000 mL.
- Functional Residual Capacity (FRC):
  The volume of air remaining in the lungs after a normal expiration (ERV + RV).
- Inspiratory Capacity (IC):
  The total amount of air that can be inhaled after a normal expiration (TV + IRV).

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3. Respiratory Rate and Frequency

- Normal Respiratory Rate
  Respiratory Abnormalities
  - Tachypnea: Breathing rate greater than 20 breaths/min.
  - Bradypnea: Breathing rate less than 12 breaths/min.
  - Dyspnea: Difficult or labored breathing.
  - Apnea: Absence of breathing.

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4. Pulmonary Ventilation and Respiratory Flow

- Ventilatory Flow: The amount of air ventilated by the lungs per minute. It is calculated by multiplying tidal volume (TV) by the respiratory rate. For an adult with a tidal volume of 500 mL and a respiratory rate of 12 breaths per minute, the ventilatory flow is 6 L/min.
- Maximal Respiratory Flow: During physical exertion, the ventilatory flow can increase to 80-100 L/min.

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5. Respiratory Function Tests

5.1. Pulse Oximetry

5.2. Spirometry

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6. Practical Experiments and Demonstrations

6.1. Measurement of Respiratory Volumes

6.2. Pulse Oximetry Demonstration

6.3. Spirometry Test

Course 11: The Respiratory System
Sub-topic: Respiration and Gas Exchange

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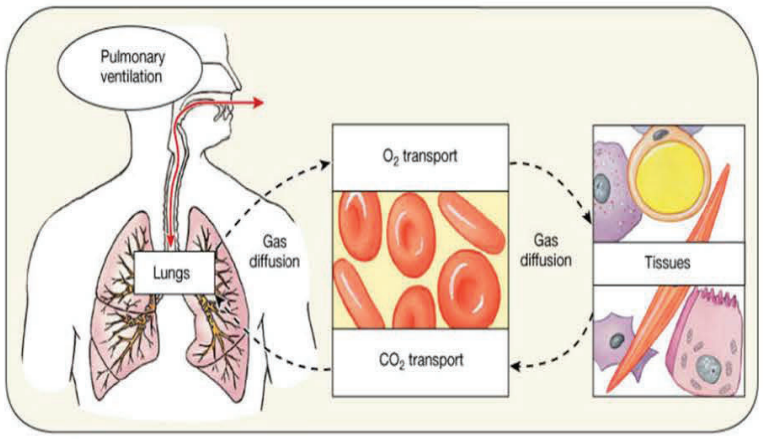
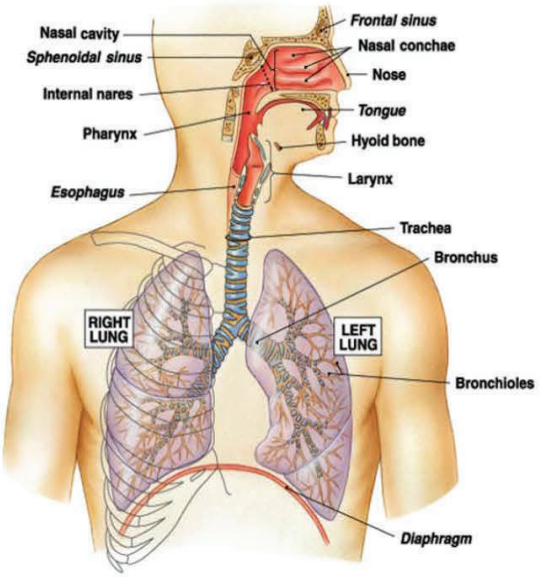
1. Overview of the Respiratory System

The respiratory system supplies oxygen to the body and removes carbon dioxide. Respiration is the process by which the body takes in and utilizes oxygen (O2) and gets rid of carbon dioxide (CO2). It involves multiple processes, including ventilation (the movement of air in and out of the lungs), gas exchange in the alveoli, and the transport of gases between the lungs and the tissues. Additionally, the respiratory system regulates blood pH, produces voice, and protects against pathogens.





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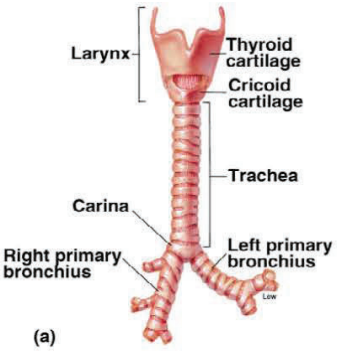
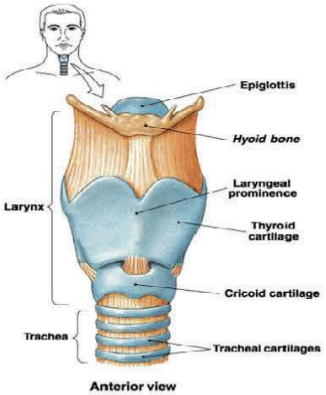
2. Anatomy of the Respiratory System

The respiratory system is divided into the upper and lower tracts:

2.1. Upper Respiratory Tract

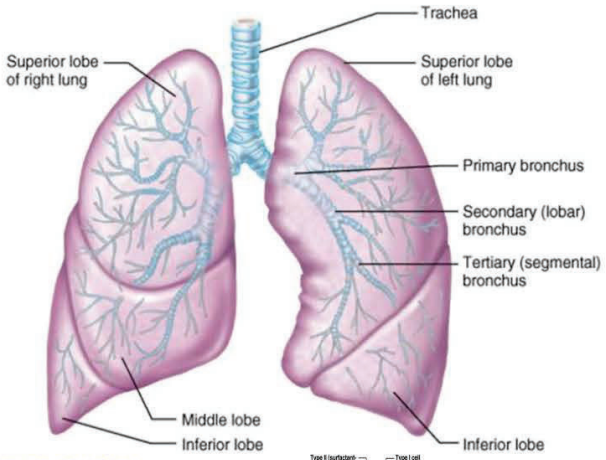
- Nose: Primary entry for air; filters, humidifies, and warms incoming air. Nares (nostrils), external opening. Functions: passageway for air, cleans the air, humidifies, warms air, smell, along with paranasal sinuses are resonating chambers for speech
- Choane, openings into the pharynx
- Nasal septum divides the cavity into left and right halves
- Hard palate, floor of the nasal cavity
- Conchae, prominent bony ridges on the lateral wall of each nasal cavity - increase surface area
- Paranasal sinuses, air-filled spaces within the bone (skull)
- Maxillary, frontal, ethmoidal and sphenoidal - Open into the nasal cavity, reduce weight, produce mucus, and act as resonating chambers, susceptible to infection and inflammation
- Nasolacrimal duct
- Pharynx: Passageway for air and food. Common opening for digestive and respiratory systems. Three regions: Nasopharynx, Oropharynx and Laryngopharynx
- Larynx: Contains the vocal cords and is essential for phonation and airway protection. Functions: maintain an open passageway for air movement; Epiglottis and vestibular folds prevent swallowed material from moving into the larynx. Vocal folds are the primary source of sound production.

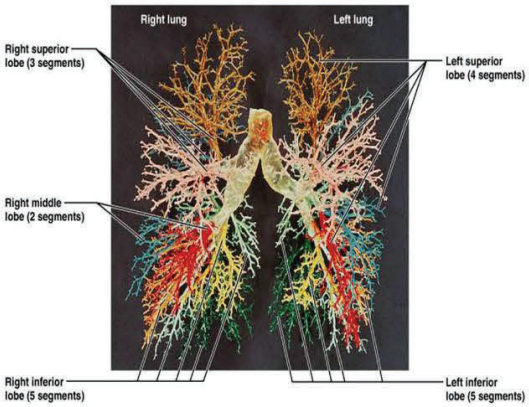




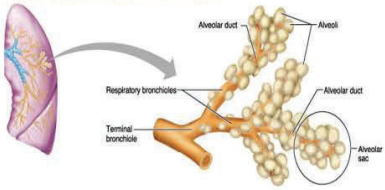
2.2. Lower Respiratory Tract

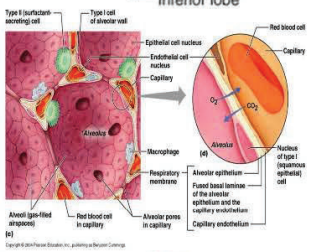
- Trachea: A cartilaginous tube that conducts air towards the lungs.
- Bronchi: The main airways that branch into smaller bronchioles within the lungs.
- Lungs: Consist of alveoli where gas exchange occurs. The right lung has three lobes, while the left lung has two. Anatomically and functionally divided into lobes, which are divided into segments, lobules, and acini.
- Alveoli: Tiny air sacs with thin walls that facilitate oxygen and carbon dioxide exchange.



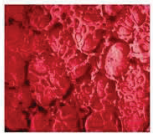


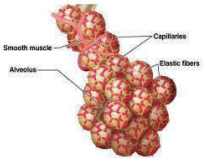
Lower Respiratory Tract
Tracheobronchial Tree





- The tissue surrounding the alveoli contain elastic fibers that allow the alveoli to expand and recoil.
- Type I pneumocytes - form 90% of alveolar wall, gas exchange
- Type II pneumocytes - secretory cells that produce surfactant

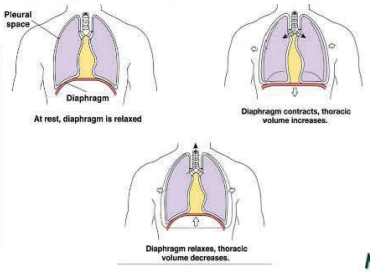


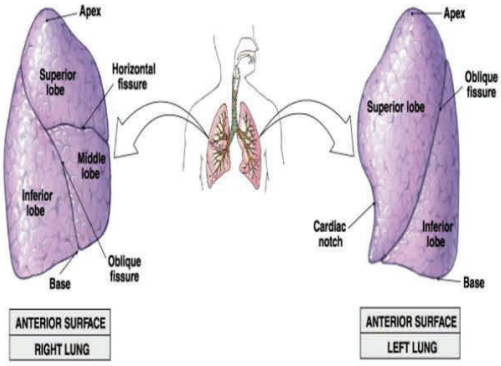


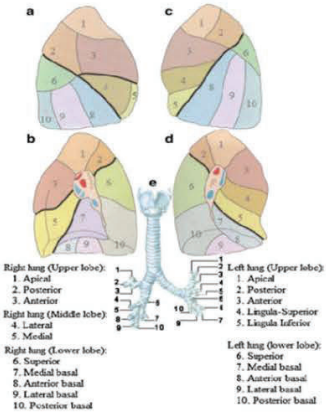
Muscles of Respiration

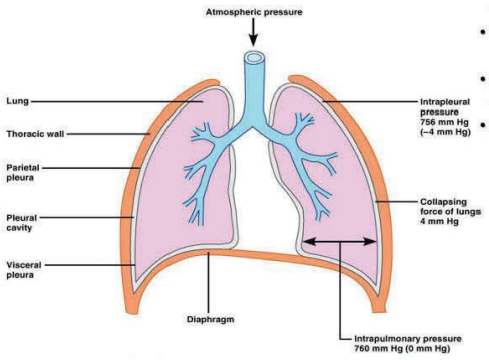
- Diaphragm - dome shaped, attaches to the inner circumference of the inferior thoracic wall.
- Inspiration - diaphragm, external intercostals pectoralis minor, and scalenes.
- Expiration - diaphragm, abdominal muscles and internal intercostals.

	Sequence of events	Changes in anterior-posterior and superior-inferior dimensions	Changes in lateral dimensions
Inspiration	① Inspiratory muscles contract (diaphragm descends; rib cage rises) ② Thoracic cavity volume increases ③ Lungs stretched; intrapulmonary volume increases ④ Intrapulmonary pressure drops (to −1 mm Hg) ⑤ Air (gases) flows into lungs down its pressure gradient until intrapulmonary pressure is 0 (equal to atmospheric pressure)	Ribs elevated and sternum flares as external intercostals contract Diaphragm moves inferiorly during contraction	External intercostals contract









Minute and Alveolar Ventilation

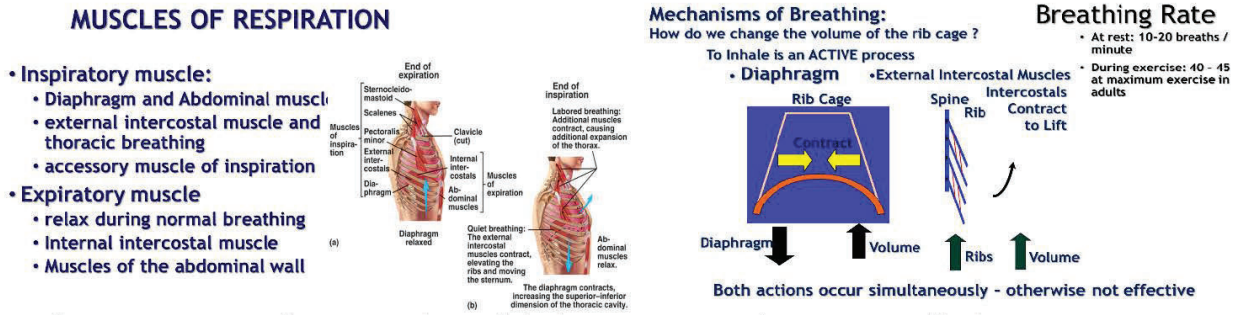
- **Minute ventilation**: Total amount of air moved into and out of respiratory system per minute
- **Respiratory rate or frequency**: Number of breaths taken per minute
- **Anatomic dead space**: Part of respiratory system where gas exchange does not take place
- **Alveolar ventilation**: How much air per minute enters the parts of the respiratory system in which gas exchange takes place

3. The Process of Respiration

3.1. Pulmonary Ventilation

- Inspiration (Inhalation): An active process where the diaphragm and external intercostal muscles contract, increasing the thoracic volume and decreasing the pressure in the lungs. This allows air to flow into the lungs.
- Expiration (Exhalation): At rest, this is passive and results from relaxing inspiratory muscles. In forced expiration, the internal intercostal and abdominal muscles contract.

Pleural fluid produced by pleural membranes acts as lubricant and helps hold parietal and visceral pleural membranes together



Ventilation: movement of air into and out of the lungs. Air moves from an area of higher pressure to an area of lower pressure. Pressure is inversely related to volume.

Pulmonary ventilation – represents the mechanical processes by which the gas exchange between the atmosphere and the lungs is ensured. Oxygen-rich air is introduced into the lung alveoli by inspiration, and carbon dioxide-rich air is expelled from the lungs into the atmosphere by expiration. Gas exchange is possible due to pressure differences, the air flows from a high-pressure environment to a low-pressure environment. The 2 phases of ventilation inspiration and expiration follow one another rhythmically, with a frequency of 12-18 cycles/minute (respiratory rate).

During inspiration, atmospheric air enters the lungs due to pressure differences between atmospheric and intrapulmonary air. A pressure lower than atmospheric pressure is called sub-atmospheric pressure / infra-atmospheric pressure or incorrectly called "negative pressure". During a resting breath, the intrapulmonary pressure decreases by 3 mmHg compared to the atmospheric pressure; the expiration occurs when the intrapulmonary pressure becomes more than 3 mmHg higher than the atmospheric pressure

INSPIRATION is triggered by stimuli generated by the inspiratory center of the spinal bulb, which reach the motor neurons in the anterior horns of the spinal cord. The spinal nerves control the contraction of the inspiratory muscles.

Inspiration at rest: the diaphragm is the main respiratory muscle. By its contraction, the craniocaudal diameter of the thoracic box is increased, as well as the basal part and the transverse diameter. It allows the largest part of the current volume to be introduced into the lungs. The external intercostal muscles, by their contraction, determine the horizontalization and rotation, as well as the anterior displacement of the sternum, which increases the anteroposterior and transverse diameter. By increasing the 2 diameters of the thoracic box, its volume is increased, causing the decrease in intrapulmonary pressures by 3-4 mmHg. Consequently, air will enter the lungs to equalize the 2 pressures. The volume of air entering or exiting the lungs under conditions of relaxed breathing or rest is called CURRENT VOLUME (TV).

Forced inspiration - the accessory muscles: scalpels, pectoral, sternocleidomastoid, trapezius. ± the muscles of the nasal fins, palatine veil, and tongue, thus facilitating the passage of air through the upper airways

They achieve a further decrease in intrapulmonary pressure by elevating the upper portion of the thoracic box, increasing the thorax-pulmonary volume, and lowering the pressure further. The volume thus introduced into the lungs is called the INSPIRATORY RESERVED VOLUME

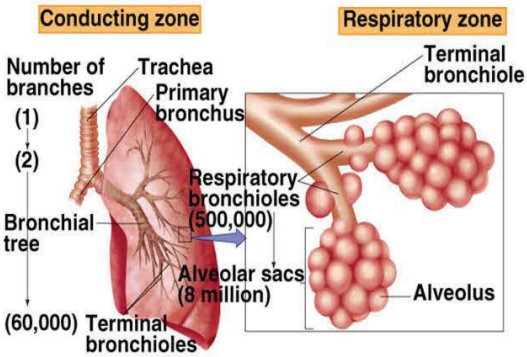
Expiration

Expiration at rest it is accomplished passively. It consists in returning to the initial position of the thoracic-pulmonary structures after the deforming force has stopped its action. It is due to the elasticity of the thoracic

components. As a result, the lung shrinks, and the intrapulmonary pressure increases (763-764 mmHg), becoming higher than atmospheric pressure by 3-4 mmHg. The consequence is the elimination of a volume of CO2-charged air from the lungs into the atmosphere.
Forced expiration - active phase. Contraction of the expiratory muscles, represented in particular by the internal abdominal and intercostal muscles. By contraction of the abdominal muscles, the intraabdominal pressure increases, and the thoracic-pulmonary volume is further reduced, increasing the intrapulmonary pressure, and an additional amount of air will be expired EXPIRATORY RESERVED VOLUME

3.2. Respiratory Volumes and Capacities

- Tidal Volume (TV): The amount of air inhaled or exhaled during a normal breath (~500 mL).
- Inspiratory Reserve Volume (IRV): The additional volume that can be inhaled after a normal inspiration (~3000 mL).
- Expiratory Reserve Volume (ERV): The extra volume that can be exhaled after a normal expiration (~1200 mL).
- Residual Volume (RV): The air remaining in the lungs after a maximal exhalation (~1200 mL).
- Vital Capacity (VC): The total amount of air that can be exhaled after maximal inhalation (TV + IRV + ERV).
- Total Lung Capacity (TLC): The sum of all lung volumes, including residual volume (VC + RV).



	Name	Division	Diameter (mm)	How many?	Cross-sectional area (cm)
Conducting system	Trachea	0	15-22	1	2.5
	Primary bronchi	1	10-15	2	
	Smaller bronchi	2	1-10	4	
		3			
		4			
		5			
		6-11		1×10^4	
Exchange surface	Bronchioles	12-23	0.5-1	2×10^4 – 8×10^7	100 – 5×10^3
	Alveoli	24	0.3	$3\text{-}6 \times 10^8$	$>1 \times 10^6$

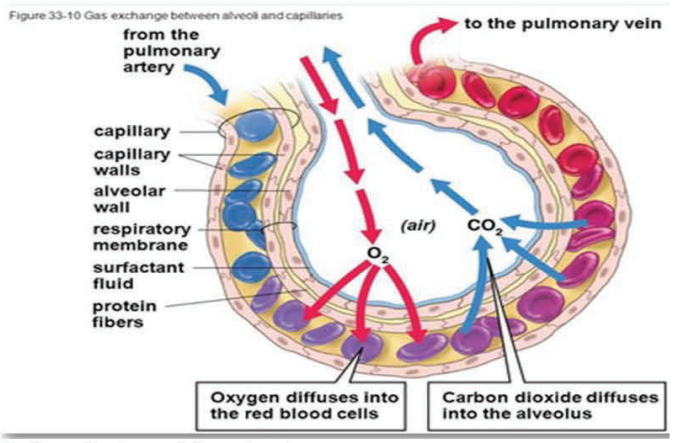
4. Gas Exchange and Transport

4.1. Pulmonary Diffusion

Gas exchange occurs by diffusion across the alveolar-capillary membrane. Oxygen diffuses from the alveoli into the blood, while carbon dioxide diffuses from the blood into the alveoli. The driving force is the difference in partial pressures of gases between the alveoli and blood.

4.2. Oxygen and Carbon Dioxide Transport in the Blood

- Oxygen Transport:
  - Most oxygen is transported by hemoglobin in red blood cells (~98.5%), with the rest dissolved in plasma.
  - The oxygen-hemoglobin dissociation curve shows the relationship between oxygen partial pressure and hemoglobin saturation.
- Carbon Dioxide Transport:
  - CO2 is transported in three forms: dissolved in plasma (~7%), chemically bound to hemoglobin as carbaminohemoglobin (~23%), and as bicarbonate ions (~70%) after reacting with water (facilitated by the enzyme carbonic anhydrase).



5. Regulation of Respiration

5.1. Neural Control of Breathing

- Respiratory Centers: Located in the brainstem, specifically in the medulla and pons. The medullary respiratory centers include the dorsal respiratory group (inspiratory neurons) and the ventral respiratory group (both inspiratory and expiratory neurons).
- Pontine Centers: The pneumotaxic center controls the rate of breathing by regulating the inspiratory signals, while the apneustic center promotes prolonged inspiration.

5.2. Voluntary and Involuntary Control

- Voluntary Control: Breathing can be consciously controlled by higher brain centers (cerebral cortex), allowing us to hold our breath or change our breathing rate.
- Involuntary Control: Reflexive control of breathing responds to blood gas levels (CO_2, O_2, pH) and is regulated by chemoreceptors and mechanoreceptors.

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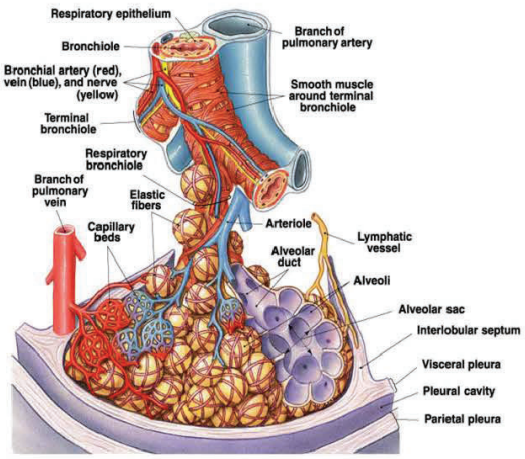
6. Pulmonary Circulation and Perfusion

6.1. Pulmonary Circulation

- The pulmonary circulation begins at the right ventricle, where deoxygenated blood is pumped to the lungs via the pulmonary arteries. In the lungs, the blood is oxygenated and returns to the left atrium via the pulmonary veins.



6.2. Perfusion of the Lungs

- Perfusion refers to the blood flow in the pulmonary capillaries, which must be matched to ventilation (airflow) for effective gas exchange. Imbalances between ventilation and perfusion can lead to conditions like hypoxemia.

Two separate blood supplies:

Pulmonary circulation

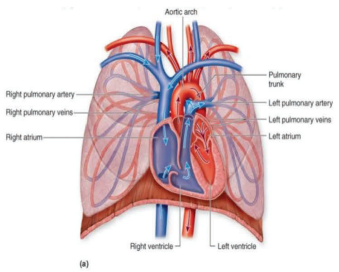
- Brings deoxygenated blood from the right ventricle to the gas-exchange units
- At the gas-exchanging units, oxygen is picked up and carbon dioxide is removed from the blood
- The oxygenated blood returned to the left atrium for distribution to the rest of the body

Bronchial circulation

- Arise from the aorta
- Provides nourishments to the lung parenchyma

PULMONARY CIRCULATION/ perfussion (Q)

- **Functional** represented by pulmonary circulation or small circulation
- Roles of pulmonary circulation:
- ensures oxygenation of blood and elimination of CO2;
- represents a filter for emboli;
- at its level there are a number of active substances (prostaglandins, angiotensin II);
- constitutes a blood reservoir for the left ventricle.



PULMONARY DIFFUSION

The passage of pulmonary gases, in the sense of the concentration gradient (from the higher concentration, to the reduced one), which takes place between the alveolar gas environment and the blood in the pulmonary capillary.

Factors that influence pulmonary diffusion are

- the qualities of the alveolo-hematic barrier;
- the pressure gradient;
- gas diffusion constant;
- the size of the exchange surface;
- the contact time between the two environments.

The alveolo-hematic barrier consists of:

- the pulmonary surfactant layer lining the alveoli
- the alveolar epithelium
- the alveolar basement membrane
- the interstitial fluid
- the capillary basal membrane
- the capillary endothelial cells
- the plasma layer
- the blood cells membrane.

Nutritional ensured by the bronchial arteries (come from the thoracic aorta) and the internal thoracic artery: irrigates bronchial tree walls and supporting lung tissue (stroma). The bronchial arteries only reach the level of the respiratory bronchioles, where they end in the capillary network, from which the bronchial veins start and the blood from the pulmonary nutrient circulation drains through the bronchial veins into the pulmonary veins, reducing the saturation in O2 of the blood from the small circulation.

7. Non-Respiratory Functions of the Lungs
   - Regulation of Blood pH: By regulating CO_2 levels, the lungs play a crucial role in maintaining acid-base balance.
   - Filtering of Blood: The lungs help remove small clots or emboli from the bloodstream.
   - Metabolism of Compounds: The lungs synthesize and metabolize various bioactive compounds, such as prostaglandins and angiotensin-converting enzyme (ACE).

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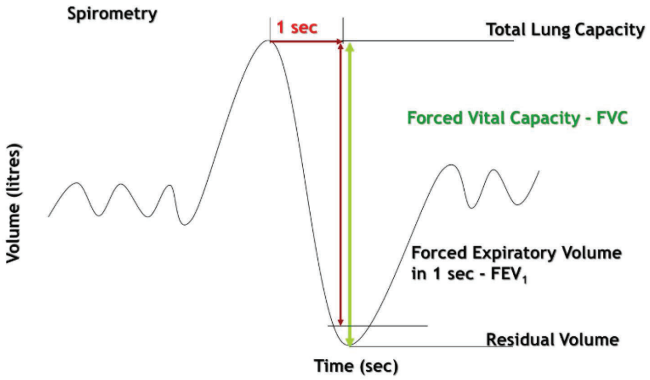
8. Practical Applications and Clinical Implications

8.1. Respiratory Disorders
   - Chronic Obstructive Pulmonary Disease (COPD): A progressive lung disease characterized by obstruction of airflow, commonly caused by smoking.
   - Asthma: A condition where the airways become inflamed, leading to difficulty breathing.

8.2. Diagnostic Tools
   - Spirometry: Measures lung volumes and capacities, useful in diagnosing conditions like COPD and asthma.
   - Pulse Oximetry: A non-invasive method for measuring oxygen saturation in the blood, providing insights into respiratory efficiency.



9. Review and Case Studies
   - Case Studies:
     - A patient with COPD and its effect on gas exchange and overall oxygenation.
     - Clinical management of asthma using bronchodilators and anti-inflammatory medications.
     - Diagnosis and treatment of respiratory acidosis or alkalosis through the regulation of blood CO_2 levels.

Practical Session 11: The Respiratory System – Respiration

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1. Introduction to the Respiratory System

The respiratory system facilitates the exchange of oxygen (O_2) and carbon dioxide (CO_2) between the body and the environment. It includes the upper respiratory tract (nose, pharynx, larynx) and the lower respiratory tract (trachea, bronchi, lungs). The main purpose of the respiratory system is to provide oxygen to the tissues and remove carbon dioxide produced by metabolism. The process of respiration involves multiple steps, including pulmonary ventilation (air movement in and out of the lungs), external respiration (gas exchange between alveoli and blood), internal respiration (gas exchange between blood and tissues), and cellular respiration (use of O_2 to produce energy in cells).

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2. Pulmonary Volumes and Capacities

Pulmonary volumes and capacities measure the amount of air the lungs can hold during various phases of the respiratory cycle. They provide critical information about lung function and are used in both health and disease to assess pulmonary performance.

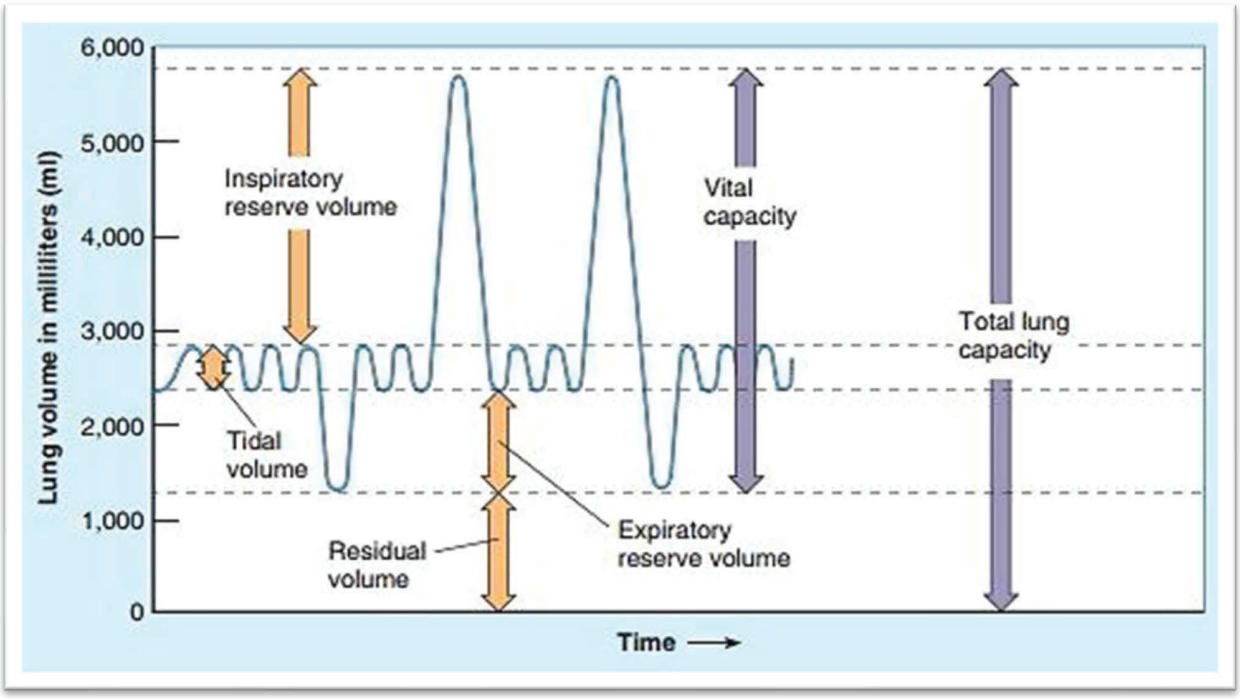
2.1. Pulmonary Volumes

- Tidal Volume (TV):
    - The amount of air that enters and exits the lungs during a normal, quiet breath. This volume is typically about 500 mL in healthy adults. It represents the regular exchange of air during rest without forced breathing.
- Inspiratory Reserve Volume (IRV):
    - The maximum volume of air that can be inhaled after a normal inspiration. The value is around 1,500 mL, depending on the individual's lung capacity. It reflects the additional air that can be drawn into the lungs during deep breathing.
- Expiratory Reserve Volume (ERV):
    - The maximum volume of air that can be exhaled after a normal expiration. The average ERV is also about 1,500 mL. This volume represents the amount of air that can be forcefully expelled from the lungs after the end of a normal, quiet expiration.
- Residual Volume (RV):
    - The volume of air remaining in the lungs after a maximal expiration. This air prevents the lungs from collapsing completely and is typically between 1,300 and 1,500 mL. Residual volume is essential for maintaining continuous gas exchange, even between breaths.

2.2. Pulmonary Capacities

- Vital Capacity (VC):
    - The total amount of air that can be exhaled after a maximal inhalation. It is the sum of tidal volume (TV), inspiratory reserve volume (IRV), and expiratory reserve volume (ERV). The typical value is between 3,500 and 4,000 mL. Vital capacity reflects the maximum functional capacity of the lungs during voluntary breathing maneuvers.
- Total Lung Capacity (TLC):
    - The sum of vital capacity and residual volume. It represents the total volume of air the lungs can hold after maximal inspiration and is generally between 5,000 and 6,000 mL. This value gives an overall estimate of lung capacity.
- Functional Residual Capacity (FRC):
    - The volume of air remaining in the lungs after a normal expiration. FRC is the sum of expiratory reserve volume and residual volume (ERV + RV). This value typically ranges between 2,300 and 2,500 mL and reflects the lung volume at the end of a passive expiration, important for gas exchange during normal respiration.
- Inspiratory Capacity (IC):

- The total amount of air that can be inhaled after a normal expiration. It is the sum of tidal volume (TV) and inspiratory reserve volume (IRV), typically around 2,000 mL. Inspiratory capacity reflects the capacity for additional inhalation after a normal breath.



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3. Respiratory Rate and Frequency

The respiratory rate is the number of breaths taken per minute, which varies based on physical activity, metabolic demands, and overall health status.

- Normal Respiratory Rate:
  - In healthy adults, the normal respiratory rate ranges from 12 to 18 breaths per minute. This rate ensures adequate oxygen intake and CO_2 removal during rest.

Respiratory Abnormalities:

- Tachypnea:
  - A condition characterized by a rapid breathing rate, typically greater than 20 breaths per minute. It can result from fever, anxiety, lung disease, or metabolic acidosis.
- Bradypnea:
  - A condition where the breathing rate is slower than 12 breaths per minute. Bradypnea can be associated with conditions like sleep, opioid overdose, or brain injury affecting respiratory centers.
- Dyspnea:
  - Refers to difficult or labored breathing, often described as shortness of breath. Dyspnea is commonly associated with respiratory and cardiac conditions, such as asthma, heart failure, and COPD.
- Apnea:
  - A complete absence of breathing. Apnea can occur temporarily during sleep (sleep apnea) or due to severe neurological impairment, trauma, or respiratory arrest.

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4. Pulmonary Ventilation and Respiratory Flow

- Ventilatory Flow:

- Ventilatory flow refers to the amount of air ventilated by the lungs per minute. It is calculated by multiplying tidal volume (TV) by the respiratory rate (RR). For an adult with a tidal volume of 500 mL and a respiratory rate of 12 breaths per minute, the ventilatory flow is: 500 mL×12 breaths/min=6,000 mL/min (6 L/min).500 \, \text{mL} \times 12 \, \text{breaths/min} = 6,000 \, \text{mL/min} \, (6 \, \text{L/min}).500mL×12breaths/min=6,000mL/min(6L/min). This is the average resting minute ventilation.

- Maximal Respiratory Flow:
  - During intense physical exertion, the ventilatory flow can increase significantly, reaching 80 to 100 L/min. This is achieved through increases in both tidal volume and respiratory rate, reflecting the body's need for more oxygen and enhanced CO_2 removal during exercise.

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5. Respiratory Function Tests

Respiratory function tests help evaluate the mechanical aspects of lung function and gas exchange efficiency.

5.1. Pulse Oximetry



- Pulse Oximetry measures the percentage of oxygen saturation in the blood (SpO_2), indicating how well oxygen is transported in the bloodstream. A sensor is placed on the finger, toe, or earlobe, where it detects changes in light absorption by oxygenated and deoxygenated hemoglobin.

Normal SpO_2 values typically range from 95% to 100%. Values below 90% suggest hypoxemia, requiring further medical evaluation.

Standard pulse oximeter probes may be placed on the fingers or earlobes of ambulatory patients.

Some oximeters use reflectance probes that can be placed on the forehead.

Fingernail polish should be removed and peripheral circulation should be maximized by warming or by applying vasodilating cream, if necessary.

Although improving, the principle of oximetry measurement by spectrophotometry is not as reliable as many practitioners believe. One side of the oximeter probe acts as a light-emitting source, and the other acts as a photodetector. The probe is placed on a finger or earlobe. A forehead reflectance probe may also be used. The relative absorption of red (absorbed by oxygenated blood) and infrared (absorbed by deoxygenated blood) light of the pulsatile (systolic) component of the absorption waveform correlates to arterial blood oxygen saturation.

Resting readings should be made for at least 5 minutes, and the stability of the reading should be characterized in the report. If a finger probe is used when standing, the hand should be placed on the chest at the level of the heart to minimize venous pulsation, which can falsely lower the reading. The correlation of the heart rate displayed on the oximeter with an ECG rate or a manually palpated pulse can help characterize the quality of the signal. Agreement within five or more beats per minute generally rules out significant motion artifacts. Ideally, pulse oximetry saturation should be correlated with a measured oxygen saturation by multiple wavelength spectrophotometry on a simultaneously obtained arterial blood gas sample.

Documentation of the type of pulse oximeter used, probe type, and probe site should be included on each report. The heart rate and SpO2 readings at rest should be reported.

When obtaining pulse oximetry readings during exercise, the type and intensity of exercise (eg: walking speed, duration of activity) along with the heart rate and SpO2 at the end of the activity should be reported. When desaturation is detected, the activity should be repeated with supplemental oxygen in place to demonstrate improvement in SpO2 values.

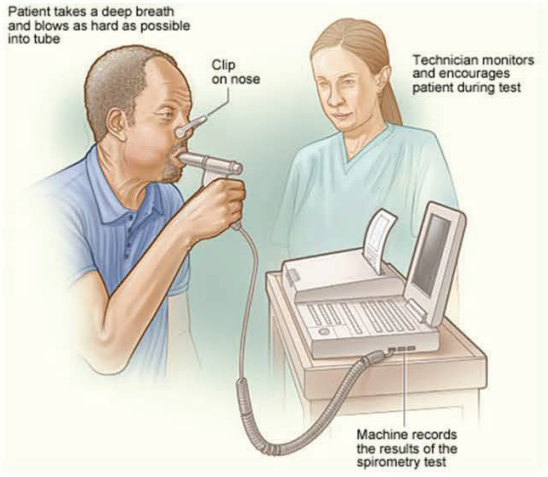
Pulse oximetry is often performed (though optional) in the setting of the 6-minute walk test, a standardized measure of functional exercise capacity. This test is a measure of the maximum distance the patient is able to walk in a hallway with a minimum of 100 feet marked in 5-foot increments.

The patient is permitted to slow down or even stop, if required. However, the elapsed time counter continues during rest periods. This test should be performed while exercise oxygen needs are being adequately met with portable oxygen delivery.
Borg dyspnea and fatigue scores are collected immediately after completion of the walk.
While SpO2 readings greater than 95% make the probability of clinically significant hypoxemia unlikely, clinical suspicion of hypoxemia should initiate the examination of ABGs.
The goal of titration of supplemental oxygen should be a stable SpO2 reading of 93% or higher.
Arterial desaturation can be considered present when the pulse oximeter saturation falls more than 4% below the baseline reading.
The role of pulse oximetry in the Medicare guidelines for reimbursement for continuous supplemental oxygen therapy is to demonstrate one of the following while at rest and breathing room air: PaO2 less than or equal to 55 mm Hg, SaO2 less than or equal to 88%, or SpO2 less than or equal to 88%.
Factors that influence the accuracy of pulse oximetry readings:

- Overestimation of SaO2 is possible with bright sunlight on the probe, fluorescent lights, operating room lights, infrared heat lamps, elevated CoHb, elevated metHb, anemia, and motion artifact if the actual SaO2 is less than 85%.
- Underestimation of SaO2 is possible because intravascular dyes, such as methylene blue and indocyanine green, produce transient reductions in SpO2. Fingernail polish, increased venous pressures, and motion artifact if the actual SaO2 is greater than 85% can also cause underestimation of the SaO2.

5.2. Spirometry

- Spirometry is a standard respiratory function test that measures lung volumes and airflow rates. It is used to diagnose and monitor lung diseases such as asthma, chronic obstructive pulmonary disease (COPD), and restrictive lung disorders. The spirometer measures ventilation and air movement into and out of the lungs. The spirogram will identify two types of abnormal ventilation patterns: obstructive and restrictive.
    - Spirometry measures forced vital capacity (FVC), the maximum amount of air that can be forcefully exhaled after a maximal inhalation, and forced expiratory volume in 1 second (FEV_1), which reflects the volume exhaled in the first second of the FVC maneuver.
    - Normal values for FEV_1/FVC ratio are around 75-80%, with lower values indicating obstructive lung diseases.



Spirometry is used to establish baseline lung function, evaluate dyspnea, detect pulmonary disease, monitor the effects of therapies used to treat respiratory disease, evaluate respiratory impairment, evaluate operative risk, and perform surveillance for occupational-related lung disease.
Relative contraindications for spirometry include hemoptysis of unknown origin, Pneumothorax, unstable angina pectoris, recent myocardial infarction, thoracic aneurysms, abdominal aneurysms, cerebral aneurysms, recent eye surgery (within 2 weeks due to increased intraocular pressure during forced expiration), recent abdominal or thoracic surgical procedures, patients with a history of syncope associated with forced exhalation. Patients with active tuberculosis should not be tested.
The determination is made in the morning, before eating, and the patient is not allowed to smoke at least one hour before the investigation. The subject (after applying the nasal clamp) is allowed to breathe normally for 1 minute, then is required to achieve maximum inspiration followed by an exhalation as slow and completely as possible. In the case of determining the dynamic volumes, a forced expirogram is performed, the subject is trained to perform a maximum inspiration after which to expire with all the force and possibility.

6. Practical Experiments and Demonstrations

6.1. Measurement of Respiratory Volumes

- Objective:
  Students will measure their own tidal volume, inspiratory reserve volume, and expiratory reserve volume using a spirometer. They will calculate their vital capacity and total lung capacity from the measured volumes.

6.2. Pulse Oximetry Demonstration

- Objective:
  Students will use pulse oximeters to monitor changes in oxygen saturation under different conditions, such as at rest and after exercise, demonstrating how respiratory rate and depth of breathing influence oxygenation.

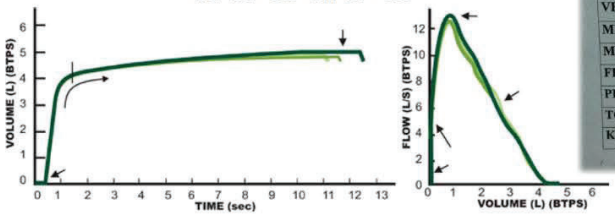
6.3. Spirometry Test

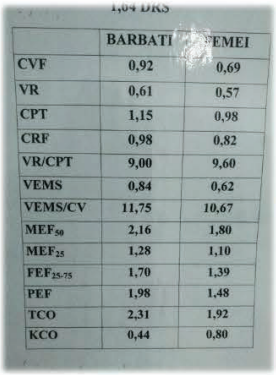
- Objective:
  Perform spirometry to assess lung function by measuring FVC, FEV_1, and the FEV_1/FVC ratio. Students will interpret the results to identify any potential airflow obstructions or lung volume restrictions.

Valid Normal Test

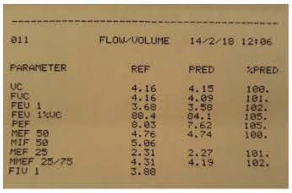
Trial	FVC (L)	FEV_1 (L)	PEF (L/sec)
1	4.81	4.09	12.1
2	4.74	4.07	12.0
3	**4.87**	**4.14**	**12.5**
Repeatability	0.06	0.05	

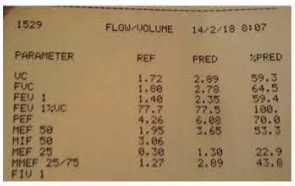
4.87-4.81 = 0.06 4.14-4.09 = 0.05

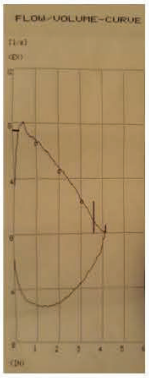




	BARBATI	EMEI
CVF	0,92	0,69
VR	0,61	0,57
CPT	1,15	0,98
CRF	0,98	0,82
VR/CPT	9,00	9,60
VEMS	0,84	0,62
VEMS/CV	11,75	10,67
MEF_{50}	2,16	1,80
MEF_{25}	1,28	1,10
FEF_{25-75}	1,70	1,39
PEF	1,98	1,48
TCO	2,31	1,92
KCO	0,44	0,80







FVC - forced vital capacity

- **Defines maximum volume of exchangeable air in lung (vital capacity)**
  - **forced expiratory breathing maneuver**
  - **requires muscular effort and some patient training**
- **Initial (healthy) FVC values approx 4 liters**
  - **slowly diminishes with normal aging**
- **Significantly reduced FVC suggests damage to lung tissue**
  - **restrictive lung disease (fibrosis)**
  - **constructive lung disease**
  - **loss of functional alveolar tissue**
- **Intra-subject variability factors**
  - **age**
  - **sex**
  - **height**
  - **ethnicity**

Course 12: Transport of Respiratory Gases, Tissue and Cellular Breathing, Respiratory Regulation, and Phonation

---

1. Transport of Respiratory Gases

1.1. Oxygen Transport

- **Carried by Hemoglobin**
- **Dissolved Oxygen**

1.2. Carbon Dioxide Transport

- **Dissolved CO_2**
- **Bicarbonate Ions (HCO_3^-)**
- **Carbaminohemoglobin**

---

2. Tissue and Cellular Breathing (Internal Respiration)

2.1. Gas Exchange at the Tissue Level

- **Oxygen Diffusion**
- **Carbon Dioxide Diffusion**

2.2. Cellular Respiration

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3. Respiratory Regulation

3.1. Neural Regulation of Breathing

- **Respiratory Centers in the Brain**
- **Pneumotaxic and Apneustic Centers (in the Pons)**

3.2. Chemical Regulation of Respiration

- **Chemoreceptors**

3.3. Mechanoreceptor Control

- **Hering-Breuer Reflex:**

3.4. Voluntary Control of Breathing

- **The cerebral cortex allows voluntary control of breathing, such as holding one's breath or controlling breathing during speech.**

---

4. Phonation (Voice Production)

4.1. The Larynx and Vocal Cords

4.2. Sound Modification

4.3. Control of Voice

---

5. Practical Applications and Clinical Implications

5.1. Respiratory Disorders

5.2. Speech Disorders

---

6. Review and Case Studies

- **Case studies on oxygen transport disorders, respiratory regulation during exercise, and the impact of CO_2 on blood pH.**
- **Clinical examples involving speech production disorders and their treatments.**

Examination and Assessment

Practical Session 12: The Respiratory System – Physical Principles of Gas Exchange

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1. Introduction to Gas Exchange

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2. Dalton's Law of Partial Pressure

---

3. Henry's Law of Gas Solubility

---

4. Gas Diffusion Through the Respiratory Membrane

4.1. Factors Influencing Diffusion

- Membrane Thickness:
  An increase in membrane thickness (e.g., due to edema or fibrosis) slows the diffusion of gases.
- Surface Area:
  A reduction in alveolar surface area (e.g., in emphysema) decreases the efficiency of gas exchange.
- Diffusion Coefficient:
  CO_2 diffuses more easily than O_2 due to its higher solubility.
- Partial Pressure Difference:
  Gas exchange efficiency is determined by the difference in partial pressures between the alveoli and blood. A large pressure difference enhances diffusion.

4.2. Ventilation-Perfusion Relationship

- Matching Ventilation with Blood Flow:
  Adequate gas exchange requires the coordination of air entering the alveoli (ventilation) and blood flow in pulmonary capillaries (perfusion). Mismatches can lead to poor gas exchange and physiologic shunting (blood bypasses the alveoli without gas exchange).

---

5. Oxygen and Carbon Dioxide Diffusion Gradients

5.1. Oxygen Transport

- Diffusion:
  Oxygen moves from the alveoli ($P_aO_2 \approx 100$ mm Hg) to the pulmonary capillaries ($P_aO_2 \approx 40$ mm Hg). Oxygen then diffuses into tissues where its partial pressure is lower.
- Transport Mechanisms:
  98.5% of oxygen is carried by hemoglobin, while 1.5% is dissolved in plasma. The oxygen-hemoglobin dissociation curve demonstrates hemoglobin's affinity for oxygen at varying partial pressures.

5.2. Carbon Dioxide Transport

- Diffusion:
  Carbon dioxide moves from the tissues ($P_aCO_2 \approx 45$ mm Hg) to the blood ($P_aCO_2 \approx 40$ mm Hg) and is transported to the lungs for elimination.
- Transport Forms:
  CO_2 is transported in the blood as bicarbonate ions (70%), bound to proteins (23%), and dissolved in plasma (7%).

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6. Practical Experiments and Demonstrations

6.1. Measurement of Gas Diffusion

6.2. Oxygen Saturation and Partial Pressure

6.3. CO_2 Transport and Blood pH

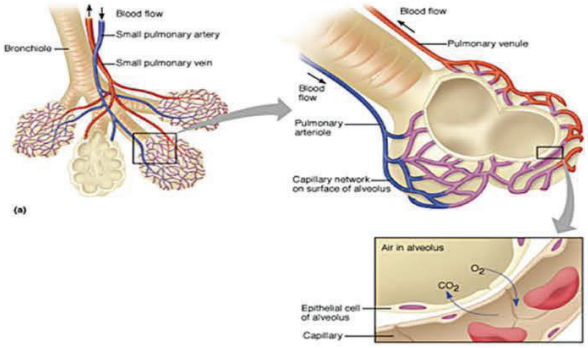
Course 12: Transport of Respiratory Gases, Tissue and Cellular Breathing, Respiratory Regulation, and Phonation

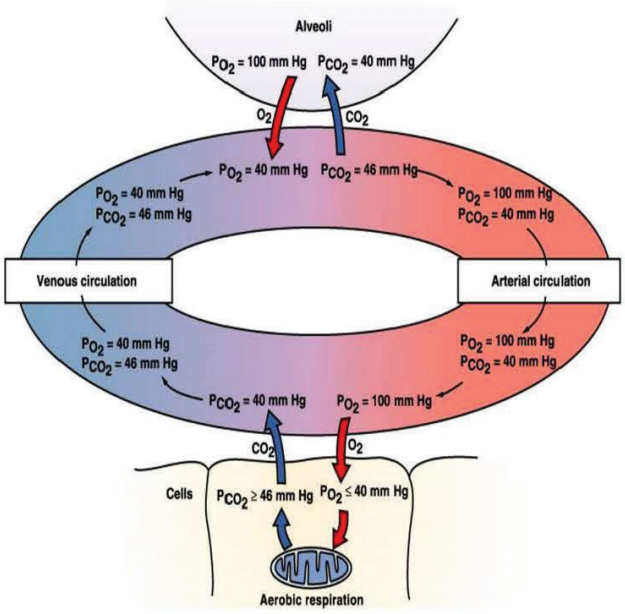
---

1. Transport of Respiratory Gases

Efficient transport of oxygen (O_2) and carbon dioxide (CO_2) between the lungs, blood, and tissues is essential for cellular respiration and homeostasis. The respiratory gases are transported in the blood by various mechanisms, facilitating the exchange of gases required for cellular metabolism. External respiration: Gas exchange between air in the lungs and blood. Transport of oxygen and carbon dioxide in the blood. Internal respiration: Gas exchange between the blood and tissues.

- Partial pressure
    - The pressure exerted by each type of gas in a mixture
    - Dalton's law
    - Water vapor pressure
- Diffusion of gases through liquids
    - Concentration of a gas in a liquid is determined by its partial pressure and its solubility coefficient
    - Henry's law





- Diffusion of gases through the respiratory membrane
    - Depends on membrane's thickness, the diffusion coefficient of gas, surface areas of membrane, partial pressure of gases in alveoli and blood
- Relationship between ventilation and pulmonary capillary flow
    - Increased ventilation or increased pulmonary capillary blood flow increases gas exchange
    - Physiologic shunt is deoxygenated blood returning from lungs

1.1. Oxygen Transport

- Moves from alveoli into blood. Blood is almost completely saturated with oxygen when it leaves the capillary
- PO_2 in blood decreases because of mixing with deoxygenated blood
- Oxygen moves from tissue capillaries into the tissues

- Carried by Hemoglobin:
  Approximately 98.5% of oxygen in the blood is carried by hemoglobin (Hb) in red blood cells (RBCs). Each hemoglobin molecule can bind to four oxygen molecules. The binding of oxygen to hemoglobin forms oxyhemoglobin (HbO_2), which allows efficient oxygen transport from the lungs to tissues. Hemoglobin releases oxygen when the partial pressure of oxygen (PO_2) decreases in tissues, facilitating oxygen delivery.
- Dissolved Oxygen:
  A small portion (1.5%) of oxygen is dissolved directly in the plasma. This dissolved oxygen contributes to the partial pressure of oxygen in the blood, which drives oxygen diffusion from the alveoli into capillaries and tissues.

1.2. Carbon Dioxide Transport. Carbon dioxide, a waste product of cellular metabolism, is transported from tissues to the lungs in three forms:

- Dissolved CO_2:
  About 7-10% of carbon dioxide is transported dissolved in the plasma, contributing to the blood's CO_2 partial pressure (PCO_2).
- Bicarbonate Ions (HCO_3^-):
  The majority (70%) of CO_2 is transported in the form of bicarbonate ions. Inside RBCs, carbon dioxide reacts with water to form carbonic acid (H_2CO_3), which dissociates into HCO_3^- and hydrogen ions (H^+) under the action of carbonic anhydrase. This reaction facilitates the removal of CO_2 from tissues and helps buffer blood pH.
- Carbaminohemoglobin ($HbCO_2$):
  About 20-23% of carbon dioxide is bound to hemoglobin, forming carbaminohemoglobin. CO_2 binds to the amino groups of hemoglobin, which does not interfere with oxygen binding sites. CO_2 is released in the lungs, where it is exhaled.

Moves from tissues into tissue capillaries. Moves from pulmonary capillaries into the alveoli

---

2. Tissue and Cellular Breathing (Internal Respiration)
Internal respiration involves the exchange of gases between systemic blood and tissues, where oxygen is delivered for cellular respiration, and carbon dioxide is removed.
2.1. Gas Exchange at the Tissue Level

- Oxygen Diffusion:
  Oxygen diffuses from the blood (where PO_2 is higher) into the tissues (where PO_2 is lower). This diffusion gradient ensures that oxygen reaches cells to support metabolic processes.
- Carbon Dioxide Diffusion:
  In the opposite direction, carbon dioxide produced by cells diffuses from tissues (higher PCO_2) into the blood (lower PCO_2). This waste product is carried to the lungs for exhalation.

2.2. Cellular Respiration
Cellular respiration occurs inside the mitochondria of cells, where oxygen is used to oxidize nutrients (primarily glucose), generating adenosine triphosphate (ATP), the energy currency of cells. Oxygen is the final electron acceptor in the electron transport chain, producing water as a byproduct. Carbon dioxide is generated as a waste product during the Krebs cycle and is removed via the bloodstream.

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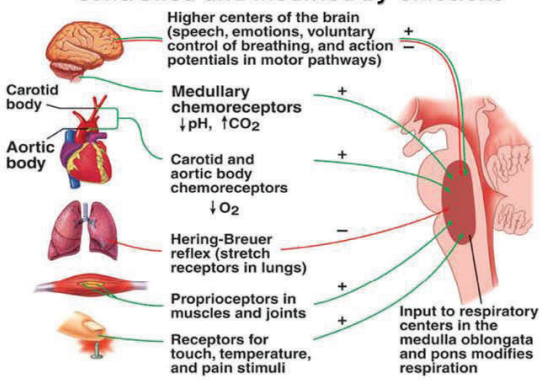
3. Respiratory Regulation
Breathing is a tightly regulated process, controlled both neurogenically and chemically to maintain optimal levels of oxygen and carbon dioxide in the blood.

Modification of Ventilation

- **Cerebral and limbic system**
  - **Respiration can be voluntarily controlled and modified by emotions**



- **Chemical control**
  - **Carbon dioxide is major regulator**
    - **Increase or decrease in pH can stimulate chemo- sensitive area, causing a greater rate and depth of respiration**
  - **Oxygen levels in blood affect respiration when a 50% or greater decrease from normal levels exists**

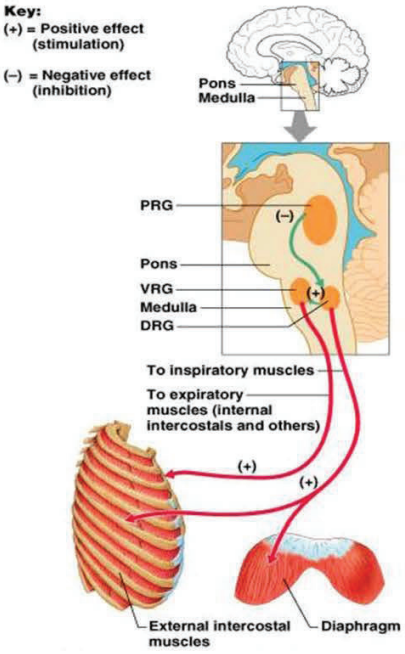
Herring-Breuer Reflex

- Limits the degree of inspiration and prevents overinflation of the lungs
- **Infants**
- Reflex plays a role in regulating basic rhythm of breathing and preventing overinflation of lungs
- **Adults**
- Reflex important only when tidal volume large as in exercise

3.1. Neural Regulation of Breathing

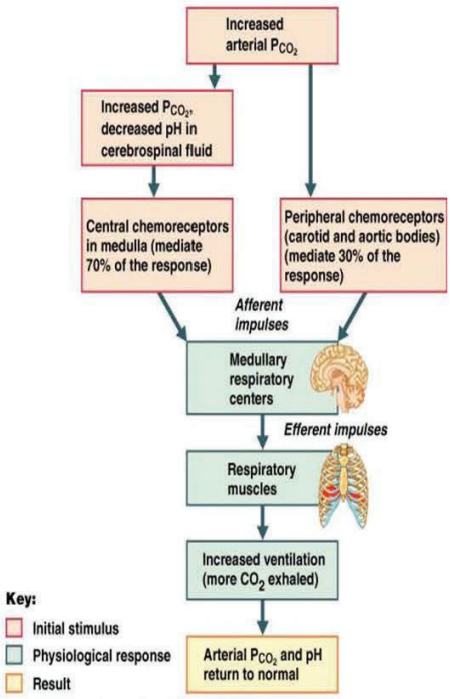
Breathing is primarily controlled by the respiratory centers in the brainstem, including the medulla oblongata and pons. These centers regulate the rhythmic pattern of breathing by sending signals to the respiratory muscles.

- Medullary Respiratory Centers: The dorsal respiratory group (DRG) controls the quiet, resting breathing rhythm by stimulating the diaphragm and external intercostal muscles. The dorsal respiratory system is most active during inspiration but is responsible for stimulating the diaphragm. The ventral respiratory group (VRG) activates during forced breathing (e.g., during exercise). The ventral respiratory group is active during both inspiration and expiration. It stimulates the external and internal intercostals and abdominal muscles.
- Pneumotaxic and Apneustic Centers (in the Pons): The pneumotaxic center inhibits inspiration, regulating the duration of inhalation to prevent over-inflation of the lungs. The apneustic center stimulates prolonged inspiration, increasing the depth of breathing when necessary. Pontine Respiratory group – neurons in the pons; some are active in expiration or inspiration and/or both.



3.2. Chemical Regulation of Respiration

- Chemoreceptors: Central chemoreceptors in the medulla oblongata monitor changes in pH and PCO_2 in the cerebrospinal fluid (CSF), triggering increased ventilation if CO_2 levels rise or pH drops. Peripheral chemoreceptors, located in the carotid bodies and aortic bodies, respond to changes in PO_2, PCO_2, and pH in the blood. A drop in PO_2 below 60 mmHg stimulates increased breathing. The Chemoreceptors involved with the regulation of respiration respond to changes in hydrogen ion concentration and PO2, or both. Chemosensitive areas are located in the medulla oblongata. Peripheral Chemoreceptors are found in the carotid and aortic bodies. The Chemoreceptors involved with the regulation of respiration responds to changes in hydrogen ion concentration and PO2, or both. Peripheral Chemoreceptors are found in the carotid and aortic bodies.
- CO_2 is the major regulator of respiration. Hypercapnia is greater than normal levels of carbon dioxide in the blood. Hypocapnia – lower than normal carbon dioxide levels.



3.3. Mechanoreceptor Control

- Hering-Breuer Reflex: Stretch receptors in the lungs prevent over-inflation by sending inhibitory signals to the respiratory centers when lung volume becomes too large, triggering exhalation. This reflex is more prominent during heavy breathing, such as exercise.

3.4. Voluntary Control of Breathing

- Cerebral Cortex Control: The cerebral cortex allows voluntary control over breathing, enabling actions such as breath-holding, speech, and conscious regulation of breathing rhythm. However, involuntary control takes over when oxygen levels drop or CO_2 levels rise significantly. It is possible to voluntarily or involuntarily control the rate of breathing through the cerebral cortex. Apnea is the absence of breathing. Voluntary apnea increases the urge to breathe due to increasing PCO2 levels.

4. Phonation (Voice Production)

Phonation, or voice production, occurs in the larynx, where vocal cords (or vocal folds) vibrate as air passes through them, producing sound.

4.1. The Larynx and Vocal Cords

- The larynx houses the vocal cords, which are composed of elastic tissue and are responsible for sound production. The glottis is the space between the vocal cords that changes size depending on their tension, influencing sound pitch.

4.2. Sound Modification

- Pitch: Controlled by the tension and length of the vocal cords. Increased tension raises the pitch, while decreased tension lowers it.
- Resonance: Sound is modified as it travels through the pharynx, oral cavity, nasal cavity, and sinuses, creating individual vocal characteristics.

4.3. Control of Voice

- The vocal cords are controlled by intrinsic muscles of the larynx, innervated by the recurrent laryngeal nerve (a branch of the vagus nerve). Fine adjustments to tension and position of the vocal cords allow control over the pitch and quality of the voice.

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5. Practical Applications and Clinical Implications

5.1. Respiratory Disorders

- Chronic Obstructive Pulmonary Disease (COPD): A group of lung diseases (e.g., emphysema and chronic bronchitis) that impede airflow, making breathing difficult. It reduces the efficiency of gas exchange, leading to chronic hypoxemia and hypercapnia.
- Asthma: Characterized by airway inflammation and hyperresponsiveness, resulting in bronchoconstriction and difficulty breathing.
- Hypoxemia and Hypercapnia: Low oxygen levels (hypoxemia) and high carbon dioxide levels (hypercapnia) can lead to serious systemic effects, such as confusion, cyanosis, and organ failure.

5.2. Speech Disorders

- Dysphonia: Difficulty or abnormality in voice production due to vocal cord damage or dysfunction, leading to changes in pitch, volume, and quality of voice.
- Aphonia: Complete loss of voice, often resulting from trauma or nerve damage affecting the vocal cords.

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6. Review and Case Studies

- Oxygen Transport Disorders: Explore case studies of patients with anemia, sickle cell disease, and pulmonary conditions that impair oxygen transport and delivery to tissues.
- Respiratory Regulation During Exercise: During physical activity, increased metabolic demands raise CO_2 levels, stimulating the respiratory centers to increase ventilation. This case study focuses on the body's adaptations to maintain gas homeostasis during exercise.
- CO_2 and Blood pH: Analyze the role of CO_2 in the regulation of blood pH, particularly in conditions such as respiratory acidosis and respiratory alkalosis, where CO_2 levels impact acid-base balance.
- Speech Production Disorders: Clinical examples of speech disorders due to neurological conditions or vocal cord damage, and discussion of therapeutic interventions such as voice therapy, speech exercises, and surgical treatments.

Practical Session 12: The Respiratory System – Physical Principles of Gas Exchange

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1. Introduction to Gas Exchange

Gas exchange is the fundamental process by which oxygen (O_2) is taken up by the blood from the alveoli, and carbon dioxide (CO_2) is removed from the blood and exhaled. This process occurs in the lungs and peripheral tissues, where gases move across cell membranes based on their partial pressure gradients. Effective gas exchange is critical for cellular respiration, energy production, and the maintenance of homeostasis.

Gas exchange relies on four key physical principles:

1. Diffusion: Gases move from areas of high partial pressure to low partial pressure.
2. Dalton's Law of Partial Pressure: Each gas in a mixture exerts a pressure proportional to its concentration.
3. Henry's Law of Gas Solubility: The amount of gas dissolved in a liquid is proportional to its partial pressure and solubility.
4. Ventilation-Perfusion Matching: Optimal gas exchange occurs when airflow (ventilation) to the alveoli is matched with blood flow (perfusion) in the capillaries.

---

2. Dalton's Law of Partial Pressure

Dalton's Law states that the total pressure exerted by a mixture of gases is the sum of the partial pressures of each individual gas. The partial pressure of a gas is directly proportional to its concentration in the mixture.

In the context of respiration, the atmosphere consists of roughly 21% oxygen (O_2) and 0.04% carbon dioxide (CO_2), along with nitrogen and trace gases. At sea level, the total atmospheric pressure is 760 mm Hg. Using Dalton's Law:

- The partial pressure of oxygen (P_aO_2) is 21% of 760 mm Hg, or 160 mm Hg.
- The partial pressure of carbon dioxide (P_aCO_2) is 0.04% of 760 mm Hg, or 0.3 mm Hg.

As air enters the lungs, the partial pressures change due to the addition of water vapor and the exchange of gases. In the alveoli:

- $P_aO_2 \approx 100$ mm Hg.
- $P_aCO_2 \approx 40$ mm Hg.

The partial pressure gradient between the alveoli and blood drives gas exchange:

- Oxygen moves from the alveoli (high P_aO_2) to the blood (low P_aO_2).
- Carbon dioxide moves from the blood (high P_aCO_2) to the alveoli (low P_aCO_2).

---

3. Henry's Law of Gas Solubility

Henry's Law states that the concentration of a gas dissolved in a liquid is proportional to its partial pressure and solubility in that liquid. Gases with higher solubility will dissolve more easily in liquids at the same partial pressure.

In the context of respiration:

- Oxygen has a relatively low solubility in plasma, so most oxygen in the blood is bound to hemoglobin rather than dissolved in plasma.
- Carbon dioxide, on the other hand, is about 20 times more soluble in blood plasma than oxygen, making it easier for CO_2 to be dissolved in plasma and transported.

The amount of O_2 and CO_2 that dissolves in the blood is influenced by both their partial pressures and solubility, as follows:

- O_2 dissolves poorly in blood; thus, hemoglobin carries 98.5% of oxygen, while only 1.5% is dissolved in plasma.
- CO_2 dissolves more readily, and about 7% is transported dissolved in plasma.

---

4. Gas Diffusion Through the Respiratory Membrane

The respiratory membrane, which consists of the alveolar and capillary walls, is the site of gas exchange between the air in the alveoli and the blood in pulmonary capillaries. Gases move across the membrane by diffusion, driven by differences in partial pressure between the alveoli and blood.

4.1. Factors Influencing Diffusion

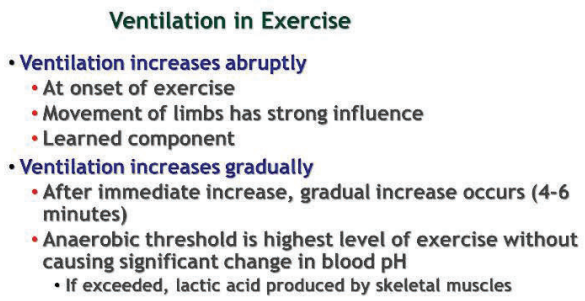
- Membrane Thickness:
  The thinner the membrane, the faster the diffusion. Normally, the respiratory membrane is extremely thin (about 0.5 micrometers). Conditions such as pulmonary edema or fibrosis increase the thickness of this membrane, slowing the diffusion of gases and leading to hypoxemia (low blood oxygen levels).
- Surface Area:
  The surface area available for gas exchange is critical for efficient diffusion. In a healthy lung, the alveoli provide a large surface area (approximately 70 m^2). In diseases such as emphysema, where alveolar walls are destroyed, surface area decreases, impairing gas exchange.
- Diffusion Coefficient:
  The diffusion rate of a gas is also influenced by its solubility and molecular weight. CO_2 diffuses more easily than O_2 because it is more soluble in plasma, even though it has a slightly higher molecular weight.
- Partial Pressure Difference:
  The greater the difference in partial pressure between two sides of the membrane, the faster the diffusion. In the lungs, the partial pressure of oxygen in the alveoli ($P_aO_2 \approx 100$ mm Hg) is higher than in the pulmonary capillaries ($P_aO_2 \approx 40$ mm Hg), promoting the diffusion of O_2 into the blood. Conversely, the partial pressure of carbon dioxide in the pulmonary capillaries ($P_aCO_2 \approx 45$ mm Hg) is higher than in the alveoli ($P_aCO_2 \approx 40$ mm Hg), promoting the diffusion of CO_2 into the alveoli for exhalation.

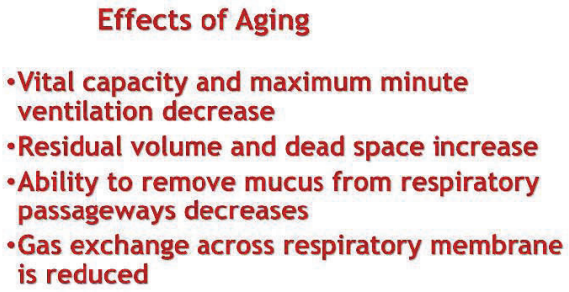
4.2. Ventilation-Perfusion Relationship

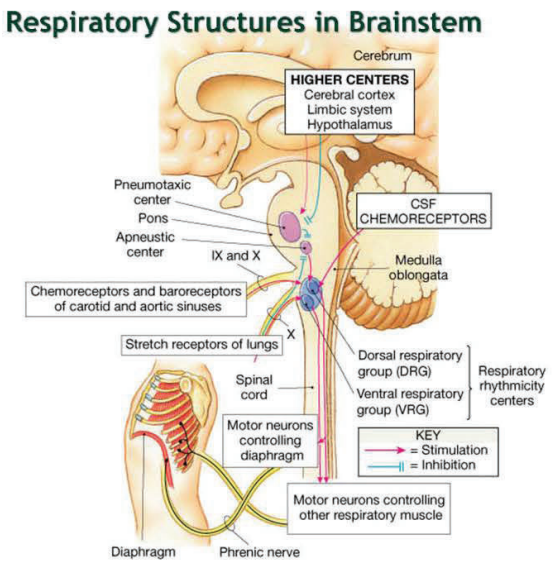
Ventilation (V) refers to the amount of air reaching the alveoli, while perfusion (Q) refers to the blood flow reaching the alveoli. For efficient gas exchange, ventilation must match perfusion. Mismatches between ventilation and perfusion can reduce the efficiency of gas exchange:

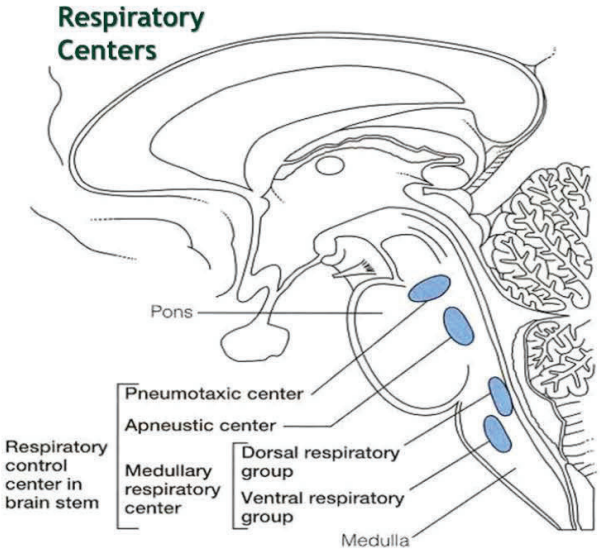
- Physiologic shunting occurs when perfusion exceeds ventilation, meaning blood bypasses under-ventilated alveoli without receiving adequate oxygen (e.g., in lung disease).
- Dead space occurs when ventilation exceeds perfusion, meaning air in the alveoli is not effectively exchanged due to insufficient blood flow (e.g., in a pulmonary embolism).

The ideal ventilation-perfusion ratio is approximately 1:1, ensuring optimal oxygen uptake and carbon dioxide removal.







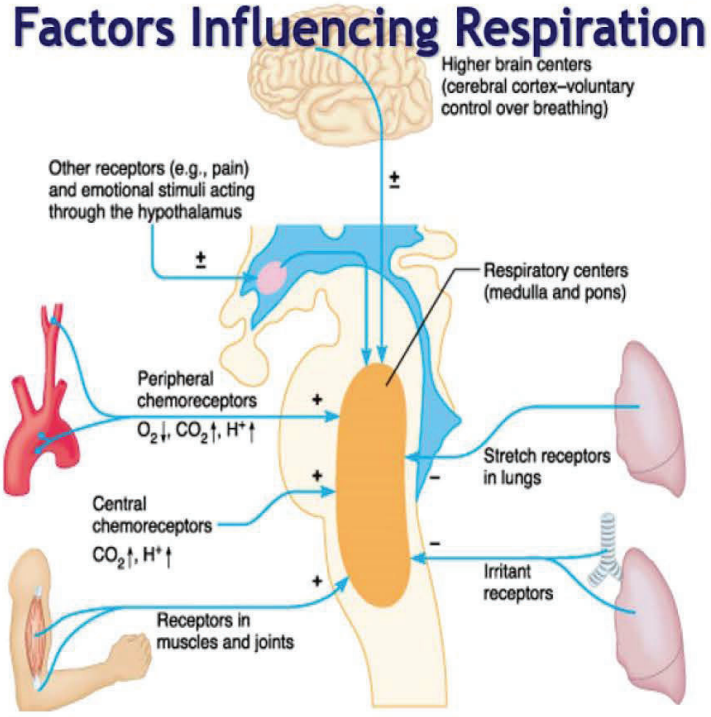


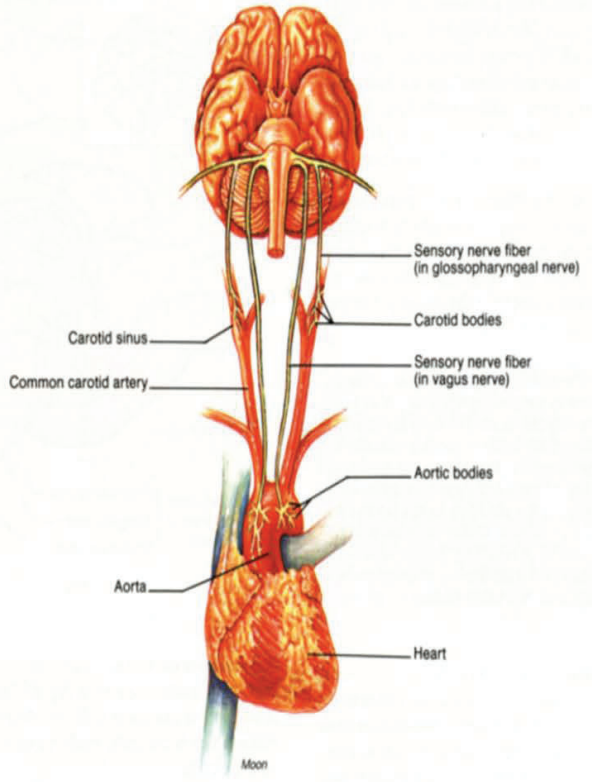
Two respiratory nuclei in medulla oblongata:

1. Inspiratory center (dorsal respiratory group, DRG)
    - The more frequently they fire, the more deeply you inhale
    - longer duration they fire, breath is prolonged, slow rate
2. Expiratory center (ventral respiratory group, VRG) - involved in forced expiration

Respiratory Centers in Pons:

3. Pneumotaxic center (upper pons) - sends continual inhibitory impulses to the inspiratory center of the medulla oblongata, as impulse frequency rises, breathe faster and shallower
4. Apneustic center (lower pons) - Stimulation causes apneusis, Integrates inspiratory cutoff information





Carotid bodies: Sensitive to: PaO2, PaCO2, and pH; Afferents in glossopharyngeal nerve.
Aortic bodies: Sensitive to: PaO2, PaCO2, but not pH; Afferents in vagus

5. Oxygen and Carbon Dioxide Diffusion Gradients

5.1. Oxygen Transport

- Diffusion: Oxygen moves from the alveoli, where $P_aO_2 \approx 100$ mm Hg, into the pulmonary capillaries, where $P_aO_2 \approx 40$ mm Hg. Oxygen then diffuses into tissues, where the P_aO_2 is even lower (approximately 40 mm Hg in resting tissues and lower in active tissues).
- Transport Mechanisms:
  - 98.5% of oxygen is carried by hemoglobin in red blood cells. Hemoglobin can bind up to four oxygen molecules, with its affinity for oxygen varying depending on the partial pressure of oxygen. The oxygen-hemoglobin dissociation curve shows that hemoglobin is nearly fully saturated at high oxygen partial pressures (as in the lungs) and releases oxygen in tissues with lower partial pressures.
  - 1.5% of oxygen is dissolved directly in plasma, which contributes to the partial pressure of oxygen in the blood.

5.2. Carbon Dioxide Transport

- Diffusion: Carbon dioxide moves from tissues, where $P_aCO_2 \approx 45$ mm Hg, into the blood, where $P_aCO_2 \approx 40$ mm Hg, and is then transported to the lungs for elimination. In the lungs, carbon dioxide diffuses from the blood (higher P_aCO_2) into the alveoli (lower P_aCO_2), where it is exhaled.
- Transport Forms:
  - Bicarbonate Ions (HCO_3^-): About 70% of CO_2 is converted into bicarbonate ions in red blood cells, which then travel in the plasma. The enzyme carbonic anhydrase catalyzes the reaction between CO_2 and water to form carbonic acid (H_2CO_3), which dissociates into HCO_3^- and H^+.
  - Carbaminohemoglobin: About 23% of CO_2 binds to hemoglobin in red blood cells to form carbaminohemoglobin.
  - Dissolved CO_2: About 7% of CO_2 is transported dissolved in plasma.

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6. Practical Experiments and Demonstrations

6.1. Measurement of Gas Diffusion

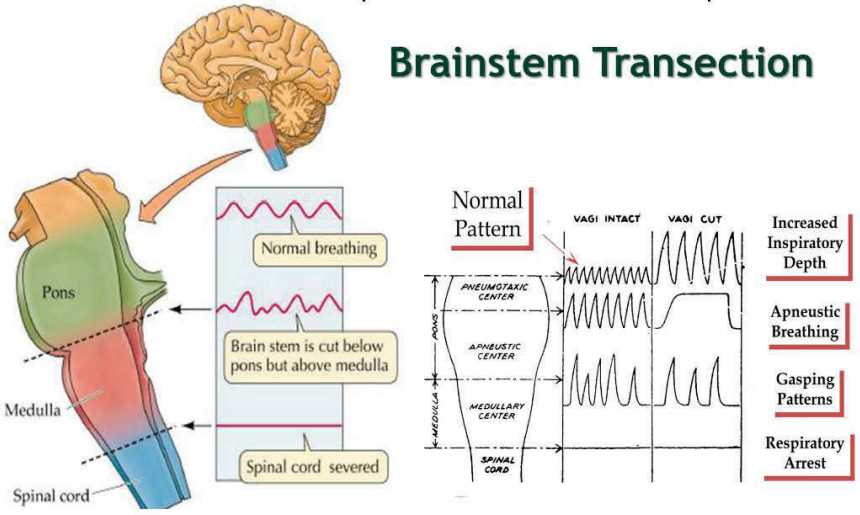
- Objective: Measure the rate of gas diffusion across a membrane under different conditions (e.g., varying membrane thickness and surface area). Students can observe how changes in these factors affect the diffusion rate of gases such as oxygen and carbon dioxide.

6.2. Oxygen Saturation and Partial Pressure

- Objective: Use pulse oximetry to measure oxygen saturation (SpO_2) in the blood. The experiment can explore how SpO_2 levels change under different conditions, such as at rest, during exercise, or at varying altitudes, reflecting the role of partial pressure in oxygen transport.

6.3. CO_2 Transport and Blood pH

- Objective: Demonstrate how CO_2 is transported in the blood and its impact on blood pH



Examination and Assessment

1	Are functions of respiration:	
a.	pulmonary ventilation, inflow and outflow of air between the atmosphere and the lung alveoli;	True
b.	diffusion of oxygen and carbon dioxide between the alveoli and the blood;	True
c.	transport of oxygen in the blood and body fluids to the body's tissue cells;	True
d.	transport of carbon dioxide in the blood and body fluids from the body's tissue cells;	True
e.	regulation of ventilation and other facets of respiration	True
f.	pulmonary expiration, which means the inflow and outflow of oxygenin the lung alveoli;	False
g.	diffusion of glycogen and carbon dioxide between the alveoli and the blood;	False
h.	transport of carbon dioxide in the blood and body fluids to the body's tissue cells;	False
i.	transport of oxygen in the blood and body fluids from the body's tissue cells to alveoli;	False
j.	regulation of ventilation and other facets of digestion	False

2	Respiration functional events:	
a.	Ventilation: Movement of air into and out of lungs	True
b.	Gas exchange between air in lungs and blood	True
c.	Transport of oxygen and carbon dioxide in the blood	True
d.	Internal respiration	True
e.	Gas exchange between the blood and tissues	True
f.	Movement of air into and out of duodenum	False
g.	Gas exchange between air in lungs and stomach	False
h.	Transport of oxygen and carbon dioxide in the endothelial space	False
i.	Artificial respiration	False
j.	Gas exchange between the blood and heart	False

3	Respiratory System Functions:	
a.	Gas exchange: Oxygen enters blood and carbon dioxide leaves	True
b.	Regulation of blood pH: Altered by changing blood carbon dioxide levels	True
c.	Voice production: Movement of air past vocal folds makes sound and speech	True
d.	Olfaction: Smell occurs when airborne molecules drawn into nasal cavity	True
e.	Protection: Against microorganisms by preventing entry and removing them	True
f.	Gas exchange: carbon dioxide enters blood and Oxygen leaves the lungs	False
g.	Regulation of blood glucose: Altered by changing blood carbon dioxide levels	False
h.	Voice antrenament: Movement of air past vocal folds makes sound and think	False
i.	Olfaction: Smell occurs when airborne molecules drawn into esophageal cavity	False
j.	Protection: Against glucose by preventing entry and removing it	False

4	Respiratory System Divisions:	
a.	Nose	True
b.	pharynx	True
c.	larynx	True
d.	trachea	True
e.	lungs	True
f.	liver	False
g.	pancreas	False
h.	duodenum	False
i.	sternum	False
j.	bones	False

5	Conducting Zone roles	
a.	All the structures air passes through before reaching the respiratory zone.	True
b.	Cartilage holds tube system open and smooth muscle controls tube diameter	True
c.	Warms and humidifies inspired air	True
d.	Filters and cleans:	True
e.	Passage of air	True
f.	digestion	False
g.	secretion	False
h.	absorbtion	False
i.	Gas exchange	False
j.	Cell division	False

6	The lung:	
a.	Anatomically and functionally divided into lobes, which in turn are divided into: segments, lobules and acini.	True
b.	Two lungs: Principal organs of respiration	True
c.	Right lung: Three lobes	True
d.	Left lung: Two lobes	True
e.	Lobes, bronchopulmonary segments, lobules	True
f.	Anatomically and functionally divided into tubules, which in turn are divided into alveoli	False
g.	Two lungs: Principal organs of transpiration	False
h.	Right lung: Three segments	False
i.	Left lung: Two segments	False
j.	Lobes, duodenal segments, lobules	False

7	Respiratory Zone	
a.	Region of gas exchange between air and blood.	True
b.	Includes respiratory bronchioles and alveolar sacs	True
c.	Mainly involves alveolar space	True
d.	There are about 500,000 bronchioles	True
e.	There are about 8 million of alveolar sacs	True
f.	Region of gas exchange between air and lymph	False
g.	Includes respiratory trachea and bronchioles	False
h.	Mainly involves bronchus	False
i.	There are about 5 bronchioles	False
j.	There are about 100 of alveolar sacs	False

8	Airway branching includes:	
a.	Trachea	True
b.	Primari bronchi	True
c.	Secondary and smaller bronchi	True
d.	Bronchioles	True
e.	Alveoli	True
f.	Nose	False
g.	pharynx	False
h.	larynx	False
i.	esophagus	False
j.	lungs	False

9	BLOOD SUPPLY TO THE LUNG	
a.	Bronchial circulation arise from the aorta and provides nourishments to the lung parenchym	True
b.	Pulmonary circulation brings deoxygenated blood from the right ventricle to gas-exchange units	True
c.	At the gas-exchanging units, oxygen is picked up and carbon dioxide is removed from the blood	True
d.	The oxygenated blood is returned to the left atrium for distribution to the rest of the body	True
e.	Blood supply to the lung includes pulmonary and bronchial circulation	True
f.	Bronchial circulation arises from the vena cava and provides nourishment to lung parenchyma	False
g.	Pulmonary circulation brings oxygenated blood from the right aorta to the gas-exchange units	False
h.	At the gas-exchanging units, carbon dioxide is picked up and oxygen is removed from the blood	False
i.	The oxygenated blood is returned to the right atrium for distribution to the lungs	False
j.	Blood supply to the lung includes arterial and bronchial circulation	False

10	MUSCLES OF RESPIRATION	
a.	Diaphragm	True
b.	Abdominal muscles	True
c.	External intercostal muscle	True
d.	Internal intercostal muscle	True
e.	Muscles of the abdominal wall	True
f.	Deltoid muscle	False
g.	Pectoralis	False
h.	Biceps	False
i.	Quadriceps	False
j.	Gluteus maximus	False

11	Mechanisms of Breathing:	
a.	At rest: 10-20 breaths / minute	True
b.	During exercise: 40 - 45 breaths / minute at maximum exercise in adults	True
c.	Inhale is an active process	True
d.	Diaphragm and ribs act simultaneously	True
e.	Ribs are moved through the intercostal muscles	True
f.	At rest: 1-2 breaths / minute	False
g.	During exercise: 2 - 5 breaths / minute at maximum exercise in adults	False
h.	Inhale is an passive process	False
i.	Diaphragm and ribs act sucessively	False
j.	Ribs are moved through the abdominal muscles	False

12	Pulmonary circulation or small circulation	
a.	ensures oxygenation of blood	True
b.	elimination of CO2	True
c.	active substances (prostaglandins, angiotensin II);	True
d.	constitutes a blood reservoir for the left ventricle.	True
e.	represents a filter for emboli	True
f.	ensures oxygenation of food	False
g.	elimination of O2	False
h.	active substances (insulin, cortisol);	False
i.	constitutes a blood reservoir for the heart	False
j.	represents a filter for glucose	False

13	Nutritional ensured by the bronchial arteries (come from the thoracic aorta) and the internal thoracic artery:	
a.	irrigates bronchial tree walls	True
b.	support lung tissue (stroma)	True
c.	the bronchial arteries only reach the level of the respiratory bronchioles	True
d.	the blood from the pulmonary nutrient circulation drains into the pulmonary veins	True
e.	reducing the saturation in O2 of the blood from the small circulation	True
f.	ensures oxygenation of blood	False
g.	elimination of glucose	False
h.	active substances (prostaglandins, angiotensin II);	False
i.	constitutes a blood reservoir for the left ventricle.	False
j.	represents a filter for emboli	False

14	Factors that influence pulmonary diffusion are:	
a.	the qualities of the alveolo-hematic barrier;	True
b.	the pressure gradient;	True
c.	gas diffusion constant;	True
d.	the size of the exchange surface;	True
e.	the contact time between the two environments.	True
f.	the qualities of the trachea	False
g.	the sodium gradient;	False
h.	gas concentration constant;	False
i.	the size of the duodenum	False
j.	the contact time with external space	False

15	The alveolo-hematic barrier include:	
a.	the pulmonary surfactant layer lining the alveoli	True
b.	the alveolar epithelium	True
c.	the alveolar basement membrane	True
d.	the interstitial fluid	True
e.	the capillary basal membrane	True
f.	Nose	False
g.	pharynx	False
h.	larynx	False
i.	esophagus	False
j.	lungs	False

16	Larynx:	
a.	Maintain an open passageway for air movement	True
b.	Epiglottis prevent swallowed material from moving into larynx	True
c.	Vestibular folds prevent swallowed material from moving into larynx	True
d.	Includes thyroid and cricoid cartilages	True
e.	Vocal folds are primary source of sound production	True
f.	Maintain a closed passageway for air movement	False
g.	Epiglottis permit swallowed material from moving into larynx	False
h.	Vestibular folds permit swallowed material from moving into larynx	False
i.	Includes thyroid	False
j.	Includes parathyroids	False

17	Lower Respiratory Tract	
a.	Tracheobronchial Tree	True
b.	The tissue surrounding the alveoli has elastic fibers - allow the alveoli to expand and recoil.	True
c.	Type I pneumocytes – form 90% of alveolar wall	True
d.	Type II pneumocytes – secretory cells that produce surfactant	True
e.	Type I pneumocytes responsible for gas exchange	True
f.	Nose	False
g.	pharynx	False
h.	larynx	False
i.	esophagus	False
j.	duodenum	False

18	Muscles of Respiration	
a.	Diaphragm – dome shaped, attaches to the inner circumference of the inferior thoracic wall.	True
b.	Inspiration – diaphragm, external intercostals pectoralis minor, and scalenes.	True
c.	Expiration – diaphragm, abdominal muscles and internal intercostals.	True
d.	Intercostal muscles	True
e.	Muscles of the abdominal wall	True
f.	Deltoid muscle	False
g.	Pectoralis	False
h.	Biceps	False
i.	Quadriceps	False
j.	Gluteus maximus	False

19	Pleura	
a.	Pleural fluid produced by pleural membranes	True
b.	Acts as lubricant	True
c.	Helps hold parietal and visceral pleural membranes together	True
d.	Important for respiration	True
e.	Mainteins lubrication	True
f.	Is part of stomach	False
g.	Is part of diaphragm	False
h.	Is a muscle	False
i.	Acts as gas exchenger	False
j.	Can be contracted	False

20	Ventilation	
a.	Movement of air into and out of lungs	True
b.	Air moves from area of higher pressure to area of lower pressure	True
c.	Pressure is inversely related to volume	True
d.	The flow of air into the lungs requires a pressure gradient from the outside of the body to the alveoli.	True
e.	Airflow from the lungs requires a pressure gradient in the opposite direction.	True
f.	Movement of air into and out of liver	False
g.	Air moves from area of low pressure to area of higher pressure	False
h.	Pressure is inversely related to air	False
i.	The flow of air into the lungs requires a pressure gradient in tissues	False
j.	Airflow from the lungs requires a pressure gradient in the air	False

21	Minute and Alveolar Ventilation	
a.	Minute ventilation: Total amount of air moved into and out of respiratory system per minute	True
b.	Respiratory rate or frequency: Number of breaths taken per minute	True
c.	Anatomic dead space: Part of respiratory system where gas exchange does not take place	True
d.	Alveolar ventilation space in which gas exchange takes place	True
e.	Alveolar ventilation represents how much air per minute enters the parts of the respiratory system	True
f.	Minute ventilation: Total amount of air moved into and out of respiratory system per hour	False
g.	Respiratory rate or frequency: Number of breaths taken per hour	False
h.	Anatomic dead space: Part of respiratory system where gas exchange is accelerated	False
i.	Alveolar ventilation space in which gas exchange is stoped	False
j.	Alveolar ventilation represents how much air per hour enters the parts of the respiratory system	False

22	Pulmonary volumes	
a.	Current volume (VT) is the volume of air that enters and exits the lungs during a quiet breath	True
b.	Inspiratory reserved volume (VIR) is the maximum volume of air that can be inhaled after regular inspiration	True
c.	Inspiratory reserved volume (VIR) has a value of 1,500 ml.	True
d.	Expiratory reserve volume (VER) is achieved by performing a maximum expiration after a regular expiration	True
e.	Expiratory reserve volume (VER) has a value of 1,500 ml.	True
f.	Current volume (VT) has a value of 1,500 ml	False
g.	Inspiratory reserved volume (VIR) is achieved by performing a maximum expiration after a regular expiration	False
h.	Inspiratory reserved volume (VIR) has a value of 6,500 ml.	False
i.	Expiratory reserve volume (VER) is the maximum volume of air that can be inhaled after regular inspiration	False
j.	Expiratory reserve volume (VER) is the volume of air that enters and exits the lungs during a quiet breath	False

23	Vital capacity (VC)	
a.	represents the volume of air that a maximum exhalation can exhale after a maximum inspiration	True
b.	It is equal to the sum of three lung volumes (TV + IRV + ERV)	True
c.	has the value of 3,500-4,000 ml air	True
d.	Vital capacity is not the total lung capacity	True
e.	Vital capacity and residual capacity represent the total lung capacity	True
f.	represents the volume of air that remains in the lungs at the end of a maximum expiration and	False
g.	has the value of 1,300-1,500 ml.	False
h.	leaves the lung only by replacing it with an inert gas (He) or with water	False
i.	Vital capacity is equal with the total lung capacity	False
j.	Vital capacity and residual capacity represent the inspiratory volume	False

24	Vital capacity varies with	
a.	age	True
b.	sex	True
c.	body position	True
d.	sports	True

e.	in clinostatism it is 5-10% lower than in orthostatism.	True
f.	Body Mass	False
g.	Body force	False
h.	Glucose level	False
i.	filtration	False
j.	Social status	False

25	Residual volume (VR)	
a.	represents the volume of air that remains in the lungs at the end of a maximum expiration and	True
b.	has the value of 1,300-1,500 ml.	True
c.	The residual volume leaves the lung only by replacing it with an inert gas (He) or with water	True
d.	when collapsed the two lungs, the amount of 200 ml of air (minimal air) remains,	True
e.	a fragment of lung float on the surface of the water	True
f.	represents the volume of air that can be exhaled by a maximum exhalation after a maximum inspiration	False
g.	It is equal to the sum of three lung volumes (TV + IRV + ERV)	False
h.	has the value of 4,500-5,000 ml air	False
i.	Residual volume is the total lung capacity	False
j.	Residual volume and Expiratory reserve volume represent the total lung capacity	False

26	The number of breaths per adult, at rest, is 16-18 breaths / min and varies according to several factors:	
a.	Health status	True
b.	Gender: in women there is a greater number of breaths-18 / min than in men 12-16 / min;	True
c.	Body position;	True
d.	Altitude: the number of breaths increases at high altitudes due to the decrease of atmospheric pressure;	True
e.	Physiological states: in sleep the number of breaths decreases;	True
f.	Body mass	False
g.	Body force	False
h.	Glucose level	False
i.	filtration	False
j.	Social status	False

27	Respiratory flow	
a.	Respiratory flow represents the amount of air ventilated by the lungs for one minute under rest conditions	True
b.	in an adult whose current volume is 500 ml and the respiratory rate is 12 cycles / min	True
c.	During physical exertion the fan flow increases to 80-100 l / min	True
d.	can be obtained by the product between the current volume (TV) and the rate of ventilation.	True
e.	voluntary breaths with maximum amplitude and frequency represents the maximum respiratory rate	True
f.	represents the volume of air that can be exhaled by a maximum exhalation after a maximum inspiration	False
g.	it is equal to the sum of three lung volumes (TV + IRV + ERV)	False
h.	has the value of 4,500-5,000 ml air	False
i.	is the total lung capacity	False
j.	can be obtained from Residual volume and Expiratory reserve volume	False

28	Pulse oximetry	
a.	Pulse oximetry is performed in the setting of the 6-minute walk test	True
b.	This test is a measure of the maximum distance the patient is able to walk	True
c.	The patient is permitted to slow down / stop, if required	True
d.	This test should be performed while exercise oxygen needs are being adequately met	True
e.	Borg dyspnea and fatigue scores are collected immediately after completion of the walk test	True
f.	establish baseline lung function	False
g.	evaluate dyspnea	False
h.	detect pulmonary disease	False
i.	monitor effects of therapies used to treat respiratory disease	False
j.	evaluate respiratory impairment	False

29	Spirometry is used to	
a.	establish baseline lung function	True
b.	evaluate dyspnea	True
c.	detect pulmonary disease	True
d.	monitor effects of therapies used to treat respiratory disease	True
e.	evaluate respiratory impairment	True
f.	To determine hemoptysis of unknown origin	False
g.	In Pneumothorax	False
h.	Detect unstable angina pectoris	False
i.	In recent myocardial infarction	False
j.	Diagnose thoracic aneurysms, abdominal aneurysms, cerebral aneurysms	False

30	Relative contraindications for spirometry include	
a.	hemoptysis of unknown origin	True
b.	Pneumothorax	True
c.	unstable angina pectoris	True
d.	recent myocardial infarction	True
e.	thoracic aneurysms, abdominal aneurysms, cerebral aneurysms	True
f.	establish baseline lung function	False
g.	evaluate dyspnea	False
h.	detect pulmonary disease	False
i.	monitor effects of therapies used to treat respiratory disease	False
j.	Evaluation of respiratory impairment	False

Course 13: The Locomotor System
Sub-topic: Bones, Joints, Muscles, and Movement

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1. Overview of the Locomotor System

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2. The Osteoarticular System – Bones
2.1. Bone Structure and Composition
2.2. Bone Development and Growth

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3. The Osteoarticular System – Joints
3.1. Types of Joints
3.2. Joint Structure

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4. The Neuromuscular System – Muscles
4.1. Muscle Types
4.2. Muscle Structure
4.3. Muscle Contraction

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5. Coordination of Movement
5.1. Agonist, Antagonist, and Synergist Muscles
5.2. Types of Muscle Contraction

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6. Bone and Joint Functions
6.1. Mechanical Functions
6.2. Biological Functions
- Hematopoiesis: Blood cell production occurs in the red bone marrow.
- Mineral Storage: Bones store calcium and phosphorus, essential for metabolic functions.

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7. Functional Role of Joints in the Body
- Postural Role: Joints help maintain body position and posture.
- Kinetic Role: Joints facilitate the movement of body segments relative to one another.
- Locomotive Role: Joints allow coordinated movements of the entire body, enabling locomotion.

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8. Practical Applications and Clinical Implications
8.1. Common Disorders of the Locomotor System
- Osteoporosis
- Arthritis: Inflammation of joints causing pain and limited mobility.
- Muscle Strains and Tears

8.2. Diagnostic Tools
- X-rays: Visualize bone fractures and joint abnormalities.
- Magnetic Resonance Imaging (MRI): Provides detailed images of soft tissues, including muscles and ligaments.
- Bone Density Scans: Assess bone mineral density, useful in diagnosing osteoporosis.

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9. Review and Case Studies
- Case studies on bone fractures, joint injuries, and muscle tears.
- Clinical scenarios involving the diagnosis and treatment of locomotor disorders.

Examination and Assessment

Practical Session 13: Human Posture and Locomotion

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1. Introduction to Human Posture and Locomotion

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2. Human Posture
2.1. Definition and Function
2.2. Gravity and Stability
2.3. Muscles Involved in Posture Maintenance

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3. Human Locomotion
3.1. Definition and Phases of Locomotion
3.2. Phases of Walking
- Stance Phase
- Swing Phase

3.3. Movements in Walking
- Flexion and Extension:
  These movements occur at the hip, knee, and ankle joints to facilitate forward motion.
- Abduction and Adduction:
  Primarily at the hip joint, these movements stabilize the pelvis during walking.
- Rotation:
  Occurs at the hip and knee joints to maintain balance and forward progression.

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4. Posture and Balance Control Mechanisms
4.1. Sensory Input
- Proprioception:
  The ability of the body to sense its position in space, providing feedback to the nervous system to maintain posture and balance.

4.2. Nervous System Control
- Central Nervous System (CNS):
  The CNS integrates sensory inputs and coordinates muscle responses to maintain balance during static posture and dynamic movements such as walking.

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5. Practical Experiments and Demonstrations
5.1. Analysis of Posture
5.2. Gait Analysis
5.3. Balance and Coordination Testing

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6. Clinical Relevance
6.1. Disorders Affecting Posture and Locomotion
- Parkinson's Disease
- Cerebellar Ataxia
- Spinal Cord Injury

6.2. Gait Abnormalities
- Hemiplegic Gait:
  Observed in stroke patients, where one leg swings in a semicircle due to weakness on one side.
- Trendelenburg Gait:
  Caused by weakness in the hip abductors, leading to a drop in the pelvis on the opposite side during the stance phase.

Course 13: The Locomotor System
Sub-topic: Bones, Joints, Muscles, and Movement

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1. Overview of the Locomotor System

The locomotor system is essential for enabling movement, providing structure and stability to the body, and allowing interactions with the environment. It consists of three main components: bones, joints, and muscles, which work together to facilitate posture, mobility, and locomotion. This system involves voluntary and involuntary movements and supports walking, running, standing, and grasping functions.

The locomotor system is composed of 2 distinct systems:

- The osteoarticular system with the role of passive support and mobilization, represented by the bones and the joints
- The neuromuscular system that acts on the first and is represented by the assembly of muscles and their somatic/motor nerve

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2. The Osteoarticular System – Bones

The osteoarticular system includes bones and joints, forming the skeletal framework that supports the body, protects vital organs, and facilitates movement by providing attachment points for muscles.

2.1. Bone Structure and Composition

- Bone Tissue:
  Bones are composed of a combination of organic (mainly collagen) and inorganic (primarily calcium phosphate) components, providing strength and flexibility.
- Types of Bone Tissue:
  - Compact Bone: Dense and forms the outer layer of bones, providing strength for weight-bearing.
  - Spongy Bone (Cancellous Bone): Found in the interior of bones, lighter than compact bone, and filled with bone marrow.
- Bone Cells:
  - Osteoblasts: Cells responsible for bone formation.
  - Osteocytes: Mature bone cells that maintain the bone matrix.
  - Osteoclasts: Cells involved in the breakdown and resorption of bone tissue.
- Structural-functional characteristics:
  - Bone vascular network
    - The bone is richly vascularized
    - Blood sources depending on the shape and size of the bone
    - The long bone has 4 sources: nutritional artery, metaphyseal artery, epiphyseal artery, and periosteal arteries (atrophied in adults)
    - The medullary venous system has a capacity of 6-8 times greater than the arterial one and plays the role of "gateway" of the young blood cells generated in the medullary hematopoietic system.
  - The somato-vegetative nervous network
    - The skeletal bone system receives an important network of nerve fibers, sensitive and vegetative, which enter the bone together with the vascular network.
- Bone system functions:
  - Mechanical functions
    - Support and protection functions
    - Head, trunk and extremity support;
    - Insertion point of the muscular tendons and ligaments;
    - Shelter for internal organs (thoracic and pelvic), brain, spinal cord and sense organs;
    - Posture and locomotion functions

- Biological functions
  - Defining and maintaining the shape of the human body
  - Participation in mineral metabolism
  - Participation in hematopoiesis and defense of the body

2.2. Bone Development and Growth

- Ossification: The process by which bones form. Two types of ossification exist:
  - Intramembranous Ossification: Formation of flat bones such as the skull, where bone forms directly from mesenchymal tissue.
  - Endochondral Ossification: Formation of long bones, where cartilage is replaced by bone tissue over time.
- Epiphyseal Plates: Growth occurs at the epiphyseal plates (growth plates), where cartilage cells divide and are gradually replaced by bone, allowing bones to lengthen during childhood and adolescence.

Factors controlling bone growth, patterning and maturation:

- Bone growth and maturation are under constant control of many modulatory factors, genetic factors, nutritional-metabolic, biochemical, pharmacological, circulatory, age and biomechanical factors.

Bone marrow

Bone cavities contain hematopoietic tissue represented by the red marrow. It participates both in the generation of blood figurative elements and in the processes of nutrition, formation and growth of bones through the high content in osteoblasts, osteoclasts, blood vessels and nerves.
Like bone, the bone marrow changes with age, during growth it turns into yellow marrow (long bones) and finally into gray bone marrow in the elderly.

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3. The Osteoarticular System – Joints

Joints are connections between bones that allow varying degrees of movement and play a key role in maintaining posture and facilitating locomotion. The assembling of the bone parts of the skeleton to form the passive device of the locomotor apparatus is accomplished through anatomical-functional formations called joints. The joint is the union organ of two or more bone pieces, their mobility, and functionality being closely related to the geometry and structural organization of the anatomical components.

3.1. Types of Joints

1. Fibrous joints, structurally "synarthrosis", allowing minimal movement (eg cranial sutures, distal tibioperonary joint)
2. Cartilaginous joints are "amphiarthrosis", moderate mobility (pubic symphysis, intervertebral joints)
3. Synovial joints are grouped under the name of "diarthrosis" and exhibit high mobility (belt joints, radio-carpal, interphalangeal). In the case of the synovial joints, the bony extremities are covered by the articular cartilage and bathed by the synovial fluid, which gives a reduced friction and an increased resistance to the compression and traction forces generated by gravity or muscle activity. The entire joint is covered by an articular capsule lined by vessels and nerves and covered by a synovial membrane.

3.2. Joint Structure

- Articular Cartilage: Covers the surfaces of bones at synovial joints, reducing friction and absorbing shock.
- Synovial Membrane: Lines the inner surface of the joint capsule and secretes synovial fluid, which lubricates the joint.
- Ligaments: Bands of dense connective tissue that connect bones, providing stability to the joint by limiting excessive movements.
- Joint Capsule: A fibrous structure that encloses the joint cavity, helping to protect and stabilize the joint.

According to the number of joint parts, the joints can be:

- Simple (interphalangeal)
- Compound (elbow joint)
- Complex (patellar joint)
- Combinate (temporo-mandibular joint)

By their form and the degree of freedom, they are classified into:

- Uniaxial joints (flat or cylindrical) can do flexion, extension, medial or lateral rotation - elbow joint
- Biaxial joints (ellipsoids and saddles) 2-way movements (flexion and extension and laterality), rotation movement are not possible (radio-carpal joint)
- Multiple joints, extension movements, flexion, rotation, laterality, adduction, abduction

Functional role of joints in the body:

- Postural, by participating in maintaining the body position;
- Kinetic, by moving some segments in relation to others;
- Locomotive, by moving the body as a whole into space.

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4. The Neuromuscular System – Muscles

About 600 skeletal muscles cover 40-50% of body weight. Muscles, in conjunction with bones and joints, allow voluntary and involuntary movements necessary for posture and locomotion. Around each muscle fiber is connective tissue called endomisium, which contains blood vessels and nerves. Several muscle fibers have a common coating made of dense collagen fibers, called perimisium. The connective tissue that organizes the fibers in the form of muscle as an organ is called epimisium. The three connective layers are in continuity and at the end of the muscle the tendons form.

The tendons are made of flexible, but practically inextensible, connective tissue, which plays an intermediary role in transmitting muscle strength to the skeleton.

The strength and movement generated by a muscle depend on the individual activities integrated over time of the component motor units.

For a fine movement a small number or even a single motor unit is used.

The increase of the contraction force is achieved by the entry into action of several motor units, simultaneously with the increase of the number of efferent nerve impulses.

The gradation of muscle activity is thus determined by the synchronous activity of the motor units throughout the muscle.

Making any movement involves the participation of several muscles, which are called agonists, synergists and antagonists.

The muscle that produces action is called the agonist, and the one that opposes it is the antagonist.

Synergistic muscles act in the same direction, but they cannot achieve the respective movement separately.

Features of muscle contraction in the body

Muscle contraction is the main internal force involved in the movement, at the production of which it participates: the neuro-muscular transmission of the message, the excitation-contraction couple, the contractile system and the energy system

As a consequence of the neuro-muscular excitability, the contraction changes the initial length of the muscular structures, leading to the development of static or dynamic tensile forces, with the entrainment of the bone-joint components in the locomotor act.

4.1. Muscle Types

- Skeletal Muscles: Voluntary, striated muscles that attach to bones and are responsible for body movement. The somatic nervous system controls them.
- Smooth Muscles: Involuntary muscles found in the walls of internal organs and blood vessels. They regulate internal movements such as digestion and blood flow.
- Cardiac Muscle: Involuntary, striated muscle found only in the heart. It contracts rhythmically to pump blood throughout the body.

4.2. Muscle Structure

- Muscle Fibers:
  Long, multinucleated cells containing myofibrils, which consist of repeating units called sarcomeres. Sarcomeres are composed of actin (thin filaments) and myosin (thick filaments), responsible for muscle contraction.
- Connective Tissue Layers:
  - Endomysium: Surrounds individual muscle fibers.
  - Perimysium: Encloses bundles of muscle fibers (fascicles).
  - Epimysium: Encloses the entire muscle.

4.3. Muscle Contraction

Muscle contraction occurs through the sliding filament theory, where actin and myosin filaments slide past each other, shortening the sarcomere and thus the entire muscle fiber. This process is initiated by neural stimulation, triggering calcium release and ATP hydrolysis.

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5. Coordination of Movement

5.1. Agonist, Antagonist, and Synergist Muscles

- Agonist (Prime Mover):
  The main muscle responsible for a specific movement (e.g., the biceps brachii in elbow flexion).
- Antagonist:
  A muscle that opposes the action of the agonist, helping to control or decelerate movement (e.g., the triceps brachii during elbow flexion).
- Synergists:
  Muscles that assist the agonist by stabilizing joints or adding extra force during a movement (e.g., brachialis during elbow flexion).

5.2. Types of Muscle Contraction

- Isotonic Contraction:
  The muscle changes length while contracting. This includes:
  - Concentric contraction: Muscle shortens as it generates force (e.g., lifting a weight).
  - Eccentric contraction: Muscle lengthens while maintaining tension (e.g., lowering a weight).
- Isometric Contraction:
  The muscle generates force without changing length, often used to maintain posture or stabilize joints.

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6. Bone and Joint Functions

6.1. Mechanical Functions

- Support: Bones provide a structural framework for the body, supporting the weight of tissues and organs.
- Protection: Bones protect vital organs (e.g., the skull protects the brain, and the rib cage protects the heart and lungs).
- Movement: Bones act as levers that muscles pull on to generate movement.

6.2. Biological Functions

- Hematopoiesis:
  The production of blood cells occurs in the red bone marrow of long bones and flat bones.
- Mineral Storage:
  Bones store essential minerals such as calcium and phosphorus, which are necessary for various metabolic processes, including nerve transmission and muscle contraction.

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7. Functional Role of Joints in the Body

Joints allow the bones of the body to move relative to one another, performing various roles:

- Postural Role:
  Joints contribute to maintaining body posture by providing stability and support during standing or sitting.
- Kinetic Role:
  Joints enable movement of body segments, such as the flexion and extension of limbs, which is critical for most physical activities.
- Locomotive Role:
  Joints facilitate coordinated movements necessary for locomotion, such as walking and running, by allowing controlled motion across different planes.

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8. Practical Applications and Clinical Implications

8.1. Common Disorders of the Locomotor System

- Osteoporosis:
  A condition characterized by decreased bone density and increased fracture risk. It commonly affects postmenopausal women and the elderly.
- Arthritis:
  Inflammation of joints, leading to pain, stiffness, and reduced mobility. Rheumatoid arthritis and osteoarthritis are the most common forms.
- Muscle Strains and Tears:
  Injuries resulting from overstretching or excessive force applied to muscles, often occurring during physical activity.

8.2. Diagnostic Tools

- X-rays:
  Useful for visualizing bone fractures, dislocations, and certain joint abnormalities.
- Magnetic Resonance Imaging (MRI):
  Provides detailed images of soft tissues, including muscles, ligaments, and cartilage, making it valuable for diagnosing musculoskeletal injuries.
- Bone Density Scans:
  Used to assess bone mineral density, particularly in diagnosing osteoporosis and evaluating fracture risk.

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9. Review and Case Studies

- Case studies on bone fractures, joint injuries, and muscle tears:
  Reviewing real-life scenarios where patients experience musculoskeletal injuries and exploring diagnostic approaches and treatments.
- Clinical scenarios involving the diagnosis and treatment of locomotor disorders:
  In-depth discussion of disorders such as arthritis, osteoporosis, and muscle injuries, focusing on current treatment options, rehabilitation strategies, and patient outcomes.

Practical Session 13: Human Posture and Locomotion

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1. Introduction to Human Posture and Locomotion

Posture and locomotion are key components of human motor function, enabling stability and movement within a gravitational environment. Posture refers to the body's alignment and positioning against gravity, allowing an upright stance with minimal energy expenditure. On the other hand, locomotion involves coordinated movements that result in the displacement of the body, with walking being the most common form of human locomotion. Both posture and locomotion are complex, integrating multiple systems, including the musculoskeletal, nervous, and sensory systems, to maintain balance and enable smooth, coordinated movements.

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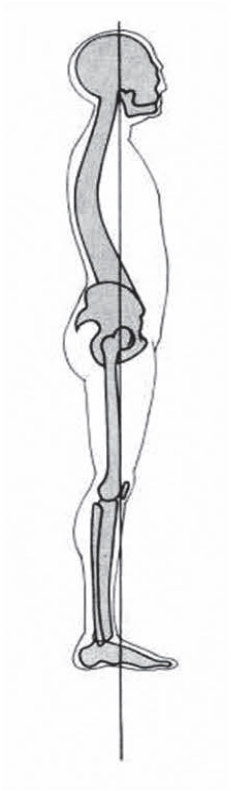
2. Human Posture

2.1. Definition and Function



Posture is the position in which the body holds itself while standing, sitting, or lying down. It involves the coordination of muscles and bones to maintain stability and balance. The primary function of posture is to provide a stable base for movement and to distribute body weight efficiently, reducing strain on muscles and joints. Proper posture minimizes the energy expenditure required to maintain an upright position, prevents injury, and supports overall function in daily activities.

2.2. Gravity and Stability

Gravity plays a fundamental role in posture. The body's center of gravity must be aligned with the base of support (usually the feet in standing) to maintain stability. The line of gravity should pass through key anatomical landmarks, including the mastoid process, the center of the shoulder, the hip joint, and just anterior to the knee and ankle joints. When the line of gravity shifts outside the base of support, compensatory muscle activity or movement (such as stepping) is required to maintain balance. Stability is further influenced by the size of the base of support—the larger the base, the more stable the posture.

2.3. Muscles Involved in Posture Maintenance

Muscle activity is essential in maintaining posture, especially in standing positions. Postural muscles are those that are active in resisting gravity and preventing the body from collapsing into a flexed position. These include:

- Paraspinal muscles: These muscles support the vertebral column and maintain the alignment of the spine.
- Abdominal muscles: Help maintain the position of the pelvis and lower back.
- Gluteal muscles: Stabilize the pelvis during standing and walking.
- Quadriceps and hamstrings: Stabilize the knee joint and maintain balance during various movements.
- Calf muscles (soleus and gastrocnemius): Play a significant role in preventing forward sway by maintaining ankle stability.

These muscles work together to maintain a vertical posture, providing small adjustments to compensate for shifts in the center of gravity.

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3. Human Locomotion

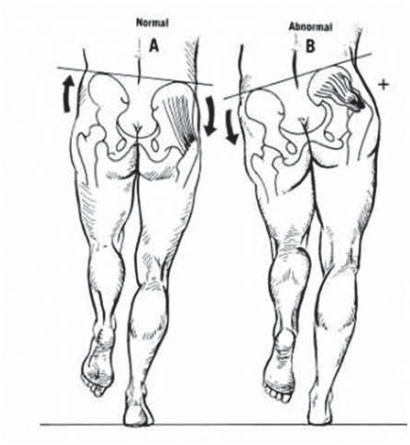
3.1. Definition and Phases of Locomotion

Locomotion refers to the ability to move from one location to another. In humans, the most common form of locomotion is walking, which involves a repetitive cycle of movements called the gait cycle. Walking is a complex process that requires the coordination of various muscles and joints to ensure smooth, efficient movement. Each step is part of a continuous process that includes periods of support (stance phase) and advancement (swing phase) of the legs.

3.2. Phases of Walking

- Stance Phase:
  This phase accounts for about 60% of the gait cycle and occurs when the foot is in contact with the ground. The stance phase begins with heel strike (the moment the heel contacts the ground), followed by mid-stance (when the body weight is directly over the supporting leg), and ends with toe-off (when the foot leaves the ground). During this phase, muscles like the quadriceps stabilize the knee, and the hip abductors maintain pelvic stability to prevent excessive tilting.
- Swing Phase:
  This phase accounts for about 40% of the gait cycle and occurs when the foot is off the ground. The swing phase begins with initial swing, where the leg moves forward, followed by mid-swing (when the foot passes under the body), and ends with terminal swing (when the leg prepares for the next heel strike). During this phase, the hip flexors and dorsiflexors of the ankle are active to clear the foot from the ground and prepare for the next stance phase.

3.3. Movements in Walking



- Flexion and Extension:
  Flexion and extension primarily occur at the hip, knee, and ankle joints. During walking, the hip and knee flex during the swing phase to bring the leg forward, and then extend during the stance phase to push off the ground and propel the body forward.
- Abduction and Adduction:
  These movements primarily occur at the hip joint. The hip abductors, particularly the gluteus medius, prevent the pelvis from dropping on the opposite side during the stance phase, ensuring stability while walking. Adduction brings the leg back towards the midline during the swing phase.
- Rotation:
  Rotation of the pelvis and spine helps to maintain balance and forward progression during walking. The pelvis rotates in the opposite direction to the movement of the legs, which reduces the lateral movement of the body and improves walking efficiency.

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4. Posture and Balance Control Mechanisms

4.1. Sensory Input

Proprioception refers to the body's ability to sense its position and movements in space. This sensory feedback comes from receptors in muscles, tendons, and joints, which send information about body position and movement to the central nervous system (CNS). Proprioception is essential for both posture and locomotion, as it allows the body to adjust its position and muscle activity in response to internal and external changes.

4.2. Nervous System Control

The central nervous system (CNS) integrates sensory information from proprioceptors, the visual system, and the vestibular system to coordinate the body's movements and maintain balance. The brainstem and cerebellum play critical roles in maintaining posture and balance, while the motor cortex coordinates voluntary movements such as walking. Reflexes, such as the stretch reflex, provide rapid adjustments to muscle length, helping to maintain posture and respond to sudden changes in body position.

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5. Practical Experiments and Demonstrations

5.1. Analysis of Posture

In this experiment, students will analyze the body's alignment during standing, paying attention to the distribution of body weight and the position of the line of gravity. They will observe muscle activity using electromyography (EMG) to understand which muscles are engaged in maintaining posture.

5.2. Gait Analysis

Students will perform gait analysis by observing the phases of walking, with a focus on the stance and swing phases. Video analysis may be used to break down the movements of the hip, knee, and ankle joints during the gait cycle, identifying any abnormalities in movement patterns.

5.3. Balance and Coordination Testing

Balance and coordination can be tested through tasks like standing on one leg or walking along a straight line. These tests evaluate the integration of sensory input, muscle coordination, and nervous system control to maintain balance during both static and dynamic activities.

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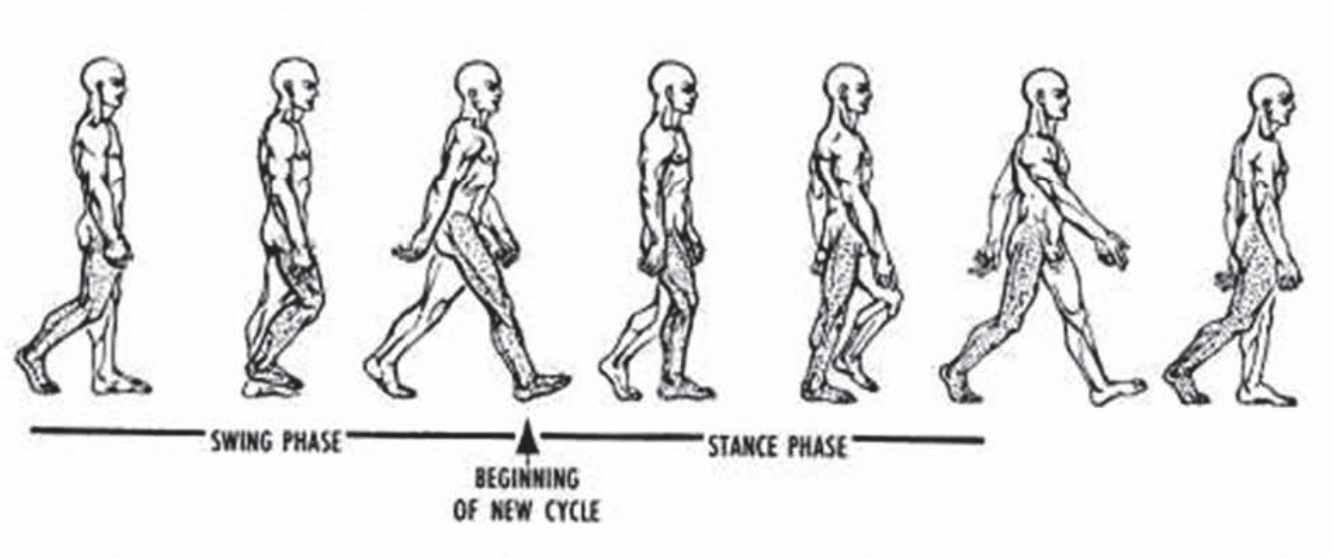
6. Clinical Relevance

6.1. Disorders Affecting Posture and Locomotion

- Parkinson's Disease:
  Parkinson's is a neurodegenerative disorder that affects the basal ganglia, leading to difficulty initiating movement, muscle stiffness, and a shuffling gait. Patients often exhibit a stooped posture and poor balance, increasing the risk of falls.
- Cerebellar Ataxia:
  Damage to the cerebellum, responsible for coordinating movement, results in uncoordinated and unsteady movements, leading to balance issues and difficulty walking.
- Spinal Cord Injury:
  Injuries to the spinal cord disrupt communication between the brain and muscles, leading to paralysis or weakness. Depending on the level of the injury, this can severely affect posture and the ability to walk.

6.2. Gait Abnormalities

- Hemiplegic Gait:
  This gait abnormality is commonly seen in stroke patients. One leg swings in a semicircular pattern due to weakness or spasticity on one side of the body. The arm on the affected side is often held close to the body with limited movement.
- Trendelenburg Gait:
  Caused by weakness of the hip abductors (especially the gluteus medius), this gait is characterized by a drop in the pelvis on the opposite side during the stance phase. The individual may compensate by leaning towards the affected side to maintain balance.



Examination and Assessment

1	The locomotor system:	
a.	Coordinates the posture and the movement activity in the most varied circumstances	True
b.	The locomotor system is composed of 2 distinct systems: osteoarticular and neuromuscular	True
c.	The osteoarticular system is represented by the bones and the joints	True
d.	The neuromuscular system is represented by the assembly of muscles and their motor nerves	True
e.	The locomotor system coordinates the posture and the movement activity	True
f.	Coordinates the mood and the movement activity in the most varied circumstances	False
g.	The locomotor system is composed of 2 distinct systems: digestive and neuromuscular systems	False
h.	The osteoarticular system is represented by osteotubes	False
i.	The neuromuscular system is represented by the assembly of muscles and their blood support	False
j.	The locomotor system coordinates the digestive and the movement activity	False

2	The Bones assures:	
a.	included along with ligaments, tendons and cartilages in the class of connective tissues.	True
b.	movement	True
c.	are an important part of the mechanical support	True
d.	maintain the skeletal structural integrity	True
e.	transmission of the force from the active to the passive elements	True
f.	included along with ligaments, muscles and hepatic tissue in the class of connective tissues.	False
g.	emotional status	False
h.	are an important part of the psychological support	False
i.	maintain the cellular structural integrity	False
j.	transmission of the force from the active structures to the passive neuro-muscular elements	False

3	Bone cells:	
a.	Chondroblasts	True
b.	Chondrocytes	True
c.	Osteoblasts	True
d.	Osteocytes	True
e.	Fibroblasts	True
f.	Myoblasts	False
g.	Erythrocytes	False
h.	Leukocytes	False
i.	Hepatocytes	False
j.	Megakaryocytes	False

4	Extracellular matrix of bones:	
a.	distinct network	True
b.	formed by the organic components	True
c.	is an intricate dynamic bio-environment	True
d.	has mechanical and biochemical properties	True
e.	predominantly responsible for bone's resistance to fracture	True
f.	Is a neural network	False
g.	formed only by the inorganic components	False
h.	is an intricate hemo-dynamic environment	False
i.	has active and passive mechanical properties	False
j.	predominantly responsible for bone's resistance to movement	False

5	Bone formation:	
a.	Intramembranous ossification	True
b.	Endochondral ossification	True
c.	Intramembranous ossification: the bones of the skull and facial bone	True
d.	Intramembranous ossification: most of the clavicle and mandible, and periosteum tissue;	True
e.	Endochondral ossification: ensures the formation of majority of the cartilaginous tissue.	True
f.	Intramembranous calcification	False
g.	Endochondral fluidification	False
h.	Intramembranous systematization	False
i.	Intramembranous contorsion	False
j.	Endochondral movement	False

6	Factors controlling bone growth, patterning and maturation:	
a.	genetic factors	True
b.	nutritional-metabolic factors	True
c.	biochemical factors	True
d.	pharmacological factors.	True
e.	circulatory, age and biomechanical factors.	True
f.	Environmental factors	False
g.	Elctrical factors	False
h.	Magnetical factors	False
i.	therapeutical factors	False
j.	Technical factors	False

7	Structural-functional characteristics of bones:	
a.	The bone consists of 2 variants of bone tissue: cortical and spongy	True
b.	Bone cavities contain hematopoietic tissue represented by the red marrow	True
c.	Like bone, the bone marrow changes with age	True
d.	Bone marrow participates in the generation of blood figurative elements	True
e.	Bone marrow during growth it turns into yellow marrow and finally into gray bone marrow in the elderly.	True
f.	The bone consists of five variants of bone tissue with different functional implications	False
g.	Bone cavities contain neuronal tissue represented by the red marrow	False
h.	Like bone, the bone marrow changes with technical factors	False
i.	Bone marrow participates in the generation of neuroendocrine elements	False
j.	Bone marrow during growth it turns into black marrow and finally into white bone marrow in the elderly.	False

8	Bone marrow:	
a.	Bone cavities contain hematopoietic tissue represented by the red marrow	True
b.	Like bone, the bone marrow changes with age	True
c.	Bone marrow participates in the generation of blood figurative elements	True
d.	Bone marrow participates in the processes of nutrition, formation and growth of bones	True
e.	Bone marrow during growth it turns into yellow marrow and finally into gray bone marrow in the elderly	True
f.	Bone cavities contain hepatic tissue represented by the red marrow	False
g.	Like bone, the bone marrow changes with environment conditions	False

h.	Bone marrow participates in the generation of nephrotic elements	False
i.	Bone marrow participates in the processes of bones fractures	False
j.	Bone marrow during growth it turns into white marrow	False

9	Bone vascular network:	
a.	The bone is richly vascularized	True
b.	Blood sources depending on the shape and size of the bone	True
c.	The long bone has 4 sources: nutritional artery, metaphyseal artery, epiphyseal artery and periosteal arteries	True
d.	The medullary venous system has a capacity of 6-8 times greater than the arterial one	True
e.	The medullary venous system plays the role of "gateway" of the young blood cells from hematopoietic system	True
f.	The bone is not vascularized	False
g.	Blood sources depending on the shape and size of the heart	False
h.	The long bone has only nutritional artery supply	False
i.	The medullary venous system has a capacity of half than the arterial one	False
j.	The medullary venous system plays the role of destructuration of the hematopoietic system	False

10	The somato-vegetative nervous network of bones:	
a.	The skeletal bone system receives an important network of nerve fibers	True
b.	Somato-vegetative nervous network of bones is sensitive and vegetative	True
c.	Nerves enter the bone together with the vascular network	True
d.	The skeleton is well-innervated	True
e.	Bone have somatic and sympathetic sensory innervations	True
f.	The skeletal bone system receives an important network of muscular fibers	False
g.	Somato-vegetative nervous network of bones is sensitive and motor	False
h.	Nerves enter the bone together with the respiratory bronchial network	False
i.	The skeleton is non-innervated	False
j.	Bone have somatic and motor innervations	False

11	Bone system functions:	
a.	Mechanical functions	True
b.	Support and protection functions	True
c.	Head, trunk and extremity support;	True
d.	Insertion point of the muscular tendons and ligaments;	True
e.	Biological functions	True
f.	Magnetic functions	False
g.	Support and electrical functions	False
h.	Head, trunk and extremity extension	False
i.	Insertion point of the blood vessels	False
j.	Sexual functions	False

12	Bone mechanical functions:	
a.	Support and protection functions	True
b.	Head, trunk and extremity support;	True
c.	Insertion point of the muscular tendons and ligaments;	True
d.	Shelter for internal organs (thoracic and pelvic), brain, spinal cord and sense organs;	True
e.	Posture and locomotion functions	True

f.	Electro-mechanical functions	False
g.	Energetic functions	False
h.	Mitochondrial functions	False
i.	Satelitar functions	False
j.	Emotional functions	False

13	Bone biological functions	
a.	Defining the shape of the human body	True
b.	Maintaining the shape of the human body	True
c.	Participation in mineral metabolism	True
d.	Participation in hematopoiesis	True
e.	Participation in defense of the body	True
f.	Magnetic functions	False
g.	Support and electrical functions	False
h.	Head, trunk and extremity extension	False
i.	Insertion point of the blood vessels	False
j.	Sexual functions	False

14	The osteoarticular system - The joints	
a.	Joints are the assembling of the bone parts of the skeleton to form the passive device of the locomotor apparatus	True
b.	The joint is the union organ of two or more bone pieces	True
c.	Joints are accomplished through anatomical-functional formations	True
d.	their mobility and functionality is closely related to the geometry of the anatomical components.	True
e.	their mobility and functionality is closely related to the structural organization of the anatomical components	True
f.	Joints are the assembling of the locomotor and vascular elements	False
g.	The joint is the union organ of two or more nerves	False
h.	Joints are accomplished through anatomical-functional satelits	False
i.	their mobility and functionality is closely related to the thelepathy	False
j.	their mobility and functionality is closely related to emotional organization of the anatomical components	False

15	Joints are classified into following types:	
a.	Fibrous joints, structurally "synarthrosis", allowing minimal movement (cranial sutures, distal tibioperonary)	True
b.	Cartilaginous joints - "amphiarthrosis"	True
c.	"amphiarthrosis" have moderate mobility (pubic symphysis, intervertebral joints)	True
d.	Synovial joints	True
e.	"diarthrosis" synovial joints that exhibit high mobility (belt joints, radio-carpal, interphalangeal)	True
f.	Fibrous joints, structurally "amphiarthrosis", allowing minimal movement	False
g.	Cartilaginous joints - "synarthrosis"	False
h.	"amphiarthrosis" have very high mobility	False
i.	Synoviomedular joints	False
j.	"diarthrosis" synovial joints that exhibit dual-mobility	False

16	In the case of the synovial joints:	

a.	Bony extremities are covered by the articular cartilage	True
b.	Bony extremities are bathed by the synovial fluid	True
c.	Synovial fluid gives a reduced friction to the compression and traction forces	True
d.	Synovial fluid gives an increased resistance to the compression and traction forces	True
e.	The entire joint is covered by an articular capsule lined by vessels and nerves	True
f.	Bony extremities are covered by mucus	False
g.	Bony extremities are bathed by the intracellular fluid	False
h.	Synovial fluid gives an increased friction to the compression and traction forces	False
i.	Synovial fluid gives a reduced resistance to the compression and traction forces	False
j.	The entire joint is covered by a nephrotic capsule	False

17	According to the number of joint parts, the joints can be:	
a.	Simple (interphalangeal)	True
b.	Compound (elbow joint)	True
c.	Complexe (patellar joint)	True
d.	Combinated	True
e.	Temporo-mandibular joint	True
f.	External	False
g.	Internal	False
h.	Convert	False
i.	Contort	False
j.	Axial	False

18	By their form and the degree of freedom, they are classified into	
a.	Uniaxial joints - flat or cylindrical	True
b.	Uniaxial joints can do flexion, extension, medial or lateral rotation - elbow joint	True
c.	Biaxial joints - ellipsoids and saddles	True
d.	Biaxial joints - 2-way movements (flexion and extension and laterality)	True
e.	Multiple joints - extension movements, flexion, rotation, laterality, adduction, abduction	True
f.	Simple (interphalangeal)	False
g.	Compound (elbow joint)	False
h.	Complexe (patellar joint)	False
i.	Combinated	False
j.	Colateral-axial	False

19	Functional role of joints in the body:	
a.	Postural	True
b.	Participating in maintaining the body position	True
c.	Kinetic	True
d.	Moving some segments in relation to others	True
e.	Locomotive, by moving the body as a whole into space	True
f.	Energetic	False
g.	Electric	False
h.	Magnetic	False
i.	Finetic	False
j.	Sintetic	False

20	The neuromuscular system:	

a.	About 600 skeletal muscles	True
b.	cover 40-50% of body weight	True
c.	Around each muscle fiber is connective tissue called endomisium	True
d.	Endomisium contains blood vessels and nerves	True
e.	Several muscle fibers have a common coating made of dense collagen fibers, called perimisium.	True
f.	About 50 skeletal muscles	False
g.	cover 90% of body weight	False
h.	Around each muscle fiber is epitelial tissue called extromisium	False
i.	Endomisium contains digestive tubules and nerves	False
j.	Several muscle fibers have a common coating made of dense collagen fibers, called endomisium	False

21	Tendons:	
a.	The connective tissue that organizes the fibers in the form of muscle as an organ is called epimisium.	True
b.	The three connective layers are in continuity and at the end of the muscle the tendons form.	True
c.	The tendons are made of flexible, but practically inextensible, connective tissue	True
d.	plays an intermediary role in transmitting muscle strength to the skeleton.	True
e.	The tendons are made of flexible, but practically inextensible connective tissue	True
f.	The connective tissue that organizes the fibers in the form of muscle as an organ is called liver	False
g.	The three connective layers are in continuity and at the end of the muscle form the skeleton	False
h.	The tendons are made of inflexible and inextensible, connective tissue	False
i.	plays an intermediary role in transmitting messages	False
j.	The tendons are made of extraflexible and extensible connective tissue	False

22	Muscle motor units	
a.	The strength and movement generated by a muscle depend on the individual activities of motor units	True
b.	For a fine movement a small number or even a single motor unit is used	True
c.	The increase of the contraction force is achieved by the entry into action of several motor units, simultaneously	True
d.	The gradation of muscle activity is determined by the synchronous activity of the motor units	True
e.	Several motor units increase of the number of efferent nerve impulses.	True
f.	The strength and movement generated by a muscle depend on the individual motor particles	False
g.	For a fine movement a small number or even a single neuron is used	False
h.	The increase of the contraction force is achieved by the entry into action of several glial cells simultaneously	False
i.	The gradation of muscle activity is determined by the synchronous activity of the brain units	False
j.	Several motor units increase of the number of muscles	False

23	Muscles and movement:	
a.	Making any movement involves the participation of several muscles	True
b.	Muscle can act as agonists, synergists and antagonists	True
c.	The muscle that produces action is called the agonist	True
d.	The muscle that opposes action is the antagonist.	True
e.	Synergistic muscles act in the same direction, but they cannot achieve the respective movement separately	True
f.	Making any movement involves the participation of several blood vessels	False
g.	Muscle can act as elonger, stronger and weaker	False

h.	The muscle that produces action is called the stronger	False
i.	The muscle that opposes action is the elonger	False
j.	Synergistic muscles act in the same direction with blood	False

24	Features of muscle contraction in the body:	
a.	Muscle contraction is the main internal force involved in the movement	True
b.	The neuro-muscular excitability - the contraction changes the initial length of the muscular structures	True
c.	the neuro-muscular permits the transmission of the motor message	True
d.	development of static or dynamic tensile forces	True
e.	the excitation-contraction couple	True
f.	Muscle contraction is the main external force involved in the movement	False
g.	The neuro-muscular excitability - the contraction changes the length of the nervous structures	False
h.	the neuro-muscular permits the transmission of the sensory message	False
i.	development of maximum tensile forces	False
j.	the sensory-contraction couple	False

25	Locomotion:	
a.	The center of gravity moves upward and downward twice during each cycle	True
b.	bobbing up and down of the head is observed during walking	True
c.	the body is lifted as each limb is extended during its stance phase	True
d.	There is also a slight side-to-side movement	True
e.	involves specific movements	True
f.	The center of gravity moves lateraly twice during each cycle	False
g.	bobbing up and down of the leg is the walking deffinition	False
h.	the body is lifted as each limb is elongated during its stance phase	False
i.	There is also a slight rotational movement	False
j.	involves patruped movements	False

26	The basic movements involved in walking are:	
a.	flexion at the hip, knee, and ankle joints and at the front part of the foot	True
b.	extension at the hip, knee, and ankle joints and at the front part of the foot	True
c.	abduction chiefly at the hip joint	True
d.	adduction at the hip joint	True
e.	rotation, mainly at the hip and knee joints.	True
f.	flexion of the front part of the body	False
g.	extension of the posterior part of the body	False
h.	abduction chiefly at the neck joint	False
i.	adduction at the carpal joint	False
j.	rotation, mainly at the thoracal joints.	False
27	Human posture and locomotion	
a.	Includes the ability of the locomotor apparatus to maintain the bipedal vertical station	True
b.	posture and balance function	True
c.	kinetic function - to move its various segments and the whole body	True
d.	performed by the participation of the musculoskeletal components	True
e.	Involves also the joints	True
f.	is very emotional	False
g.	is laboriously stoped	False

h.	becomes almost entirely vegetative	False
i.	disturbances of gait are important signs in many muscular activities	False
j.	a healthy gait pattern depends on an array of psychological features	False

28	Posture:	
a.	Standing involves a series of relatively immobile positions separated by brief intervals of movement	True
b.	The position of the line of gravity is determined by the distribution of body mass	True
c.	The line of gravity extends superiorly through the junctions of the curves of the vertebral column	True
d.	In the easy standing position, few muscles of the back and lower limbs are active	True
e.	In the easy standing position, the hip and knee joints are extended and are in stable positions	True
f.	Standing involves a series of relatively dynamic positions	False
g.	The position of the line of gravity is determined by the distribution of body fluids	False
h.	The line of gravity extends superiorly through the junctions of the curves of the head	False
i.	In the easy standing position, few muscles of the back and lower limbs are decuplated	False
j.	When a subject is in the easy standing position, the phalangeal joints are extended and are in external positions	False

29	Locomotion characteristics:	
a.	is very complicated	True
b.	is laboriously acquired	True
c.	becomes almost entirely automatic	True
d.	disturbances of gait are important signs in many disorders of the central nervous system	True
e.	a healthy gait pattern depends on an array of biomechanical features	True
f.	is a basic electrical activity	False
g.	is emotionally acquired	False
h.	becomes almost entirely somatic	False
i.	disturbances of gait are important signs in many activities	False
j.	a healthy gait pattern depends on an array of attraction features	False

30	Walking phases:	
a.	Lower limbs may be divided into "swing" and "stance" phases, separated by heel-strike.	True
b.	The swing phase occurs when the limb is off the ground, and the stance phase occurs when it is in contact	True
c.	A cycle of walking is the period from the heel-strike of one foot to the next heel-strike of the same foot	True
d.	At the time of heel-strike, the knee is slightly flexed on that side	True
e.	During the stance phase, the thigh abductors are active on the side of the leg that is in contact with the ground	True
f.	lower limbs may be divided into "swiming" and "elaborated" phases, which are separated by heel-strike.	False
g.	Swimming phase occurs when the limb is off the ground and the stance phase when it is in contact	False
h.	A cycle of walking is the period from the activation of one foot to the next	False
i.	At the time of heel-strike, the knee is slightly rotated on that side	False
j.	During the second phase, the thigh abductors are on the ground	False

Course 14: The Musculoskeletal System
Sub-topic: Structure, Function, and Energetics of Muscles and Bones

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1. Overview of the Musculoskeletal System

---

2. Bones
2.1. Types of Bones

---

3. Joints
3.1. Joint Types and Functions
3.2. Joint Structure

---

4. Muscles
4.1. Types of Muscles
- Skeletal Muscles: Voluntary muscles responsible for body movement, posture, and heat production.
- Smooth Muscles: Involuntary muscles found in the walls of internal organs, responsible for regulating their functions.
- Cardiac Muscle: Involuntary muscle found only in the heart, responsible for pumping blood.

4.2. Muscle Structure
- Muscle Fibers: Long, multinucleated cells that contain contractile proteins (actin and myosin).
- Connective Tissue Layers:
  - Endomysium: Surrounds individual muscle fibers.
  - Perimysium: Groups fibers into bundles (fascicles).
  - Epimysium: Encloses the entire muscle.

---

5. Muscle Contractions and Energetics
5.1. Properties of Muscle Tissue
5.2. Muscle Contraction Mechanism
- Excitation-Contraction Coupling
- Crossbridge Cycling

5.3. Muscle Energetics
- ATP Hydrolysis: Provides the energy for muscle contraction.
- Sources of ATP Production

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6. Movement and Muscular Control
6.1. Muscle Roles in Movement
- Agonist (Prime Mover): Muscle primarily responsible for a specific movement.
- Antagonist: Muscle that opposes the action of the agonist.
- Synergists: Muscles that assist the prime mover in performing its action.

6.2. Types of Muscle Contractions
- Isotonic Contraction: Muscle changes length to produce movement.
- Isometric Contraction: Muscle tension increases but length remains unchanged.

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8. Review and Case Studies
- Clinical discussions on diagnosing and managing musculoskeletal diseases such as arthritis and osteoporosis.

Examination and Assessment

Course 14: The Musculoskeletal System
Sub-topic: Structure, Function, and Energetics of Muscles and Bones

---

1. Overview of the Musculoskeletal System

The musculoskeletal system is a complex framework responsible for support, movement, protection, and mineral storage. It includes bones, muscles, joints, cartilage, tendons, and ligaments. Together, these elements provide structural support for the body, facilitate movement, and protect internal organs. Additionally, bones store essential minerals like calcium and phosphorus and are involved in hematopoiesis (blood cell formation).

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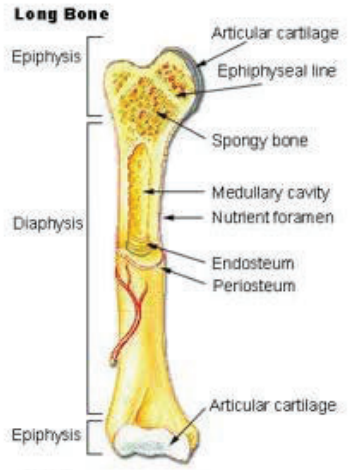
2. Bones

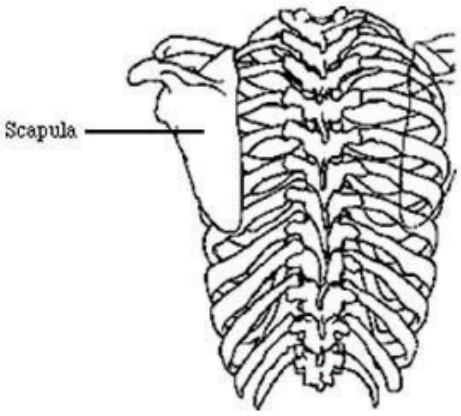
Bones serve multiple roles, including supporting the body, protecting organs, and providing a framework for muscle attachment. They are metabolically active and participate in mineral homeostasis and blood cell production.

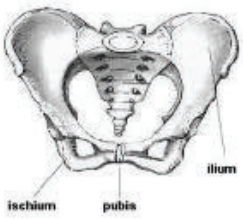
2.1. Types of Bones

1. Long Bones:
   Found in the arms and legs (e.g., femur, tibia, humerus). These bones act as levers, providing strength and facilitating movement.
2. Short Bones:
   Cube-shaped bones found in the wrists and ankles, facilitating shock absorption and transferring forces across joints.
3. Flat Bones:
   Flat structures that provide broad surfaces for muscle attachment (e.g., cranial bones, ribs). They offer protection to internal organs.
4. Irregular Bones:
   Bones with complex shapes, such as vertebrae and certain facial bones. They often serve specialized functions, such as supporting weight and protecting the spinal cord.
5. Sesamoid Bones:
   Small, rounded bones embedded within tendons (e.g., the patella). These bones reduce friction and modify pressure to enhance tendon movement.

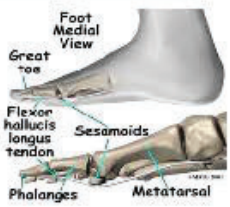














3. Joints

Joints are crucial for providing mobility and flexibility to the body, connecting bones and allowing different types of movement.

3.1. Joint Types and Functions

1. Fibrous Joints:
   Immovable joints connected by fibrous tissue (e.g., skull sutures).
2. Cartilaginous Joints:
   Semi-movable joints where bones are united by cartilage, providing flexibility and support (e.g., intervertebral discs).
3. Synovial Joints:
   Freely movable joints filled with synovial fluid. These joints are the most common and allow various movements such as flexion, extension, abduction, and rotation (e.g., knee, elbow).

3.2. Joint Structure

Joints consist of multiple components:

- Articular Cartilage: Covers the surfaces of bones within the joint, reducing friction and acting as a cushion during movement.
- Synovial Membrane: Lines the joint capsule and secretes synovial fluid, which lubricates the joint.
- Ligaments: Connect bones and stabilize the joint, preventing excessive movement.

---

4. Muscles

Muscles provide the force necessary for movement, posture maintenance, and heat production. Based on structure and function, they are classified into three types.

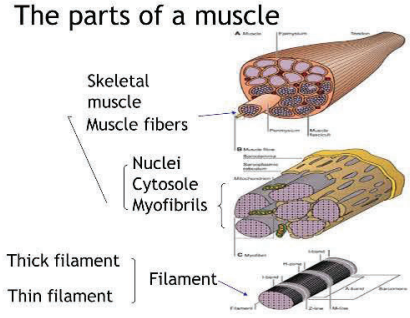
4.1. Types of Muscles

- Skeletal Muscles:
  Voluntary muscles are attached to bones via tendons. These muscles contract to facilitate body movement and maintain posture. They are striated and multinucleated, with contractions initiated by neural stimuli.
- Smooth Muscles:
  Involuntary muscles are found in hollow organs' walls (e.g., digestive tract, blood vessels). These muscles regulate internal processes like digestion and blood flow.
- Cardiac Muscle:
  Involuntary muscle is found exclusively in the heart. It is responsible for rhythmic contractions, pumping blood throughout the body. Cardiac muscle fibers are striated and connected by intercalated discs, which allow synchronized contraction.

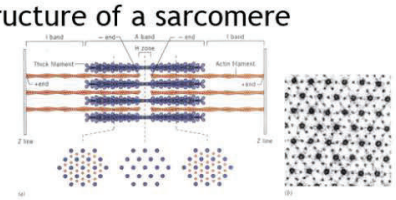
4.2. Muscle Structure

- Muscle Fibers:
  Muscle fibers are long, cylindrical cells containing multiple nuclei and contractile proteins (actin and myosin). These fibers are organized into myofibrils, which are responsible for muscle contraction.

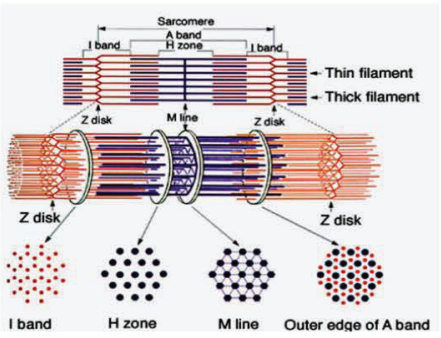
The parts of a muscle



Structure of a sarcomere



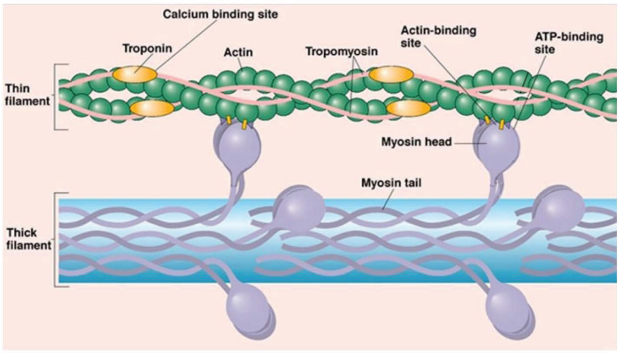
1. Actin and myosin filaments(A-band,)
2. Myosin filaments only (H-zone)
3. Actin filaments only (I-band)
4. M line
5. Z line



Molecular Structure of Myofilament

Myofilament
- Thick filament: Myosin
  - Head consists of 4 light, two heavy chain
  - Tail consist of two heavy chains
- Thin filament
  - Actin has binding sites of myosin
  - Tropomyosin
  - Trponin has affinities for actin, tropomyosin and Ca^{2+}

- Thick filament: Myosin (head and tail)
- Thin filament: Actin, Tropomyosin, Troponin (calcium binding site)



- Connective Tissue Layers:
  Layers of connective tissue surround each muscle fiber:
  - Endomysium: Surrounds individual muscle fibers.
  - Perimysium: Groups muscle fibers into bundles called fascicles.
  - Epimysium: Encloses the entire muscle, providing structure and support.

---

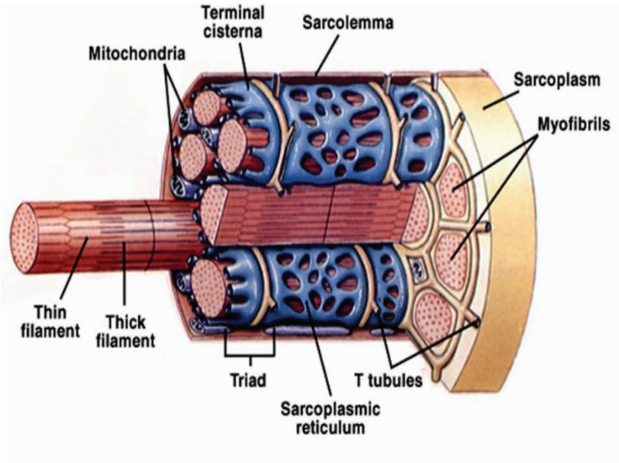
5. Muscle Contractions and Energetics

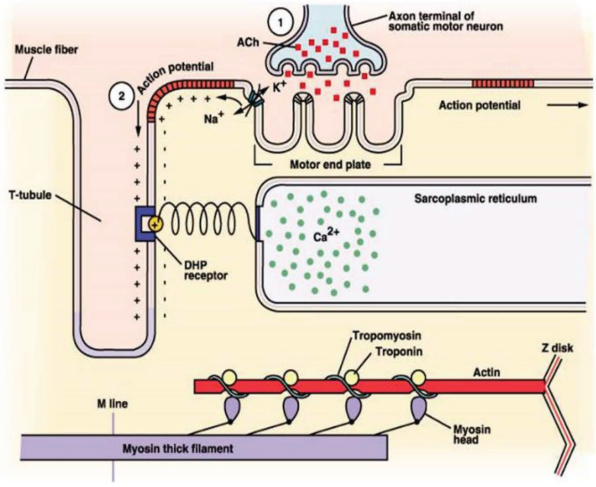
5.1. Properties of Muscle Tissue

- Excitability: The ability of muscle fibers to respond to neural stimuli by generating an action potential.
- Contractility: The ability to shorten and generate force.
- Extensibility: The ability to be stretched without damage.
- Elasticity: The ability to return to the original length after stretching.

5.2. Muscle Contraction Mechanism

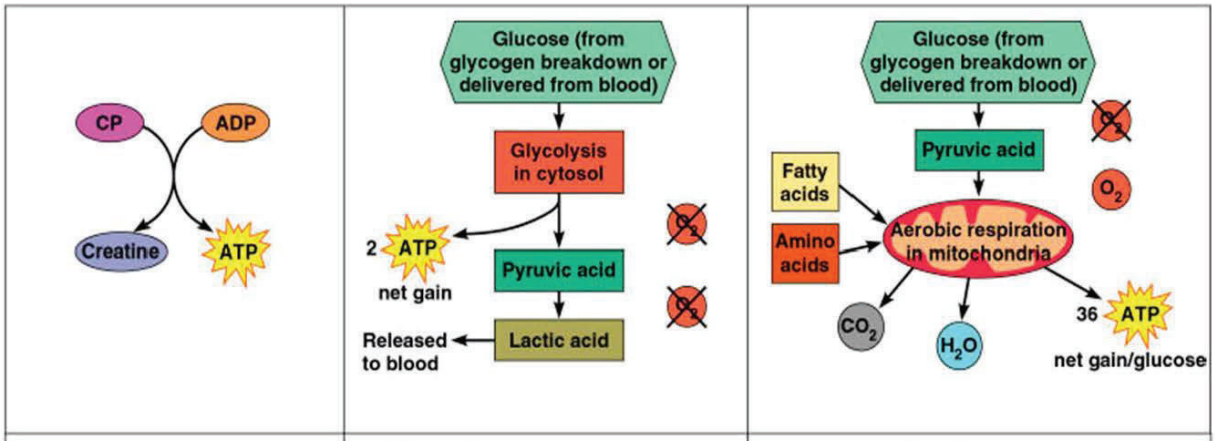
- Excitation-Contraction Coupling:
  Neural stimulation triggers the release of calcium ions from the sarcoplasmic reticulum, initiating muscle contraction. Calcium binds to troponin, causing a shift in tropomyosin and exposing active sites on actin filaments.
- Crossbridge Cycling:
  Myosin heads bind to actin, forming cross-bridges. ATP hydrolysis powers the myosin heads to pull the actin filaments, generating force. The cycle repeats as long as calcium and ATP are available.





5.3. Muscle Energetics

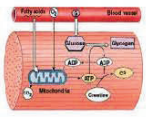
- ATP Hydrolysis:
  ATP is the primary energy source for muscle contraction. Breaking down ATP releases the energy the myosin heads need to perform the power stroke during cross-bridge cycling.
- Sources of ATP Production:
  1. Creatine Phosphate: A high-energy compound that rapidly regenerates ATP in the initial seconds of muscle activity.
  2. Aerobic Metabolism: Produces ATP through the oxidation of glucose and fatty acids in the presence of oxygen.
  3. Anaerobic Glycolysis: Generates ATP in the absence of oxygen, producing lactate during high-intensity exercise.



(a) Direct phosphorylation (coupled reaction of creatine phosphate [CP] and ADP)	(b) Anaerobic mechanism (glycolysis and lactic acid formation)	(c) Aerobic mechanism (aerobic cellular respiration)
Energy source: CP	Energy source: glucose	Energy source: glucose; pyruvic acid; free fatty acids from adipose tissue; amino acids from protein catabolism
Oxygen use: None Products: 1 ATP per CP, creatine Duration of energy provision: 15 sec.	Oxygen use: None Products: 2 ATP per glucose, lactic acid Duration of energy provision: 30–60 sec.	Oxygen use: Required Products: 36 ATP per glucose, CO_2, H_2O Duration of energy provision: Hours

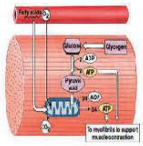
In a resting skeletal muscle

- The demand for ATP is low
- Resting muscle fibers absorb fatty acids and glucose that are delivered by the bloodstream
- The extra ATP is used to build up reserves of Creatine Phosphate (CP) and glycogen



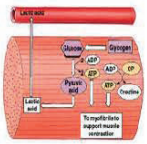
At moderate levels of activity

- the demand for ATP increases, of which demand is met by the mitochondria
- As the rate of mitochondrial ATP production rises, so does the rate of oxygen consumption.
- As all the ATP produced is needed by the muscle fiber, and no surplus is available, the skeletal muscle now relies primarily on the aerobic metabolism of pyruvic acid to generate ATP



At peak levels of activity

- the ATP demands are enormous and mitochondrial ATP production rises to a maximum
- At peak levels of exertion, mitochondrial activity can provide only about 1/3 of the ATP needed.
- The remainder is produced through glycolysis



Skeletal Muscle Innervation

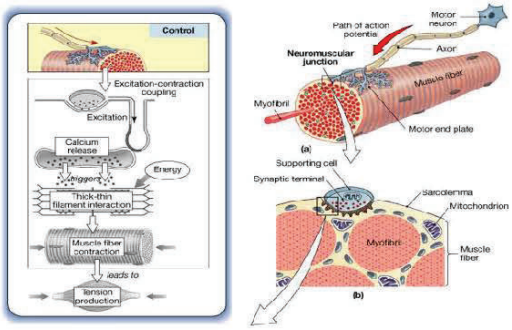
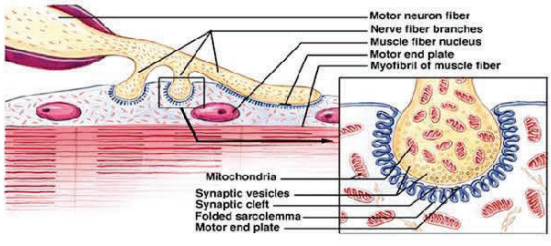
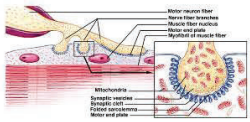


Illustration of the Neuromuscular Junction (NMJ)



New Ion Channel Players

- Voltage-gated Ca^{2+} channel
  - in presynaptic nerve terminal
  - mediates neurotransmitter release
- Nicotinic Acetylcholine Receptor Channel
  - in muscle neuromuscular junction (postsynaptic membrane, or end plate)
  - mediates electrical transmission from nerve to muscle

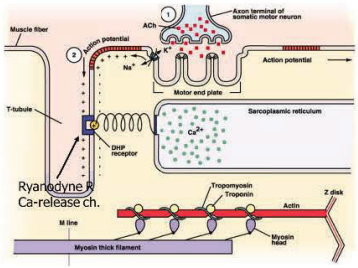


Nerve Terminal Ca^{2+} channels

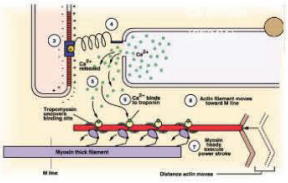
- Structurally similar to Na^+ channels
- Functionally similar to Na^+ channels except
  - activation occurs at more positive potentials
  - activation and inactivation much slower than Na^+ channels

Ca^{2+} release during Excitation-Contraction coupling

- Action potential on motor endplate travels down T tubules



- Voltage -gated Ca^{2+} channels open, Ca^{2+} flows out SR into cytoplasm
- Ca^{2+} channels close when action potential ends. Active transport pumps continually return Ca^{2+} to SR



Excitation-Contraction Coupling

- Depolarization of motor end plate (excitation) is coupled to muscular contraction
  - Nerve impulse travels along sarcolemma and down T-tubules to cause a release of Ca^{2+} from SR
  - Ca^{2+} binds to troponin and causes position change in tropomyosin, exposing active sites on actin
  - Permits strong binding state between actin and myosin and contraction occurs
  - ATP is hydrolyzed and energy goes to myosin head which releases from actin

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6. Movement and Muscular Control

6.1. Muscle Roles in Movement

- Agonist (Prime Mover):
  The primary muscle responsible for generating a specific movement (e.g., biceps in elbow flexion).
- Antagonist:
  The muscle that opposes the action of the agonist, helping to control and smooth out the movement (e.g., triceps in elbow flexion).
- Synergists:
  Muscles assist the agonist in performing a specific action, often stabilizing the movement (e.g., brachialis during elbow flexion).

6.2. Types of Muscle Contractions

- Isotonic Contraction:
  Muscle changes length during contraction to move. It can be concentric (muscle shortens) or eccentric (muscle lengthens under tension).
- Isometric Contraction:
  Muscle generates tension without changing length. This type of contraction is essential for maintaining posture and joint stability.

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7. Review and Case Studies

- Clinical Discussions:
  - Arthritis: A condition characterized by inflammation of joints, leading to pain and reduced mobility.
  - Osteoporosis: A bone disease that results in weakened bones and an increased risk of fractures due to decreased bone density. Treatments focus on increasing calcium intake, weight-bearing exercise, and medication to slow bone resorption.

Examination and Assessment

1	MUSCULOSKELETAL SYSTEM includes:	
a.	Bones	True
b.	Joints	True
c.	Ligaments	True
d.	Cartilage	True
e.	Muscles	True
f.	Glial Cells	False
g.	Neurons	False
h.	Nephrons	False
i.	Secretory cells	False
j.	Hepatocytes	False

2	MUSCULOSKELETAL SYSTEM functions:	
a.	Support	True
b.	Protection	True
c.	Movement	True
d.	Hematopoiesis	True
e.	Storage	True
f.	Absorption	False
g.	Digestion	False
h.	Excretion	False
i.	Secretion	False
j.	Circulation	False

3	Bones classification includes:	
a.	Long bones	True
b.	Short bones	True
c.	Flat bones	True
d.	Irregular bones	True
e.	Sesamoid bone	True
f.	Inverted bones	False
g.	Extra bones	False
h.	Inner bones	False
i.	External bones	False
j.	Mini bones	False

4	Structure of a sarcomere:	
a.	Actin and myosin filaments(A-band,)	True
b.	Myosin filaments only (H-zone)	True
c.	Actin filaments only (I-band)	True
d.	M line	True
e.	Z line	True
f.	T line	False
g.	V line	False
h.	Microfibers	False
i.	Excitative elements	False
j.	Calcium	False

5	The Muscles:	
a.	Determine a person's body shape	True
b.	Aiding in body movement	True
c.	Blood circulation	True
d.	Heat production	True
e.	Support	True
f.	Storage	False
g.	Absorbtion	False
h.	Digestion	False
i.	Excretion	False
j.	Secretion	False

6	Muscle Contractions:	
a.	Contractility - the ability to shorten and to become thicker	True
b.	Extensibility - the ability to stretch	True
c.	Elasticity - the ability to return to normal length after stretching	True
d.	Irritability - the ability to respond to stimulus, often a nerve impulse that originates in the spinal cord	True
e.	Do not respond without stimuli	True
f.	Determine a person's body shape	False
g.	Absorbtion	False
h.	Digestion	False
i.	Excretion	False
j.	Secretion	False

7	Power Source of muscle contraction	
a.	Glycogen	True
b.	A special form of stored glucose the body uses to fuel	True
c.	Fatty acids	True
d.	ATP	True
e.	Adenosine triphosphate	True
f.	Lipids	False
g.	Vitamins	False
h.	Calcium	False
i.	Potassium	False
j.	Proteins	False

8	The Crossbridge Cycle	
a.	Muscle is a chemomechanical transducer	True
b.	Ability to convert chemical energy	True
c.	Energy stored in the terminal phosphate group of ATP into mechanical work	True
d.	The myosin crossbridge, or myosin molecular motor, is the site for this energy conversion	True
e.	In addition to generating force and shortening, myosin is an enzyme that hydrolyzes ATP	True
f.	Muscle is a chemomagnetic ransducer	False
g.	Ability to convert magnetic energy	False
h.	Energy stored in the terminal phosphate group of ATP into thermic forces	False
i.	The myosin crossbridge, or myosin molecular motor, is the site for water conversion	False
j.	In addition to generating force and shortening, myosin is an ribosome that produces ATP	False

9	Biochemical Cycle for ATP Hydrolysis:	
a.	Hydrolysis occurs while myosin is detached	True
b.	Hydrolysis of ATP primes myosin for attachment.	True
c.	Once attached to actin, the products of ATP hydrolysis are released and myosin has a conformational change	True
d.	Conformational change believed to be the force generating step or powerstroke.	True
e.	Myosin detaches from actin upon binding of ATP to complete one cycle of the actomyosin ATPase.	True
f.	Hydrolysis occurs while myosin is hydrolised	False
g.	Hydrolysis of ATP primes myosin for agglutination	False
h.	Once attached to actin, the products of ATP hydrolysis are absorbed	False
i.	Conformational change is nephrotic powerstroke.	False
j.	Myosin detaches from actin upon producing ATP	False

10	In a resting skeletal muscle:	
a.	The demand for ATP is low	True
b.	Resting muscle fibers absorb fatty acids and glucose	True
c.	Fatty acids and glucose are delivered by the bloodstream	True
d.	The extra ATP is used to build up reserves of Creatine Phosphate	True
e.	The extra ATP is used to build up reserves of glycogen	True
f.	The demand for ATP is maximum	False
g.	Resting muscle fibers absorb insulin	False
h.	Fatty acids and glucose are delivered by the urinary duct	False
i.	The extra ATP is used to build up reserves of muscles	False
j.	The extra ATP is used to build up reserves of DNA	False

11	At moderate levels of activity of muscles:	
a.	The demand for ATP increases	True
b.	ATP demand is met by the mitochondria	True
c.	As the rate of mitochondrial ATP production rises, so does the rate of oxygen consumption.	True
d.	ATP produced is needed by the muscle fiber, and no surplus is available	True
e.	The skeletal muscle now relies primarily on the aerobic metabolism of pyruvic acid to generate ATP	True
f.	The demand for ATP decreases	False
g.	ATP demand is met by the ribosomes	False
h.	As the rate of mitochondrial ATP production rises, increases carbon dixide consumption	False
i.	ATP produced is needed by the bones	False
j.	The skeletal muscle now relies primarily on ADP	False

12	At peak levels of activity of muscles:	
a.	The ATP demands are enormous	True
b.	Mitochondrial ATP production rises to a maximum	True
c.	At peak levels of exertion, mitochondrial activity is at maximum level	True
d.	At peak levels of exertion, mitochondrial activity can provide only about 1/3 of the ATP needed.	True
e.	The remainder energy is produced through glycolysis	True
f.	The demand for ATP is low	False

g.	Resting muscle fibers absorb fatty acids and glucose	False
h.	Fatty acids and glucose are delivered by the bloodstream	False
i.	The extra ATP is used to build up reserves of Creatine Phosphate	False
j.	The extra ATP is used to build up reserves of glycogen	False

13	Ion Channel Players in muscular activity:	
a.	Voltage-gated Ca2+ channel and Nicotinic Acetylcholine Receptor Channel	True
b.	Voltage-gated Ca2+ channel in presynaptic nerve terminal	True
c.	Voltage-gated Ca2+ channel mediates neurotransmitter release	True
d.	Nicotinic Acetylcholine Receptor Channel in muscle neuromuscular junction (postsynaptic membrane)	True
e.	Nicotinic Acetylcholine Receptor Channel mediates electrical transmission from nerve to muscle	True
f.	Voltage-gated Na+ channel and Dopaminic Receptor Channel	False
g.	Voltage-gated K+ channel in presynaptic nerve terminal	False
h.	Voltage-gated Ca2+ channel mediates neurotransmitter degradation	False
i.	Dopaminic Receptor Channel in muscle neuromuscular junction (postsynaptic membrane)	False
j.	Dopaminic Receptor Channel mediates electrical transmission from nerve to muscle	False

14	Nerve Terminal Ca2+ channels	
a.	Structurally similar to Na+ channels	True
b.	Functionally similar to Na+ channels with exceptions	True
c.	Functionally similar to Na+ channels except activation occurs at more positive potentials	True
d.	Functionally similar to Na+ channels except activation and inactivation are much slower than Na+ channels	True
e.	Structurally and functionally similar to Na+ channels	True
f.	Structurally similar to Cl- channels	False
g.	Functionally similar to Zn2+ channels	False
h.	Functionally similar to electrical channels except activation occurs at more positive potentials	False
i.	Functionally similar to magnetic channels	False
j.	Structurally and functionally similar to electronic channels	False

15	Thin filaments:	
a.	Backbone: two strands of polymerized globular actin – fibrous actin	True
b.	Each actin has myosin binding site	True
c.	Thin filament: Actin, Tropomyosin, Troponin	True
d.	Have calcium binding sites	True
e.	Thin filaments are a polymer of actin with tightly bound regulatory proteins troponin and tropomyosin	True
f.	Backbone: two strands of polymerized fibrous myosin	False
g.	Each actin has myosin structures	False
h.	Thin filament includes myosin, tropomyosin, actinin	False
i.	Have sodium binding sites	False
j.	Thin filaments are a polymer of myosin with tightly bound regulatory proteins	False

16	Troponin:	
a.	Binds Ca2+	True
b.	Regulates muscle contraction	True

c.	Thin filament: Actin, Tropomyosin, Troponin (calcium binding site)	True
d.	Troponin plays a central role in the calcium-regulation of muscle contraction	True
e.	Upon binding calcium, troponin moves tropomyosin away from the myosin-binding sites on actin	True
f.	Binds Na+	False
g.	Regulates muscle relaxation	False
h.	Thin filament includes myosin, tropomyosin, actinin	False
i.	Troponin plays a central role in the calcium metabolism	False
j.	Upon binding calcium, troponin moves tropomyosin away from cells	False

17	Tropomyosin:	
a.	Lies in groove of actin helix	True
b.	Blocks myosin binding	True
c.	Thin filament: Actin, Tropomyosin, Troponin (calcium binding site)	True
d.	In the absence of Ca2+ is bound in a position along the actin filament that blocks its interaction with myosin.	True
e.	Tropomyosin acts to block the myosin binding sites on actin	True
f.	Binds Na+	False
g.	Regulates muscle relaxation	False
h.	Thin filament includes myosin, tropomyosin, actinin	False
i.	plays a central role in the calcium metabolism	False
j.	Upon binding calcium, tropomyosin is excreted from cells	False

18	Thick filament:	
a.	Myosin (head and tail)	True
b.	The thick filament consists largely of myosin	True
c.	Myosin is an asymmetric protein composed of two globular heads attached to a long tail	True
d.	Thick filaments in muscle produce tension via their myosin motors	True
e.	Myosin is the major component of the thick filaments	True
f.	Myosin is a globular amino acid	False
g.	The thick filament consists largely of actin	False
h.	Six carbohydrates make up myosin	False
i.	Thick filaments in muscle produce extension	False
j.	Actin is the major component of the thick filaments	False

19	Nerve Activation of Individual Muscle Cells:	
a.	Muscle cells innervated by motor neurons that arise from spinal cord	True
b.	Activation of motor neuron triggers contraction of muscle cell	True
c.	The axon of motor neurons form synapse on the surface of skeletal muscle cells at the neuromuscular junction	True
d.	The neuromuscular junction is composed of a pre-synaptic axon terminus and a post-synaptic muscle cell	True
e.	Acetylcholine binds to receptors on the post-synaptic membrane	True
f.	Muscle cells are innervated only by sensory neurons that arise from spinal cord	False
g.	Activation of motor neuron triggers relaxation of muscle cell	False
h.	The axon of motor neurons form plexus at surface of skeletal muscle junction	False
i.	The neuromuscular junction is composed of a plurisynaptic axon terminals	False
j.	Acetylcholine binds to external ligands	False

20	Ca2+ release during Excitation-Contraction coupling	
a.	Action potential on motor endplate travels down T tubules	True
b.	Voltage -gated Ca2+ channels open, Ca2+ flows out SR into cytoplasm	True
c.	Ca2+ channels close when action potential ends. Active transport pumps continually return Ca2+ to SR	True
d.	The action potential triggers the sarcoplasmic reticulum to release of Ca2+, which activate troponin	True
e.	Calcium ions (Ca2+) link action potentials in a muscle fiber to contraction	True
f.	Action potential on motor endplate travels down excretory tubules	False
g.	Voltage -gated Ca2+ channels close, Ca2+ flows out cytoplasm in the nucleus	False
h.	Ca2+ channels close when action potential arrive	False
i.	The action potential triggers the sarcoplasmic reticulum to collect Ca2+	False
j.	Calcium ions (Ca2+) link action potentials in a muscle fiber to bone mineralization	False

21	Excitation-Contraction Coupling	
a.	Depolarization of motor end plate (excitation) is coupled to muscular contraction	True
b.	Nerve impulse travels along sarcolemma and down T-tubules to cause a release of Ca2+ from SR	True
c.	Ca2+ binds to troponin and causes position change in tropomyosin, exposing active sites on actin	True
d.	Permits strong binding state between actin and myosin and contraction occurs	True
e.	ATP is hydrolyzed and energy goes to myosin head which releases from actin	True
f.	Depolarization of motor end plate (excitation) is coupled to muscular digestion	False
g.	Nerve impulse travels along sarcolemma and down T-tubules to cause a Ca2+ depletion	False
h.	Ca2+ binds to myosin and causes change in tropomyosin	False
i.	Permits strong binding state between actin and troponin	False
j.	ATP is hydrolyzed and energy goes to action potential of muscles	False

22	Excitation-Contraction Coupling Key Points	
a.	neuromuscular junction	True
b.	motor-end plate	True
c.	neurotransmitter acetylcholine diffuses across the synaptic cleft	True
d.	depolarization of the sarcolemma	True
e.	sarcoplasmic reticulum to release Ca2+, which causes the muscle to contract	True
f.	Sodium channels	False
g.	Motor activities	False
h.	Dopamine diffuses across the synaptic cleft	False
i.	repolarization of the sarcolemma	False
j.	sarcoplasmic reticulum release Ca2+, which causes the muscle to relax	False

23	Excitation-Contraction Coupling Key terms	
a.	motor-end plate	True
b.	acetylcholine receptors exposed to the synaptic cleft	True
c.	sarcolemma	True
d.	converting an electrical stimulus to a mechanical response	True
e.	excitation–contraction coupling	True
f.	Sodium channels	False

g.	Motor activities	False
h.	Dopamine diffuses across the synaptic cleft	False
i.	repolarization of the sarcolemma	False
j.	sarcoplasmic reticulum release Ca2+, which causes the muscle to relax	False

24	Muscle Contraction	
a.	Muscle is a highly specialized soft tissue that creates tension, which leads to strength generation	True
b.	Muscle cells, or myocytes, contain myofibrils, which are made up of actin and myosin myofilaments	True
c.	Excitation-contraction coupling is the process of converting an electrical stimulus into a mechanical reaction	True
d.	muscle contraction is a result of an action potential	True
e.	when a muscle is at rest, actin and myosin are separated	True
f.	Muscle is a highly specialized soft tissue that creates body problems	False
g.	Muscle cells, or myocytes, contain myofibrils, which are made up of troponin and fibromiozin myofilaments	False
h.	Excitation-contraction coupling is the process of converting a magnetic stimulus into impulses	False
i.	muscle contraction is a result of a genetically transmitted code	False
j.	when a muscle is at rest, actin and myosin are closely coupled in a syncitium	False

25	MUSCULOSKELETAL SYSTEM includes:	
a.	Muscles	True
b.	Joints	True
c.	Ligaments	True
d.	Cartilage	True
e.	Bones	True
f.	Digestive muscles	False
g.	Gastrointestinal plexus	False
h.	Neuroendocrine axis	False
i.	Ion channels	False
j.	Fluids	False

26	MUSCULOSKELETAL SYSTEM functions:	
a.	Movement	True
b.	Protection	True
c.	Support	True
d.	Hematopoiesis	True
e.	Storage	True
f.	Relaxation	False
g.	Emotion	False
h.	Immunity	False
i.	Activation	False
j.	Sensitivity	False

27	Structure of a sarcomere:	
a.	Actin and myosin filaments	True
b.	Thick filaments	True

c.	Thin filaments	True
d.	M line	True
e.	Z line	True
f.	N line	False
g.	P line	False
h.	Microfibers	False
i.	Excitative elements	False
j.	Sodium	False

28	Myosin filaments	
a.	Myosin molecules have helical tails and globular head groups that hydrolyze ATP - act as motors	True
b.	Energy of ATP hydrolysis is invested in bending the myosin molecule around a pivot point	True
c.	Molecular motor converts chemical into mechanical energy	True
d.	Smooth muscle uses actin and myosin filaments for contraction	True
e.	Myosin is the prototype of a molecular motor— converts chemical energy to mechanical energy	True
f.	All myosin molecules have helical tails and globular head groups that hydrolyze glucose	False
g.	Energy of ATP hydrolysis is invested in bending the myosin molecule around a fibroblast	False
h.	Molecular motor converts electrical energy into thermal energy	False
i.	Smooth muscle uses actin and myosin filaments for balance	False
j.	Myosin is the prototype of a molecular radiator—a protein that converts thermal energy to electrical energy	False

29	Actin filaments:	
a.	Actin filaments are linear polymers of globular actin subunits and occur as thin filaments	True
b.	Actin filaments, usually in association with myosin, are responsible for movements	True
c.	Actin participates in many important cellular processes, including muscle contraction	True
d.	Actin plays a role in muscle cells, which consist of repeated bundles of actin and myosin	True
e.	To move along the actin thread, myosin must hydrolyze ATP	True
f.	Actin filaments are linear polymers of globular actin subunits and occur as thick filaments	False
g.	Actin filaments, usually in association with myosin, are responsible for cell division	False
h.	Actin participates in many important cellular processes, including neuroendocrin secretion	False
i.	Actin plays a particularly role in muscle cells by accumulating oxygen	False
j.	To move along the actin thread, myosin must hydrolyze glucose	False

30	Myosin motors	
a.	Myosin II contains: a head domain - the motor domain, that binds to actin; a neck domain; and a tail domain	True
b.	Like actin, myosin II proteins also form filaments	True
c.	when activated, the motor domains grab actin filaments and pull against them in a 'powerstroke'	True
d.	actin is a multi-functional protein found in almost all eukaryotic cells	True
e.	actin filaments are involved in the contraction of muscles together with myosin	True
f.	Myosin II contains: a head domain, a neck domain; and a tail domain - the motor domain	False
g.	Like actin, myosin II proteins also form vesicles	False
h.	when activated, the motor domains grab cell membranes and pull against them in a 'powerstroke'	False
i.	actin is a multi-functional protein found in almost all microorganisms	False
j.	only actin filaments are involved in the contraction of muscles	False

Physiopatology Exam Questions

I-1	The causes of cellular changes can be:	
A	Low oxygen intake	True
B	Respiratory diseases	True
C	Cardiovascular diseases	True
D	Anemias	True
E	Radiations	True
F	Normal oxygen intake	False
G	Normal cardiovascular system	False
H	Normal respiratory system	False
I	Normal blood values	False
J	Light	False

I-2	The causes of cellular changes can be toxins generated by:	
A	Bacteria	True
B	Plants	True
C	Animals	True
D	Snakes	True
E	Spiders	True
F	Air	False
G	Water	False
H	Light	False
I	Heat	False
J	Moisture	False

I-3	The cellular changes are:	
A	Necrosis	True
B	Gangrene	True
C	Clear intumescence	True
D	Steatosis	True
E	Atrophy	True
F	Thrombosis	False
G	Embolism	False
H	Myocardial infarction	False
I	Phagocytosis	False
J	Healing	False

I-4	The cellular changes are:	
A	Fatty degeneration	True
B	Amyloid degeneration	True
C	Calcifications	True
D	Atrophy	True
E	Necrosis	True
F	Healing	False
G	Embolism	False
H	Thrombosis	False
I	Myocardial infarction	False

J	Phagocytosis	False

I-5	Necrosis:	
F	It represents the death of some cells	True
G	It is found only in a living organism	True
H	It is a cellular change	True
I	It can be liquefied	True
J	It can be coagulation	True
F	It represents the shrinking of some cells	False
G	It represents the shrinking of some organs	False
H	It is a chronic inflammation	False
I	It is related to phagocytosis	False
J	It is not related to gangrene	False

I-6	As a result of cell death:	
A	Enzymes from the cells are released into the blood	True
B	It increases the amount of enzymes in the blood	True
C	The increase in the amount of enzymes in the blood is a diagnostic test	True
D	The nucleus shrinks	True
E	The nucleus disappears	True
F	Enzymes remain in the cells	False
G	Enzymes from the cells are not released into the blood	False
H	The nucleus enlarges	False
I	Two nuclei appear	False
J	The color of the cell does not change on microscopic examination	False

I-7	Coagulation necrosis:	
A	Occurs in case of myocardial infarction	True
B	Occurs in case of splenic infarction	True
C	Occurs in case of renal infarction	True
D	It causes a swollen area	True
E	Determines a hard zone	True
F	It occurs mostly in the brain	False
G	Determines a soft zone	False
H	It causes a collection of fluid	False
I	It is the rarest type of necrosis	False
J	It frequently occurs in organs that contain a large amount of fluids	False

I-8	In the area of necrosis:	
A	Cells maintain their shape	True
B	The cytoplasm becomes opaque	True
C	The nucleus shrinks	True
D	The nucleus is fragmented	True
E	The nucleus disappears	True
F	Cells lose their shape	False
G	The cytoplasm becomes more transparent	False
H	The cytoplasm becomes paler	False
I	The nucleus enlarges	False

J	The nucleus doubles	False

I-9	Gangrene:	
A	It is a complication of necrosis	True
B	It represents the invasion of necrotic tissue by microbes	True
C	It causes necrotic tissues to be colored black	True
D	Microbes invading necrotic tissue will cause gas production	True
E	It determines the green coloring of necrotic tissues	True
F	It causes necrotic tissues to turn white	False
G	It causes necrotic tissues to turn yellow	False
H	It causes necrotic tissues to stain red	False
I	It is the cause of necrosis	False
J	It is not related to necrosis	False

I-10	Caseification necrosis:	
A	It is specific to chronic tuberculosis	True
B	The necrotic tissue has a cheesy appearance	True
C	The necrotic tissue is yellowish-white in color	True
D	The necrotic tissue has a fine granular appearance	True
E	The necrotic tissue has an amorphous appearance	True
F	It is specific to myocardial infarction	False
G	It is specific to renal infarction	False
H	It is specific to splenic infarction	False
I	Necrotic tissue is black	False
J	It is specific to the brain	False

I-11	Necrotic tissue:	
A	It is rarely cured	True
B	It only heals if the blood vessels remain intact	True
C	It is replaced by fibrous tissue	True
D	It is replaced by scars	True
E	Contains compensatory enlarged cells	True
F	It always heals	False
G	It heals even if the blood vessels are not intact	False
H	Contains normal cells	False
I	It has normal color	False
J	It contains many blood vessels	False

I-12	Gangrene occurs:	
A	In the fingers of the lower limbs (toes)	True
B	In people with diabetes	True
C	Due to very low temperatures	True
D	After climbing the mountain in winter	True
E	As a consequence of arterial occlusion	True
F	As a consequence of venous occlusion	False
G	In young people	False
H	Due to normal or slightly elevated temperatures	False

I	After easy walking	False
J	On the shoulders or hips	False

I-13	Clear intumescence:	
A	It is the mildest form of cell destruction	True
B	It is reversible	True
C	It can be seen in the kidney	True
D	The cells look like boiled meat	True
E	The cells hypertrophy	True
F	The cells atrophy	False
G	The cells stain intensely	False
H	It is irreversible	False
I	It is the most severe form of cell destruction	False
J	It is seen in the toes	False

I-14	Steatosis is the accumulation of fat:	
A	In the liver	True
B	In the kidneys	True
C	In the myocardium	True
D	In skeletal muscle	True
E	In tissues with very active metabolism	True
F	In tissues with slow metabolism	False
G	In the subcutaneous tissue	False
H	In the skin	False
I	In the fingers of the lower limbs (toes)	False
J	In the fingers of the upper limbs	False

I-15	Causes of hepatic steatosis:	
A	Lack of oxygen intake	True
B	Toxins	True
C	Alcoholism	True
D	Organic solvents	True
E	Infections	True
F	Increased oxygen intake	False
G	Excessive light	False
H	Increased temperature	False
I	Low temperature	False
J	Gangrene	False

I-16	Atrophy represents:	
A	Reduction in the number of cells	True
B	Reduction of cell size	True
C	Shrinking tissue	True
D	Shrinkage of the organ	True
E	It is most common in the elderly	True
F	Increase in the number of cells	False
G	Increase in cell size	False
H	Increase in tissue volume	False

I	Increasing the volume of the organ	False
J	It is frequently found in young people	False

I-17	The causes of atrophy are:	
A	Reduction of blood supply	True
B	Reduction of oxygen intake	True
C	Reducing nutrient intake	True
D	Narrowing of the arteries	True
E	Reduction in usage	True
F	Increased blood supply	False
G	Increasing oxygen intake	False
H	Increasing nutrient intake	False
I	Narrowing of veins	False
J	Intense physical effort	False

I-18	Atrophy can be caused by:	
A	Nerve sectioning	True
B	injury	True
C	Poliomyelitis	True
D	Endocrine disorders	True
E	Compression on the arteries	True
F	Compression on the veins	False
G	Vein sectioning	False
H	Increasing muscle volume	False
I	Increase in the diameter of the arteries	False
J	Increase in the diameter of the veins	False

I-19	Amyloid degeneration	
A	It is also called amyloidosis	True
B	It represents the deposition of a waxy substance	True
C	It represents the deposition of a substance around the blood vessels	True
D	It represents the deposition of a substance around the basement membranes	True
E	It represents the deposition of a substance around the connective fibers	True
F	It is also called atrophy	False
G	It represents the thinning of the connective fibers	False
H	It represents the thinning of blood vessels	False
I	It represents thinning of the basement membranes	False
J	It is also called caseification necrosis	False

I-20	Amyloidosis can be caused by:	
A	An unknown cause	True
B	Chronic infections	True
C	Tuberculosis	True
D	Syphilis	True
E	Hodgkin's disease	True
F	Atrophy	False
G	Hypertrophy	False
H	Increased caloric intake	False

I	Intense light	False
J	Low temperature	False

I-21	Amyloidosis causes:	
A	Renal insufficiency	True
B	Oliguria	True
C	Decreased permeability of vessels	True
D	Decreased absorption of nutrients from the intestines	True
E	Diarrhea	True
F	Obesity	False
G	fatty	False
H	Increase in the size of the heart	False
I	Increased blood supply to the heart muscle	False
J	Increased absorption of nutrients from the intestines	False

I-22	Calcifications can occur:	
A	In old tuberculous lesions	True
B	In old infarct areas	True
C	In old thrombi	True
D	In dead parasites	True
E	In old pus collections	True
F	In recent pus collections	False
G	In areas of recent infarction	False
H	In recent thrombi	False
I	In live parasites	False
J	In recent tuberculous lesions	False

I-23	Calcifications can occur due to excess calcium in the blood through:	
A	Excessive vitamin D administration	True
B	Bone destruction	True
C	Osteoporosis by immobilization in bed	True
D	Excess parathyroid hormone	True
E	Chronic kidney disease	True
F	Insufficient intake of vitamin D	False
G	Bone growth	False
H	Increased physical exertion	False
I	Adrenaline overload	False
J	Sleep	False

I-24	Excess calcium is deposited:	
A	In the arteries	True
B	In the walls of the left ventricle	True
C	In the kidneys	True
D	In the liver	True
E	In the walls of the stomach	True
F	In the veins	False
G	In the walls of the right atrium	False
H	In the brain	False

I	In the lung	False
J	In the muscles	False

I-25	Calcifications are deposited:	
A	Especially in the tissues of the elderly	True
B	In atheroma plaques	True
C	In fibrous tissue	True
D	In the cartilage	True
E	In tissues undergoing progressive degeneration	True
F	Especially in the tissues of young people	False
G	In thin dishes	False
H	In nervous tissue	False
I	In the spleen	False
J	In the skin	False

I-26	Inflammation:	
A	It represents the process by which living organisms respond to the action of a pathogenic agent	True
B	It is triggered by microbes	True
C	It is triggered by viruses	True
D	It is triggered by toxins	True
E	It is triggered by parasites	True
F	It is triggered by light	False
G	It is triggered by air	False
H	It is triggered by water	False
I	It is triggered by sleep	False
J	It is triggered by rest	False

I-27	Inflammation occurs in response to:	
A	Chemical agents: strong acids	True
B	Chemical agents: strong bases	True
C	Chemical agents: organic solvents	True
D	Immunological agents: antigen-antibody complexes	True
E	Immunological agents: cell-mediated reactions	True
F	The light	False
G	Rest	False
H	Relaxation	False
I	Sleep	False
J	Walking	False

I-28	Inflammation occurs in response to physical agents:	
A	Injuries	True
B	Falling	True
C	Excess heat	True
D	Excessive cold	True
E	The radiations	True
F	Easy ride	False
G	Walking	False

H	Rest	False
I	Relaxation	False
J	Sleep	False

I-29	Inflammation proceeds:	
A	In the connective tissue	True
B	Around arterial type blood vessels	True
C	Around capillary blood vessels	True
D	Around arteriole-type blood vessels	True
E	Around specialized cells of various organs	True
F	Inside specialized cells in the myocardium	False
G	Inside specialized cells in the liver	False
H	Inside specialized cells in the pancreas	False
I	Inside specialized cells in the brain	False
J	Inside specialized cells in the kidney	False

I-30	Acute inflammation has the following signs:	
A	Redness	True
B	Increase in volume	True
C	Pain	True
D	Heat	True
E	Loss of function	True
F	Blushing	False
G	Relaxation	False
H	Well being	False
I	Walking	False
J	Calcifications	False

I-31	Acute inflammation also has the following signs:	
A	Rubor	True
B	Tumor	True
C	Dolor	True
D	Calor	True
E	Functio laesa	True
F	Blushing	False
G	Relaxation	False
H	Well being	False
I	Walking	False
J	Calcifications	False

I-32	Hyperemia occurs:	
A	By dilating the blood capillaries	True
B	By dilating blood arterioles	True
C	When we press a hard object on the skin	True
D	Through a direct effect on blood vessels, it causes vasodilatation	True
E	Through an indirect effect on the nerves, it causes vasodilatation	True
F	Through sleep	False

G	By light movement	False
H	Through proper nutrition	False
I	Through proper hydration	False
J	By relaxing	False
I-33	Hyperemia occurs:	
A	By vasodilatation generated by pressing a hard object on the skin	True
B	By destroying cells, which produces vasodilatation	True
C	By releasing chemical mediators, which produce vasodilatation	True
D	By vasodilatation, generated by direct effect on blood vessels	True
E	Through vasodilatation, generated by an indirect effect on the nerves	True
F	During sleep	False
G	During easy walk	False
H	In stand by	False
I	During relaxation	False
J	Only during the daytime	False

I-34	Hyperemia:	
A	It explains the local redness	True
B	It explains the "rubor" sign	True
C	It explains the increase in local temperature	True
D	It explains the "calor" sign	True
E	Occurs in acute inflammation	True
F	Appears only during sleep	False
G	Appears only during relaxation	False
H	Appears only during daytime	False
I	Appears only during nighttime	False
J	Appears only during morning	False
I-35	Exudation:	
A	It represents the passage of an increased amount of protein-rich fluid from the blood through the vascular wall into the interstitial tissue	True
B	It causes an increase in the amount of fluid in the tissues	True
C	It causes the dilution of toxins	True
D	It causes an increase in the amount of local antibodies	True
E	It causes an increase in the amount of local fibrin	True
F	Appears only during sleep	False
G	Appears only during relaxation	False
H	Appears only during daytime	False
I	Appears only during nighttime	False
J	Appears only during morning	False

I-36	Exudation:	
A	Increases the amount of protein in the tissues	True
B	Increases the amount of globulins in the tissues	True
C	Increases the amount of fibrin in the tissues	True
D	Increases the amount of antibodies in the tissues	True
E	Causes the local volume to increase	True
F	Appears only during morning	False

G	Appears only during evening	False
H	Appears only during sleeping	False
I	Appears only during daytime	False
J	Appears only during intense physical activity	False
I-37	Through exudation there pass from the blood vessels into the surrounding interstitial tissue:	
A	Antibodies	True
B	Proteins	True
C	Albumin	True
D	Globulins	True
E	Fibrinogen	True
F	Vitamins	False
G	Carbohydrates	False
H	Lipids	False
I	Red blood cells	False
J	Platelets	False

I-38	In acute inflammation, through the vascular wall there pass:	
A	Neutrophils	True
B	Eosinophils	True
C	Basophils	True
D	Lymphocytes	True
E	Monocytes	True
F	Vitamins	False
G	Carbohydrates	False
H	Lipids	False
I	Red blood cells	False
J	Platelets	False
I-39	The migration of leukocytes through the vascular wall is produced by:	
A	Exudation of fluid from the blood into the tissues	True
B	Increased blood viscosity	True
C	Reducing the speed of blood flow through the vessels	True
D	The deposition of leukocytes on the wall of blood vessels	True
E	The gradual passage of leukocytes through the spaces between the cells of the blood vessel	True
F	Steatosis	False
G	Necrosis	False
H	Calcifications	False
I	Gangrene	False
J	Clear intumescence	False

I-40	After passing through the vascular wall, during leukocyte migration, the movement of leukocytes is determined by:	
A	Chemotaxis	True
B	Increased concentrations of proteins in destroyed bacteria	True
C	Increased concentrations of proteins in destroyed leukocytes	True
D	Increased concentrations of toxins from bacteria	True

E	Increased concentrations of toxins from destroyed leukocytes	True
F	Sleep	False
G	Relaxation	False
H	Easy walks	False
I	Rest	False
J	The right diet	False
I-41	Phagocytosis is a mechanism:	
A	Of defense, very important, especially in bacterial infections	True
B	By which polymorphonuclear cells engulf cellular debris	True
C	Through which macrophages engulf cellular debris	True
D	Through which polymorphonuclear cells swallow particles foreign to the body	True
E	Through which macrophages swallow particles foreign to the body	True
F	To sleep	False
G	To recover	False
H	To make steady efforts	False
I	To increase brain capacity	False
J	To walk	False

I-42	Polymorphonuclears:	
A	They have a life cycle of 1-3 days	True
B	They phagocytose bacteria	True
C	They can destroy phagocytosed bacteria	True
D	They can be destroyed by phagocytosed bacteria (tuberculosis)	True
E	They can digest phagocytosed bacteria	True
F	Transport O2 to tissues	False
G	Transport CO2 to tissues	False
H	Transport O2 from the tissues to the lungs	False
I	Transport CO2 from the tissues to the lungs	False
J	Transport O2 and CO2 from the tissues to the lungs	False

I-43	Macrophages:	
A	They have a life cycle of months or even years	True
B	They phagocytize bacteria	True
C	They can destroy phagocytosed bacteria	True
D	They can be destroyed by phagocytosed bacteria (tuberculosis)	True
E	They can digest phagocytosed bacteria	True
F	Transport O2 to tissues	False
G	Transport CO2 to tissues	False
H	Transport O2 from the tissues to the lungs	False
I	Transport CO2 from the tissues to the lungs	False
J	Transport O2 and CO2 from the tissues to the lungs	False

I-44	Acute inflammation can progress to:	
A	Resolution	True
B	Suppuration	True
C	Reparation	True
D	Organization	True
E	Chronic inflammation	True

F	Relaxation	False
G	Sleep	False
H	Easy ride	False
I	Proper nutrition	False
J	Adequate hydration	False

I-45	Resolution:	
A	It means returning to normal after acute inflammation	True
B	It occurs when there are few dead cells	True
C	It occurs when there is minimal tissue damage	True
D	Occurs when rapid elimination of the pathogen (bacteria) occurs	True
E	It occurs when local conditions favor the rapid elimination of cellular debris	True
F	It means the patient's determination	False
G	Appears only after maximum effort	False
H	It occurs only in the elderly	False
I	It occurs only in winter	False
J	It occurs only in spring	False

I-46	Resolution in a lobar pneumonia includes:	
A	Destruction of bacteria by PMN	True
B	Fibrin fragmentation by enzymes in PMN lysosomes	True
C	Drainage of fluid by blood and lymphatic capillaries	True
D	Phagocytosis of all debris by macrophages	True
E	Reduction of capillary hyperemia	True
F	Bacterial multiplication	False
G	Uncontrolled division of bacteria	False
H	Lack of leukocytes	False
I	Lack of macrophages	False
J	Lack of erythrocytes	False

I-47	Suppuration:	
A	It means the accumulation of pus	True
B	Where pus accumulates, an abscess forms	True
C	Pus is most commonly produced by staph infection	True
D	The pus contains a fluid supernatant	True
E	Pus contains a solid deposit of PMN and bacteria, live and dead	True
F	It means healing	False
G	It means the accumulation of water	False
H	It means the accumulation of glucose	False
I	It means the accumulation of vitamins	False
J	It means the accumulation of neurons	False

I-48	The evolution of the abscess includes:	
A	Just below the surface of the skin, bacteria cause cellular damage	True
B	Just below the surface of the skin, the bacteria cause necrosis	True
C	Bacteria multiply and attract PMN	True
D	PMN accumulate in the central area	True
E	Hyperemia and edema occur in the central area	True

F	Division of viruses	False
G	Multiplication of viruses	False
H	PMNs attract neurons	False
I	Pus attracts neurons	False
J	Macrophages attract neurons	False

I-49	The evolution of the abscess also includes:	
A	The pus in the center is pushed to the surface	True
B	The abscess is delimited by the formation of a pyogenic membrane	True
C	The abscess breaks out	True
D	The pus is removed	True
E	A small final scar results	True
F	Division of viruses	False
G	Multiplication of viruses	False
H	PMNs attract neurons	False
I	Pus attracts neurons	False
J	Macrophages attract neurons	False

I-50	Chronic inflammation:	
A	It follows acute inflammation	True
B	It occurs if the action of the pathogen continues	True
C	It sometimes causes the formation of giant cells	True
D	It causes the formation of new capillaries from the old ones, by budding	True
E	Through the proliferation of fibroblasts, it causes the production of collagen and consequent fibrosis	True
F	Appears after healing	False
G	Appears after resting	False
H	Appears in sleep	False
I	Appears after meals	False
J	It only appears at night	False

I-51	Organization, after acute inflammation:	
A	It occurs when a large amount of exudate is produced	True
B	Occurs when large amount of necrosis is generated	True
C	It occurs when local conditions do not allow rapid resorption of the exudate	True
D	It occurs when local conditions do not allow rapid resorption of cellular debris	True
E	It is a type of evolution of acute inflammation	True
F	Appears after healing	False
G	It appears due to deep inspiration	False
H	It occurs due to deep exhalation	False
I	It occurs due to red blood cells	False
J	It occurs due to platelets	False

I-52	In the organization after acute inflammation occur:	
A	Same changes as in wound healing	True
B	Growth of new capillaries in the inert material	True
C	Growth of new capillaries in the exudate	True
D	Growth of new capillaries in thrombosis area	True

E	Migration of macrophages	True
F	Migration of erythrocytes	False
G	Migration of platelets	False
H	Migration of neurons	False
I	Migration of liver cells	False
J	Migration of cardiac cells	False

I-53	In curing pleurisy after pneumonia:	
A	The lung recovers quickly	True
B	The pleura undergoes the process of organization	True
C	Pleural exudate cannot be removed quickly	True
D	Fibrin cannot be removed quickly	True
E	Fibrous adhesions form between the two pleural sheets	True
F	The pleura recovers quickly	False
G	Fibrin is rapidly removed from between the pleural sheets	False
H	Neurons accumulate	False
I	Cardiac cells accumulate	False
J	Liver cells accumulate	False

I-54	A sinus:	
A	It's a channel	True
B	It joins a cavity to the surface of the skin	True
C	It can be associated with osteomyelitis	True
D	Appears after bone necrosis	True
E	It allows the pus to be evacuated to the surface of the skin	True
F	It belongs to the muscular system	False
G	It belongs to tendons	False
H	It belongs to the ligament	False
I	Appears after sleep	False
J	Appears at rest	False

I-55	A fistula:	
A	It is a communication opened on both ends	True
B	It is an abnormal communication between two surfaces	True
C	It can be congenital or acquired	True
D	It can occur after trauma	True
E	It can occur after inflammation	True
F	Appears in sleep	False
G	Appears after a light walk	False
H	It occurs only in children	False
I	It only appears in the morning	False
J	Disappears after resting	False

I-56	Infections:	
A	They represent the invasion of the body by living microorganisms	True
B	They are produced by bacteria	True
C	They are produced by viruses	True
D	They are produced by fungi	True

E	Most of them are produced by bacteria	True
F	They appear during sleep	False
G	They appear after a light walk	False
H	They only appear in children	False
I	They only appear in the morning	False
J	They disappear after resting	False

I-57	Bacteria:	
A	They are normally present on the skin	True
B	They are normally present on mucous membranes	True
C	Most of them are harmless	True
D	Some of them are useful for the body	True
E	There is a competition between bacteria normally present in the body and those that cause disease	True
F	They are not found on clean skin	False
G	They are not found in the intestines	False
H	They are not found in raw foods	False
I	They are not found in the air	False
J	They are not found in drinking water	False

I-58	Bacteria can enter the body:	
A	Through skin wounds	True
B	Through insect bites	True
C	Through reused syringe needles	True
D	By drinking contaminated water from unverified sources	True
E	Through food	True
F	With the help of the nose hairs	False
G	With the help of hydrochloric acid from the gastric juice	False
H	Through the mucus in the respiratory system	False
I	Through tears	False
J	Through urine	False

I-59	Factors that prevent and limit infection:	
A	Intact skin	True
B	Filtering by nose hairs	True
C	Urine	True
D	Mucus from the respiratory system	True
E	Tears	True
F	Insect stings	False
G	Reused syringe needles	False
H	Contaminated water drunk from unverified sources	False
I	Spoiled food	False
J	Wounds on the skin	False

I-60	Microorganisms can enter the body:	
A	Through intact skin (STDs)	True
B	Through contaminated water (dysentery)	True
C	Through contaminated water/food (cholera)	True

D	Through insect bites (typhoid)	True
E	By inhalation (flu)	True
F	On nose hairs	False
G	With the help of hydrochloric acid from the gastric juice	False
H	Through the mucus in the respiratory system	False
I	Through tears	False
J	Through urine	False

I-61	Secretions of the human body:	
A	Protect against infections	True
B	Wash away and eliminate pathogens	True
C	They may be represented by tears	True
D	They may be represented by urine	True
E	They may be represented by the mucus in the respiratory tract	True
F	Decrease immune response of the body	False
G	Decrease calorie intake	False
H	Decrease waking time	False
I	Decrease muscle relaxation	False
J	Decrease muscle contractility	False

I-62	Virulence of bacteria:	
A	Stimulates their invasive capacity	True
B	It means the ability of bacteria to resist phagocytosis by PMN	True
C	It means the ability of bacteria to resist phagocytosis by macrophages	True
D	It means the ability of bacteria to resist the enzymatic attack generated by PMN	True
E	It usually means a very thick and tough bacterial capsule	True
F	It means the ability of bacteria to resist to phagocytosis tempted by erythrocytes	False
G	It means the ability of bacteria to resist to phagocytosis tempted by neurons	False
H	It means the ability of bacteria to resist to phagocytosis tempted by platelets	False
I	It means the ability of bacteria to resist to phagocytosis tempted by epithelial cells	False
J	It means the ability of bacteria to resist to phagocytosis tempted by adipocytes	False

I-63	Bacterial virulence means:	
A	The ability to produce enzymes	True
B	Production of enzymes that destroy host tissues	True
C	Production of hyaluronidase by streptococci	True
D	Coagulase production by staphylococci	True
E	Toxin production by bacteria	True
F	Production of antibodies by bacteria	False
G	Production of hemoglobin by bacteria	False
H	Production of collagen by bacteria	False
I	Production of platelets by bacteria	False
J	Production of red blood cells by bacteria	False

I-64	The skin, as a protective barrier against microbes, is overcome by:	
A	Insect stings	True
B	Syringe needles	True
C	Wounds	True
D	Scratches	True
E	Dryness and cracking of the skin	True
F	Sleep	False
G	Rest	False
H	Healthy food	False
I	Proper hydration	False
J	Moderate physical exercises	False

I-65	In the respiratory tract, the infection is stimulated:	
A	By smoking	True
B	By nicotine	True
C	By reducing the movement of respiratory cilia due to nicotine	True
D	By increasing the amount of mucus produced due to nicotine	True
E	By not wearing protective masks when facing patients sick with COVID-19	True
F	By healthy food	False
G	By relaxation	False
H	By proper hydration	False
I	By moderate physical exercises	False
J	By resting	False

I-66	In the stomach:	
A	Bacteria arrive with the food	True
B	Infections are stimulated by the decrease in the amount of acid in the gastric juice	True
C	Infections are stimulated by conditions such as chronic gastritis, which decrease the amount of acid in the gastric juice	True
D	Infections are stimulated by conditions such as atrophic gastritis, which decrease the amount of acid in the gastric juice	True
E	The bacteria are destroyed by the acidity of the gastric juice	True
F	Microbes do not penetrate	False
G	Germs disappear by resting	False
H	Germs disappear in the morning	False
I	Germs disappear in children	False
J	Germs disappear in adults	False

I-67	Low resistance to infection occurs in:	
A	Diabetes	True
B	Cancer	True
C	Malnutrition	True
D	Chronic renal failure	True
E	Hereditary lack of some enzymes	True
F	Performance sportsmen	False
G	Athletes	False
H	Deep sleep	False
I	Holidays	False

J	Proper nutrition	False

I-68	Bacteremia:	
A	It means that only a few bacteria end up in the blood	True
B	It can occur after the extraction of an infected tooth	True
C	Bacteria in the blood are immediately destroyed by leukocytes	True
D	Bacteria can attach to the atrio-ventricular valves	True
E	Bacteria can cause bacterial endocarditis	True
F	It means very high number of bacteria in the blood	False
G	It means very high number of bacteria in the stomach	False
H	It means very high number of bacteria in the kidneys	False
I	It means very high number of bacteria in the joints	False
J	It means very high number of bacteria in the muscles	False

I-69	Septicemia:	
A	It is a serious condition accompanied by shock	True
B	It is a serious condition accompanied by toxemia	True
C	It means that there is a large number of bacteria in the blood	True
D	It means that the bacteria in the blood multiply and enter the tissues	True
E	It requires immediate antibiotic therapy	True
F	It means that only a few bacteria end up in the blood	False
G	It can occur after the extraction of an infected tooth	False
H	Bacteria in the blood are immediately destroyed by leukocytes	False
I	Bacteria can attach to the atrio-ventricular valves	False
J	Bacteria can cause bacterial endocarditis	False

I-70	Septicemia occurs:	
A	Due to some virulent bacteria	True
B	Due to meningococci	True
C	Due to serious diseases of the digestive tract	True
D	Due to the bacteria Escherichia coli	True
E	Due to some medical maneuvers in patients with very low immunity	True
F	In perfectly healthy patients	False
G	In sleep	False
H	In stand by	False
I	After a healthy meal	False
J	After adequate hydration	False

I-71	Piemia:	
A	Means there are very many bacteria in the blood	True
B	Means that blood bacteria are crowded in larger aggregates	True
C	It means that blood bacteria can generate thrombi	True
D	It means that blood bacteria can generate abscesses in the brain	True
E	It means that blood bacteria can generate abscesses in the lungs	True
F	It means that only a few bacteria end up in the blood	False
G	It can occur after the extraction of an infected tooth	False
H	Bacteria in the blood are immediately destroyed by leukocytes	False
I	Bacteria can attach to the atrio-ventricular valves	False

J	Bacteria can cause bacterial endocarditis	False

I-72	In piemia, the aggregates of microorganisms in the blood:	
A	Form thrombi	True
B	Form micro emboli	True
C	Generate septic abscesses in the brain	True
D	Generate septic abscesses in the heart	True
E	Generate septic abscesses in the kidneys	True
F	Are immediately destroyed by leukocytes	False
G	Are immediately destroyed by platelets	False
H	Are immediately destroyed by erythrocytes	False
I	Are immediately destroyed by epithelial cells	False
J	Are immediately destroyed by neurons	False

I-73	A virus:	
A	Is a particle that does not have the ability to survive by itself	True
B	Is a particle that does not have the ability to multiply by itself	True
C	Is a particle completely dependent on a living cell	True
D	Penetrate into a living cell and control the cell's metabolic processes	True
E	Penetrates into a living cell whose metabolic processes he diverts for its benefit	True
F	Is an independent cell	False
G	Is a cell that produces substances needed for the human body	False
H	Is a cell that determines the correct functioning of the human body's cells	False
I	Is a cell that produces nutrients	False
J	Is a cell that produces only antibodies	False

I-74	A virus can determine:	
A	Severe infections when very virulent	True
B	Severe infections when body immunity is very low	True
C	Generally only mild infections	True
D	Mild infections, because the multiplication of the virus is blocked by the defense mechanisms of the organism	True
E	Mild infections because virus diffusion is blocked by organism defense mechanisms	True
F	Bacteremia	False
G	Piemia	False
H	Septicemia	False
I	Relaxing sleep	False
J	Relaxation	False

I-75	Changes that occur in cells infected with viruses:	
A	Cell degeneration	True
B	Loss of function	True
C	Cell death	True
D	Abnormal cell proliferation	True
E	Accumulation of intracellular substances	True
F	Bacteremia	False
G	Piemia	False

H	Septicemia	False
I	Hemoglobin production	False
J	Glomerular ultra-filtrate production	False

I-76	Changes that may also occur in cells infected with viruses:	
A	Apparently no change	True
B	The virus remains latent in cells	True
C	The virus can be activated later	True
D	The malignant transformation of the cell	True
E	Accumulation of inclusions of inclusion, containing fragments of cellular degeneration	True
F	Thrombosis	False
G	Embolism	False
H	Myocardial infarction	False
I	Intestinal infarction	False
J	Division of the nucleus of the host cell	False

I-77	General effects of infection on the body:	
A	Fever	True
B	Imbalance between the production and loss of body heat	True
C	Fragments of bacteria influence the center of the thermoregulation in the hypothalamus	True
D	Leukocyte fragments influence the center of the thermoregulation of the hypothalamus	True
E	Chills	True
F	Relaxation	False
G	Improving of the general condition of the body	False
H	Increasing intellectual capacity	False
I	Increasing effort capacity	False
J	Increasing muscle capacity	False

I-78	In infections, fever generates:	
A	Increased heart rate	True
B	Tendency to dehydration	True
C	Over 41 ° C destroys neurons	True
D	Increases the phagocytosis capacity of leukocytes	True
E	Increasing the body's defense capacity	True
F	Relaxation	False
G	Improving of the general condition of the body	False
H	Increasing intellectual capacity	False
I	Increasing effort capacity	False
J	Increasing muscle capacity	False

I-79	In infections there are metabolic changes:	
A	Decreased appetite	True
B	Decrease of carbohydrate deposits in tissues	True
C	Decrease of protein deposits in tissues	True
D	Decrease of fat deposits in tissues	True

E	Dehydration	True
F	Increase of carbohydrate deposits in tissues	False
G	Increase of protein deposits in tissues	False
H	Increase of fat deposits in tissues	False
I	Appropriate hydration	False
J	Weight gain	False

I-80	In infections it occurs:	
A	Increased use of proteins	True
B	Increased elimination of nitrogenous products in the urine	True
C	Increasing the removal of products resulting from the fragmentation of proteins in the urine	True
D	Eliminating an increased amount of water in the urine	True
E	Formation of kidney stones	True
F	Increased muscle mass	False
G	Increased intellectual capacity	False
H	Increased breathing amplitude	False
I	The perfect functioning of the nervous system	False
J	The perfect functioning of the digestive system	False

I-81	Healing occurs:	
A	In smooth muscle cells	True
B	In cardiac striated muscle cells	True
C	In skeletal striated muscle cells	True
D	In nerves	True
E	In bone	True
F	In case of necrosis	False
G	In case of gangrene	False
H	In case of embolism by amniotic fluid	False
I	In case of intestinal infarction	False
J	In case of liquefying necrosis in the brain	False

I-82	Muscle repair:	
A	Muscle fibers have limited regeneration capacity	True
B	Muscle fibers have limited healing capacity	True
C	When a large part of the muscle is destroyed, repair occurs by producing scars	True
D	Repairing cardiac muscle after heart attack means scar production	True
E	Cardiac muscle regeneration after viral infections is possible	True
F	When much of the heart muscle is destroyed, healing occurs immediately	False
G	When much of the skeletal muscle is destroyed, healing occurs immediately	False
H	When much of the smooth muscle is destroyed, healing occurs immediately	False
I	Smooth muscle fibers have 100% regeneration capacity	False
J	Cardiac muscle fibers have 100% regeneration capacity	False

I-83	Muscle regeneration and healing:	
A	Smooth muscle fibers have limited regenerative capacity	True
B	Skeletal striated muscle fibers have limited regenerative capacity	True
C	Cardiac striated muscle fibers have limited regenerative capacity	True

D	Smooth muscle fibers have limited healing capacity	True
E	Skeletal striated muscle fibers have limited healing capacity	True
F	Skeletal muscle fibers have 100% regenerative capacity	False
G	After total destruction, skeletal muscle fibers regenerate 100%	False
H	After total destruction, cardiac muscle fibers regenerate 100%	False
I	After total destruction, smooth muscle fibers regenerate 100%	False
J	Cardiac muscle fibers have 100% regenerative capacity	False

I-84	Myocardial healing:	
A	After viral infections, the myocardium can fully recover	True
B	After the effects of diphtheria toxin, the myocardium can fully recover	True
C	Regeneration of certain muscle fibers is possible, if the disease diffusely affects all muscle fibers	True
D	Regeneration of certain muscle fibers is possible, if the disease affects all muscle fibers to varying degrees	True
E	In the case of a myocardial infarction, recovery involves the formation of scars	True
F	It occurs in all cases	False
G	It occurs regardless of the number of muscle cells affected	False
H	It occurs only in the elderly	False
I	It occurs only during intense physical exertion	False
J	It is produced in a very short time	False
I-85	Destruction of neurons:	
A	In the central nervous system, it is not followed by regeneration	True
B	It leads to a functional loss that exceeds the initial function of the destroyed neurons	True
C	It leads to reactive changes in the surrounding tissues	True
D	The disappearance of reactive changes around the destroyed neurons allow the functions of neighboring neurons to be restored	True
E	Causes liquefaction necrosis	True
F	It is followed by complete healing	False
G	It is followed by 100% regeneration of the destroyed neurons	False
H	It causes hepatic steatosis	False
I	It causes atrophy of the heart	False
J	It determines the improvement of the physical condition of the patients	False

I-86	After a small cerebral infarction:	
A	A small area of neuronal necrosis remains	True
B	The area of necrosis is surrounded by an area of edema	True
C	The area of necrosis is surrounded by a congestive zone	True
D	The area of edema influences the neighboring motor area	True
E	The area of congestion influences the adjacent motor area	True
F	All neurons return to normal	False
G	Total healing occurs	False
H	A 100% healing of neurons occurs	False
I	The patient's motor function is intact	False
J	The patient's neurological function is intact	False
I-87	After a small stroke, there also is:	
A	Damage to the motor area immediately causes hemiplegia	True

B	Damage to the motor area causes immediate loss of function	True
C	Within a few weeks, the small area of necrosis remains	True
D	In a few weeks, the edema disappears	True
E	Within a few weeks, the congestion disappears	True
F	All neurons return to normal	False
G	Total healing occurs	False
H	A 100% healing of neurons occurs	False
I	The patient's motor function is intact	False
J	The patient's neurological function is intact	False

I-88	After a small cerebral infarction, after a few weeks:	
A	Part of the motor area is recovering	True
B	New synapses are established between the remaining neurons	True
C	The paralysis disappears completely	True
D	The paralysis partially disappears	True
E	The area of liquefaction necrosis remains	True
F	All neurons return to normal	False
G	Total healing occurs	False
H	A 100% healing of neurons occurs	False
I	The patient's motor function is intact	False
J	The patient's neurological function is intact	False

I-89	In the peripheral nervous system, when a peripheral nerve is destroyed:	
A	The axon degenerates rapidly	True
B	The myelin sheath of the axon rapidly degenerates	True
C	The connective sheath of the axon slowly degenerates	True
D	The endonerve of the axon degenerates slowly	True
E	Axon regeneration can occur	True
F	The axon cannot regenerate	False
G	The axon will not regenerate	False
H	The myelin sheath remains intact	False
I	The conjunctival sheath remains intact	False
J	The endonerve remains intact	False

I-90	Sectioning, by trauma, of a spinal motor nerve, initially causes:	
A	Mild degenerative changes in motor neurons in the anterior horns of the spinal cord	True
B	Atrophy of the muscles innervated by that nerve	True
C	Gradual destruction of Nissl corpuscles in the neuronal body	True
D	Gradual destruction of the rough endoplasmic reticulum in the neuronal body	True
E	Axon disintegration	True
F	Keeping axons intact	False
G	Permanent maintenance of the myelin sheath	False
H	Maintaining the innervation of the appropriate muscle	False
I	Maintaining the trophicity of the corresponding muscle	False
J	Maintaining the strength of the corresponding muscle	False

I-91	Sectioning, by trauma, of a spinal motor nerve, subsequently causes:	

A	Disintegration of the myelin sheath	True
B	Survival of only Schwann cells	True
C	Budding of the distal end of the axon	True
D	Axon growth of about 20mm per week	True
E	Axon growth along the path of the former nerve	True
F	Keeping axons intact	False
G	Permanent maintenance of the myelin sheath	False
H	Maintaining the innervation of the appropriate muscle	False
I	Maintaining the tonus of the corresponding muscle	False
J	Maintaining the strength of the corresponding muscle	False

I-92	After the destruction of a spinal nerve:	
A	The best healing results are obtained if the nerve has been cut with clean edges	True
B	The best healing results are obtained through microsurgery	True
C	The best healing results are obtained by end-to-end suturing of the nerve	True
D	If the two damaged ends of the nerve have not been brought together, the axon buds that form do not reach the appropriate muscles	True
E	If the two destroyed ends of the nerve have not been put together, only a chaotic multiplication of Schwann cells occurs, called a traumatic neuroma	True
F	All axons return to normal	False
G	Total healing occurs	False
H	A 100% healing of axons occurs	False
I	The patient's motor function is intact	False
J	The patient's neurological function is intact	False

I-93	Bone healing after fracture:	
A	The fracture is accompanied by destruction in the surrounding soft tissues	True
B	The fracture is accompanied by hemorrhage in the surrounding soft tissues	True
C	Destruction of adjacent soft tissues is repaired by organization	True
D	Adjacent soft tissue hemorrhage is repaired by organization	True
E	The destroyed bone fragments are united by regeneration	True
F	It occurs independently of the movement of bone fragments	False
G	It occurs regardless of age	False
H	It is produced independently of protein intake	False
I	It is produced independently of vitamin intake	False
J	It occurs independently of the damage to the nutritive artery of the bone	False

I-94	Organization, after bone fracture, includes:	
A	Growth of new capillaries from the healthy tissue to the inert material	True
B	Growth of new capillaries from healthy tissue to the hematoma	True
C	Growth of new capillaries from healthy tissue to damaged tissue	True
D	Migration of macrophages, which remove the hematoma	True
E	Migration of macrophages, which remove destroyed tissue	True
F	Neuron growth	False
G	Skeletal muscle growth	False
H	Growth of heart muscle	False
I	Smooth muscle growth	False
J	Tendon growth	False

I-95	Immediately after the fracture occurs:	
A	The ends of the bone become necrotic	True
B	The surrounding soft tissue is destroyed	True
C	Hemorrhage occurs	True
D	Hematoma occurs	True
E	Fibrin is deposited	True
F	The continuity of the bone is preserved	False
G	The continuity of the adjacent muscles is preserved	False
H	Continuity of neighboring nerves is preserved	False
I	Continuity of the adjacent adipose tissue is preserved	False
J	The continuity of the neighboring blood vessels is preserved	False

I-96	After bone fracture:	
A	The first reaction is inflammatory	True
B	Phagocytosis of debris takes place	True
C	Phagocytosis of necrotic tissues occurs	True
D	Capillary formation takes place	True
E	Fibroblasts multiply	True
F	The continuity of the bone is preserved	False
G	The continuity of the adjacent muscles is preserved	False
H	Continuity of neighboring nerves is preserved	False
I	Continuity of the adjacent adipose tissue is preserved	False
J	The continuity of the neighboring blood vessels is preserved	False

I-97	One week after the fracture:	
A	Bone regeneration begins	True
B	The osteoblasts on the periphery of the bone marrow multiply	True
C	The osteoblasts in the periosteum multiply	True
D	Osteoblasts produce the temporary callus	True
E	Temporary callus joins the ends of the bone	True
F	The bone is completely healed	False
G	The adjacent muscle is completely healed	False
H	The surrounding adipose tissue is completely healed	False
I	The surrounding nerve tissue is completely healed	False
J	The cord is completely healed	False

I-98	Temporary callus:	
A	It is produced by osteoblasts	True
B	Join the ends of the bone	True
C	Contains unmineralized bone	True
D	May contain fragments of cartilage	True
E	It may gradually contain cancellous bone	True
F	It is produced by macrophages	False
G	It is produced by skeletal muscle cells	False
H	It is produced by neurons	False
I	It is produced by the tendon	False
J	It is produced by the heart	False

I-99	At least three weeks after the fracture:	
A	The callus is permanent	True
B	The callus is mineralized	True
C	The union of the bone ends is solid	True
D	The activity of osteoblasts continues	True
E	The activity of callus remodeling of osteoblasts continues	True
F	New synapses are established between the remaining neurons	False
G	The paralysis disappears completely	False
H	New synapses are established between the destroyed neurons	False
I	The liquefaction necrosis area disappears	False
J	The gangrene area disappears	False

I-100	For months after the fracture:	
A	Remodeling of the callus occurs	True
B	Spongy bone gradually becomes compact bone	True
C	Recanalization of the medullary canal occurs	True
D	Osteoclasts generate bone remodeling	True
E	The fracture site becomes almost invisible	True
F	New synapses are established between the remaining neurons	False
G	The paralysis disappears completely	False
H	New synapses are established between the destroyed neurons	False
I	The area of liquefaction necrosis disappears	False
J	The area of gangrene disappears	False

I-101	Complications of fractures can be:	
A	Fat embolism	True
B	Infection	True
C	Pathological fracture	True
D	Penetration of fat from the medullary cavity into the broken ends of the veins	True
E	Bone breaks easily when there is already bone disease (metastasis)	True
F	Nerve healing	False
G	Muscle healing	False
H	Bone healing	False
I	Tendon healing	False
J	Healing of the heart	False

I-102	Factors that prevent fracture healing:	
A	Local infection	True
B	The condition that causes the pathological fracture	True
C	Incorrect position of the ends of the bone	True
D	The continuous movement of the ends of the bone	True
E	Low blood supply	True
F	Balanced diet	False
G	Young age	False
H	Increased protein intake	False
I	Increased calcium intake	False
J	Increased intake of vitamin D	False

I-103	Other factors that prevent the fracture from healing:	
A	Old age	True
B	Malnutrition	True
C	Low protein intake	True
D	Low calcium intake	True
E	Low vitamin D intake	True
F	Increased intake of vitamin C	False
G	Correct position of the bone ends	False
H	Good immobilization	False
I	Maintaining the continuity of the skin above the fracture	False
J	Thorough cleaning of the open fracture	False

I-104	Factors favoring fracture healing:	
A	Good immobilization of the bone ends	True
B	Correct position of the bone ends	True
C	Adequate blood supply from the periosteum	True
D	Adequate blood supply from the nutrient artery of the bone	True
E	Adequate blood supply from adjacent soft tissues	True
F	Old age	False
G	Malnutrition	False
H	Low protein intake	False
I	Low calcium intake	False
J	Low vitamin D intake	False

I-105	A small callus results:	
A	After a bone fracture	True
B	If these bone ends are immobilized	True
C	If the immobilization of the bone ends is in the correct position	True
D	If the distance between these bone ends is as small as possible	True
E	Unless an infection occurs	True
F	In the large bones	False
G	In bones with pre-existing conditions (metastases)	False
H	If the surrounding muscles are very stressed	False
I	Due to the intense physical effort of the affected segment	False
J	Due to daily running, in case of fracture in the lower limbs	False

I-106	Thrombosis:	
A	It represents the coagulation of blood in the vessels during life	True
B	It is triggered by the release of thromboplastin from platelets	True
C	Induced by thromboplastin, thrombin is formed from the prothrombin released by the liver	True
D	Induced by thrombin, the soluble fibrinogen in the blood turns into an insoluble fibrin network	True
E	The fibrin network traps red blood cells, leukocytes and blood platelets and generates the thrombus	True
F	It represents the death of cells in a living organism	False
G	It represents the blockage of blood circulation in the vessels, due to air	False

H	It represents the blockage of blood circulation in the vessels, due to some fat particles	False
I	It represents the accumulation of lipids in liver cells	False
J	It represents the accumulation of microbes in macrophages	False

I-107	The extension of the thrombus into the vessels is produced by:	
A	Stagnation of blood proximal to the thrombus	True
B	Stagnation of blood distal to the thrombus	True
C	Extension of the fibrin network proximal to the thrombus	True
D	Extension of the fibrin network distal to the thrombus	True
E	The thrombus extends in both directions until it meets a blood vessel	True
F	Phagocytosis, by macrophages	False
G	Phagocytosis, by neutrophils	False
H	Liver steatosis	False
I	Clear intumescence	False
J	Cardiac steatosis	False

I-108	The extension of the thrombus at the junction with the second blood vessel depends on:	
A	Blood flow velocity in the second vessel	True
B	The amount of fibrin that is formed	True
C	The number of blood platelets that collide	True
D	Shutting off the blood flow in this second vessel	True
E	Successive episodes of thrombosis	True
F	The force of heart contractions	False
G	The frequency of heart contractions	False
H	Respiratory rate	False
I	Cardiac steatosis	False
J	Clear intumescence	False

I-109	Factors that cause thrombosis:	
A	Changes in blood flow	True
B	Reducing the speed of blood flow	True
C	Turbulence of the blood	True
D	Destruction of the vascular endothelium	True
E	Changes in blood composition	True
F	The number of macrophages in the lungs	False
G	The right diet	False
H	Relaxation	False
I	Good sleep	False
J	Increased tonus of the heart muscle	False

I-110	Reduction in blood flow speed:	
A	It causes thrombosis	True
B	It occurs in heart failure	True
C	Occurs in bedridden patients	True
D	It does not allow blood cells to remain in the axis of the vessel	True
E	It causes blood cells to accumulate near the vascular wall	True

F	It is beneficial for the heart	False
G	It is beneficial for the brain	False
H	It is beneficial for the muscle subjected to physical effort	False
I	It is beneficial for children	False
J	It is beneficial for the elderly	False

I-111	Turbulence of the blood:	
A	It causes thrombosis	True
B	It appears in the area of the venous valves	True
C	Appears in the area of varicose veins	True
D	Appears in the area of vascular aneurysms	True
E	It appears in areas of dilation of blood vessels	True
F	It is beneficial for the heart	False
G	It is beneficial for the brain	False
H	It is beneficial for the muscle subjected to physical effort	False
I	It is beneficial for children	False
J	It is beneficial for the elderly	False

I-112	Blood turbulence also:	
A	It appears in areas of narrowing of blood vessels	True
B	It causes blood cell vortices	True
C	It causes blood platelets to collide with each other	True
D	It causes blood platelets to collide with the vascular walls	True
E	It causes blood platelets to exit from the central blood stream	True
F	Improves memory	False
G	Improves gastric function	False
H	Improves kidney function	False
I	Improves brain function	False
J	Improves visual acuity	False

I-113	Destruction of the vascular endothelium:	
A	It causes thrombosis	True
B	It causes platelets to adhere to the blood vessel wall	True
C	It can be generated by an atheroma plaque	True
D	It can be generated by toxins	True
E	It may be generated by the surrounding inflammation	True
F	It is beneficial for the heart	False
G	It is beneficial for the brain	False
H	It is beneficial for the muscle subjected to physical effort	False
I	It is beneficial for children	False
J	It is beneficial for the elderly	False

I-114	Changes in blood composition:	
A	They cause thrombosis	True
B	They appear after giving birth	True
C	They appear after surgical interventions	True
D	They appear around the 10th day after giving birth	True
E	They appear about the 10th day after surgery	True

F	They do not affect the heart	False
G	They do not affect the brain	False
H	They do not affect the skeletal muscles	False
I	They do not affect the small intestine	False
J	They are not dangerous	False

I-115	Changes in the composition of the blood, which cause thrombosis, mean:	
A	Increase in the number of blood platelets	True
B	Increase in the amount of fibrinogen in the blood	True
C	Increase in the amount of prothrombin in the blood	True
D	Increase in the amount of thrombin in the blood	True
E	Increase in the adhesiveness of blood platelets	True
F	Decreased blood glucose levels	False
G	Lowering blood lipid levels	False
H	Decreased blood protein levels	False
I	Proper hydration	False
J	Lowering the level of bad cholesterol (LDL-cholesterol) in the blood	False

I-116	Thrombi can be of several types:	
A	White	True
B	Red	True
C	Mixed	True
D	Composed mainly of blood platelets	True
E	Composed mainly of leukocytes and red blood cells	True
F	Yellow	False
G	Green	False
H	Orange	False
I	Black	False
J	Blue	False

I-117	White thrombus:	
A	It is mainly composed of blood platelets	True
B	It forms in the arteries	True
C	It forms in vessels where blood circulation is fast	True
D	It does not obstruct the lumen	True
E	It is called a parietal thrombus	True
F	It is mainly composed of red blood cells and leukocytes	False
G	It forms in the veins	False
H	It forms in vessels where blood circulation is slow	False
I	It obstructs the lumen	False
J	It contains a gradually expanding fibrin network	False

I-118	Red thrombus:	
A	It is mainly composed of red blood cells and leukocytes	True
B	It forms in the veins	True
C	It forms in vessels where blood circulation is slow	True
D	It obstructs the lumen	True
E	It contains a gradually expanding fibrin network	True

F	It is mainly composed of blood platelets	False
G	It forms in the arteries	False
H	It forms in vessels where blood circulation is fast	False
I	It does not obstruct the lumen	False
J	It is called a parietal thrombus	False

I-119	Red thrombus:	
A	It is frequently encountered	True
B	It is dry	True
C	It is granular	True
D	It's crumbly	True
E	It adheres to the vascular wall at the point of onset of thrombosis	True
F	It is rarely encountered	False
G	It occurs mainly in the arteries	False
H	It's a small thrombus	False
I	It's a parietal thrombus	False
J	Contains predominantly blood platelets	False

I-120	Thrombi can be:	
A	Cardiac thrombi, located in the atria	True
B	Cardiac thrombi, located in the ventricles	True
C	Cardiac thrombi, located on the atrio-ventricular valves	True
D	Arterial thrombi	True
E	Venous thrombi	True
F	Located under the skin	False
G	Located in the gastric cavity	False
H	Located in bone	False
I	Located in skeletal muscle cells	False
J	Located in liver cells	False

I-121	Cardiac thrombi:	
A	Ventricular ones are the result of an infarction of the ventricular wall	True
B	The ventricular ones are red	True
C	The ones on the heart valves are white thrombi	True
D	In case of bacterial endocarditis, small thrombi form	True
E	In case of bacterial endocarditis, thrombi which also contain numerous bacteria, are formed	True
F	They are only white ones	False
G	They are only red ones	False
H	They are just small ones	False
I	They form only in children	False
J	They form only in men	False

I-122	Arterial thrombi:	
A	They are commonly found in the aorta	True
B	They form due to atheroma plaques	True
C	They are parietal ones	True
D	They form where the blood pressure is high	True

E	They form where the blood flow is fast	True
F	They are only white ones	False
G	They are only red ones	False
H	They are just small ones	False
I	They form only in children	False
J	They form only in women	False

I-123	Small thrombi occur in:	
A	Aortic aneurysms	True
B	Coronary arteries	True
C	Middle cerebral arteries	True
D	Small arteries of the limbs	True
E	Small arteries of the fingers	True
F	Only in veins	False
G	Only in capillaries	False
H	Only in children	False
I	Only in men	False
J	Only in women	False

I-124	Venous thrombi:	
A	They are the most numerous ones	True
B	They form in vessels with low flow velocity	True
C	They form in vessels with low blood pressure	True
D	They form in vessels with increased compressibility of the vessels	True
E	They form in vessels where vortices form (venous valves)	True
F	They are only white ones	False
G	They form only in men	False
H	They are just small ones	False
I	They form only in children	False
J	They form only in women	False

I-125	The formation of thrombi in veins is favored by:	
A	Abdominal operations	True
B	Giving birth (labor)	True
C	Heart disease	True
D	Varicose veins	True
E	Inflammatory processes	True
F	Daily walk	False
G	Daily climbing up the stairs	False
H	Proper hydration of the body	False
I	Correct nutrition	False
J	Daily running	False

I-126	The evolution of the thrombus is towards:	
A	Organization	True
B	Calcification	True
C	Incorporation	True
D	Inclusion in an atheroma plaque	True

E	Embolism	True
F	Recovery	False
G	Regeneration	False
H	Atrophy	False
I	Hypertrophy	False
J	Steatosis	False

I-127	The embolus can be:	
A	A fragment of thrombus	True
B	A fragment of an atheroma plaque	True
C	Air	True
D	Amniotic fluid	True
E	Fat	True
F	Bone	False
G	Cartilage	False
H	Muscle	False
I	Nerve	False
J	Tendon	False

I-128	The solid embolus can consist of:	
A	Tumor cells from a liver cancer	True
B	Tumor cells from a bone cancer	True
C	Bullets	True
D	Aggregations of bacteria	True
E	Vermin	True
F	Bone	False
G	Cartilage	False
H	Muscle	False
I	Nerve	False
J	Tendon	False

I-129	Emboli from the left heart end up blocking:	
A	Arteries in the brain	True
B	Arteries in the kidney	True
C	Arteries in the spleen	True
D	Arteries in the lower limbs	True
E	Arteries in the intestine	True
F	Veins in the brain	False
G	Veins in the kidney	False
H	Veins in the spleen	False
I	Veins in the lower limbs	False
J	Veins in the intestine	False

I-130	Emboli originating from veins:	
A	They usually block the pulmonary arteries	True
B	If they are of the gaseous type, they are malleable	True
C	If they are fluid, they are malleable	True

D	If they are of the gaseous type, they can pass through the pulmonary circulation	True
E	If they are fluid, they can pass through the pulmonary circulation	True
F	They're only blood clots	False
G	They are only the solid type ones	False
H	They are only white ones	False
I	They are only parietal ones	False
J	They are only fragments of atheroma plaques	False

I-131	Simple gaseous embolism:	
A	It occurs when sectioning the veins at the base of the neck	True
B	Occurs when sectioning the cranial veins	True
C	Inspiration causes air aspiration through the sectioned veins	True
D	Air enters the left ventricle	True
E	Air in the ventricle causes disorders of ventricular contraction	True
F	Appears after giving birth	False
G	Occurs after bone fracture	False
H	It occurs due to a thrombus	False
I	It occurs only in children	False
J	It occurs only in the elderly	False

I-132	Multiple gaseous embolism:	
A	Appears in divers	True
B	It occurs due to rapid decompression	True
C	Gases dissolved in the blood suddenly turn into gas bubbles	True
D	It causes multiple heart attacks	True
E	It causes cerebral infarcts	True
F	Appears after giving birth	False
G	Occurs after bone fracture	False
H	It occurs due to a thrombus	False
I	It occurs only in children	False
J	It occurs only in the elderly	False

I-133	Fat embolism:	
A	It occurs when a long bone is fractured	True
B	The fat globules enter the veins of the bone	True
C	The fat globules reach the pulmonary arteries	True
D	Fat globules prevent oxygenation of the blood	True
E	It causes a feeling of suffocation	True
F	Appears after giving birth	False
G	Appears in divers	False
H	It occurs due to a thrombus	False
I	It occurs only in children	False
J	It occurs only in the elderly	False

I-134	Amniotic fluid embolism:	
A	Appears during giving birth (labor)	True
B	It occurs when the uterine veins are open	True

C	It occurs due to penetration of amniotic fluid into the uterine veins	True
D	It occurs due to penetration of baby hairs from amniotic fluid into the uterine veins	True
E	It occurs due to penetration of baby scales from amniotic fluid into the uterine veins	True
F	Appears after fractures	False
G	Appears in divers	False
H	It occurs due to a thrombus	False
I	It occurs only in men	False
J	It occurs only in the elderly	False

I-135	The heart attack:	
A	It is due to thrombosis	True
B	It is due to embolism	True
C	It is an area of necrosis due to ischemia	True
D	It affects an area on the periphery of the heart	True
E	It can heal slowly, by scarring	True
F	It causes the death of the patient in all cases	False
G	It causes the patient to be cured in all cases	False
H	It occurs only in children	False
I	It occurs only in women	False
J	It occurs only in men	False

I-136	The heart attack:	
A	It is usually caused by thrombosis	True
B	It causes necrosis of the myocardium	True
C	It causes destruction of the endocardium	True
D	It causes the formation of an intracardiac thrombus over the area of necrosis	True
E	It can progress to a non-contractile fibrous scar	True
F	It causes the death of the patient in all cases	False
G	It causes the patient to be cured in all cases	False
H	It occurs only in children	False
I	It occurs only in women	False
J	It occurs only in men	False

I-137	The heart attack causes the death of the patient if:	
A	Thrombosis occurred in a major coronary vessel	True
B	Thrombosis stopped the blood supply through the collateral vessels as well	True
C	The external third of the myocardium is also destroyed	True
D	Transmural infarction occurs	True
E	Cardiac tamponade occurs	True
F	The patient is young	False
G	The patient is healthy	False
H	The patient has a balanced diet	False
I	The patient is a child	False
J	The patient is a newborn	False

I-138	Cerebral infarction:	

A	It is usually caused by thrombosis	True
B	The middle cerebral artery is affected	True
C	The posterior cerebral artery is affected	True
D	The basilar artery is affected	True
E	Causes liquefaction necrosis	True
F	It mostly affects children	False
G	It mostly affects women	False
H	It mostly affects men	False
I	Appears only during the day	False
J	It only appears during the night	False

I-139	Cerebral infarction can occur:	
A	Due to embolism	True
B	Due to hypotension	True
C	In case of shock	True
D	Without arterial occlusion	True
E	At the border between territories vascularized by two neighboring arteries	True
F	Only in children	False
G	Only in newborns	False
H	Only in young people	False
I	Only during the day	False
J	Only during the night	False

I-140	Pulmonary infarction:	
A	It is conical in shape	True
B	It is located under the pleura	True
C	It can be produced by embolism	True
D	It is usually produced by a thrombus from the right atrium	True
E	It occurs in heart failure	True
F	It mainly affects children	False
G	It mostly affects women	False
H	It mostly affects men	False
I	Appears only during the day	False
J	It only appears during the night	False

I-141	Renal infarction:	
A	It may occur due to embolism	True
B	It may occur due to a thrombus	True
C	It is due to atrial fibrillation	True
D	It is due to bacterial endocarditis	True
E	It causes hematuria	True
F	It mainly affects children	False
G	It mostly affects women	False
H	It mostly affects men	False
I	Appears only during the day	False
J	It only appears during the night	False

I-142	Intestinal infarction:	

A	It is quite rare	True
B	It is prevented by the existence of vascular anastomoses	True
C	It is produced by embolism	True
D	It causes gangrene of the wall	True
E	It causes the colonization of that area by the bacteria in the intestine	True
F	Appears only during the day	False
G	It only appears during the night	False
H	It mainly affects children	False
I	It mostly affects women	False
J	It mostly affects men	False

I-143	A tumor is a proliferation of cells that is:	
A	Progressive	True
B	Without purpose	True
C	Uncorrelated with the body's needs	True
D	Stray	True
E	Self-dependent	True
F	Only from the skin	False
G	Only from the bone	False
H	Only from the nerve	False
I	Only from the cartilage	False
J	Only from the heart	False

I-144	Differentiated tumor cells:	
A	They mimic the structure of the original organ	True
B	They resemble the tissue of origin	True
C	They are uniform in size	True
D	They perform a normal function	True
E	They show few mitoses	True
F	They are arranged chaotically	False
G	There is nothing like the original tissue	False
H	They vary greatly in size and shape	False
I	They do not perform their normal function	False
J	They highlight numerous abnormal mitoses, resulting in 2-3 cells of various sizes and shapes	False

I-145	Undifferentiated tumor cells:	
A	They are arranged chaotically	True
B	There is nothing like the original tissue	True
C	They vary greatly in size and shape	True
D	They do not perform their normal function	True
E	They highlight numerous abnormal mitoses, resulting in 2-3 cells of various sizes and shapes	True
F	They mimic the structure of the original organ	False
G	They resemble the tissue of origin	False
H	They are uniform in size	False
I	They perform a normal function	False
J	They show few mitoses	False

I-146	The chondroma:	
A	It is a benign tumor	True
B	It is a tumor of cartilaginous tissue	True
C	It can be single	True
D	There may be multiple chondromas, enchondromatosis	True
E	It appears in children, at the level of the limbs	True
F	It is a malignant tumor	False
G	It is a skeletal muscle tumor	False
H	It is found only in the skull	False
I	It occurs only in the elderly	False
J	Disappears with drug treatment	False

I-147	Osteoma:	
A	It is a benign tumor	True
B	It is a tumor of bone tissue	True
C	It can be "ivory"	True
D	It may consist of compact bone	True
E	It can be made of cancellous bone	True
F	It is a malignant tumor	False
G	It is a skeletal muscle tumor	False
H	It is found only in the sacrum bone	False
I	It occurs only in the elderly	False
J	Disappears with drug treatment	False

I-148	Osteosarcoma:	
A	It occurs in young people	True
B	It is a malignant tumor	True
C	It may come from endosteum	True
D	It may come from the periosteum	True
E	It quickly produces metastases	True
F	It is a benign tumor	False
G	It is generated in the epithelial tissue	False
H	It is found only in the sacrum bone	False
I	It occurs only in the elderly	False
J	Disappears with drug treatment	False

I-149	Chondrosarcoma:	
A	It is a malignant tumor	True
B	Appears at the ends of long bones	True
C	It occurs in the bones of the hand	True
D	It occurs in the bones of the pelvis	True
E	It grows slowly	True
F	It does not recur after surgery	False
G	It does not metastasize	False
H	It is generated in the epithelial tissue	False
I	It occurs only in the elderly	False
J	Disappears with drug treatment	False

I-150	Giant cell tumor:	
A	It is a malignant tumor	True
B	It contains numerous osteoclasts	True
C	It contains numerous macrophages specialized in destroying bone	True
D	It rarely produces metastases	True
E	It produces pathological fractures	True
F	It develops only on the outside of the bone	False
G	It often generates metastases	False
H	It is generated in the epithelial tissue	False
I	It occurs only in the elderly	False
J	Disappears with drug treatment	False

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