UNIT -I

INTRODUCTION AND SCOPE OF ANATOMY AND PHYSIOLOGY

INTRODUCTION:

Anatomy and physiology concern with the structures and functions of the human body.

Anatomy describes the structures of the body -- their scientific names, composition, location, and associated structures.

Anatomy ("a cutting open") is a plan or map of the body.

Physiology studies the function of each structure, individually and in combination with other structures.

Anatomy and physiology always work together. As we examine each part of the body, always consider both its structure and its function.

The study of anatomy is divided into 2 major fields:

1. **Gross anatomy** is the study of large visible structures

2. **Microscopic anatomy** is the study of structures that are too small to see, such as cells and molecules.

1. Gross anatomy, also called macroscopic anatomy, is separated into 5 major divisions:

A. **Surface anatomy** describes surface forms and marks.

B. **Regional anatomy** describes the organization of specific areas of the body such as the head or hand. This approach is used mostly in professional schools: medical, dental, physical therapy.

C. **Systemic anatomy** describes groups of organs that function together for a single purpose.

D. **Developmental anatomy** describes the structural changes in an organism from fertilized egg to maturity. Embryology is the anatomical study of early development.

E. **Clinical anatomy** describes various medical specialties, including medical anatomy (changes that occur during illness), and radiographic anatomy.

2. Microscopic anatomy is divided into two major divisions:

A. **Cytology,** the study of cells and their structures.

B. **Histology,** the study of tissues and their structures.

Physiology has many specialties. The 4 basic divisions are:

1. **Cell physiology**, including chemical and molecular processes within and between cells.

2. **Special physiology**, the study of specific organs such as the heart.

3. **Systemic physiology,** the cooperative functions of all the organs in an organ system.

4. **Pathological physiology**, the effects of diseases on organs and organ systems.

LEVELS OF ORGANIZATION

Our bodies are organized at many different levels.

The levels of organization of living things, from smallest to largest, are:

1. **Atoms,** the smallest functional units of matter.

2. **Molecules,** active chemicals.

3. **Organelles**, specialized structures within a cell.

4. **Cells,** the smallest living units.

5. **Tissues,** a group of similar cells that work together.

6. **Organs,** two or more tissue types working together.

7. **Organ systems,** two or more organs working together.

8. **Organism,** a single individual, including all of the above.

The human body is divided into 11 interconnected organ systems. All organ systems work together, and many organs function in more than 1 organ system.

1. **The Integumentary System:** includes the skin & derived structures, it protects internal organs & helps maintain body temperature.

2. **The Skeletal System:** includes the bones & joints, it provides support & protection to internal organs.

3. **The Muscular System:** includes skeletal muscle and it provides movement.

4. **The Nervous System:** includes the brain, spinal cord, and nerves. It provides regulation of body functions & sensory perception.

5. **The Endocrine System:** includes hormone-producing cells & glands. It regulates homeostasis, growth & development.

6. **The Cardiovascular System:** includes blood, heart, & blood vessels. It is responsible for delivery of oxygen & nutrients to the tissues.

7. **The Lymphatics & Immune System:** includes lymphatic vessels & fluid. It is involved in the defence against infection.

8. **The Respiratory System:** includes lungs & airways. It is involved in the absorption of oxygen & release of carbon dioxide.

9. **The Digestive System:** includes organs of the gastrointestinal tract. It is responsible for the absorption of nutrients.

10. **The Urinary System:** includes the kidneys, ureters, and bladder. It is responsible for electrolyte balance & waste removal.

11. **The Reproductive System:** includes the reproductive organs in males and females. It controls the biological process by which new individuals are produced.

HOMEOSTASIS:

- Ability to maintain relatively stable internal conditions despite a changing external environment. Dynamic state of equilibrium, or balance.
- The body is said to be in homeostasis when its cellular needs are adequately met and functional activities are occurring smoothly.
- Virtually every organ system plays a role in maintaining the internal environment.

A homeostatic regulatory mechanism consists of 3 parts:

1. **Receptors,** sensors that respond to a stimulus. It monitors change in control condition and send the input information to control center.

2. **The control center** receives information from sensors (receptor) and sends out commands. In the body there are hundred controlled conditions. A few examples are heart rate, blood pressure, temperature and breathing rate.

3. **Effectors are the cell or organ** that responds according to output command of the control center.

Receptors, control center and effectors maintain the homeostasis by two mechanisms:

1. Negative feedback:

When the response of effectors opposes the original stimulus, it is called negative feedback because it negates the stimulus.

An example of negative feedback is the temperature thermostat in your home.

Temperature sensors turn the air conditioner off and on to maintain air temperature within a specific, limited range.

In the same way, the brain controls normal body-temperature homeostasis by negative feedback.

– Some stimulus (Stress) disrupts homeostasis (control condition) by an increase in body temperature.

– Due to this condition thermoreceptors (temperature sensitive receptors) in the skin and brain activate and send input message via nerve impulse to control center.

– Control center analyze the input message and send output message to effectors (skin).

– Effectors according to output message of control center increases sweating from sweat glands causes increased heat loss by evaporation.

– Finally, decreases the temperature in the form of response and normalize the body temperature (control condition).

2. Positive feedback:

The effector adds to the initial stimulus instead of negating it, speeding up the process.

– Labor contraction is the example of positive feedback system.

– Labor contractions force baby's head or body into birth canal.

– It produces effect on control condition and increases distention of cervix of uterus.

– It activates the stretch receptors of cervix and send input message to control center via sensory nerve impulse.

– Control center activates the hypothalamus and pituitary gland and send the output message to increase oxytocin secretion in blood.

– Oxytocin produces their effect on to the effector (cervix of uterus) and cause distention of cervix of uterus than the normal value to push the baby further into birth canal.

– Birth of the baby decreases distention of cervix of uterus and interrupts positive feedback cycle.

BODY CAVITIES AND SEROUS MEMBRANES

The body maintains its internal organization by means of membranes, sheaths, and other structures that separate compartments.

The dorsal (posterior) cavity and the ventral (anterior) cavity are the largest body compartments.

These cavities contain and protect delicate internal organs, and the ventral cavity allows for significant changes in the size and shape of the organs as they perform their functions.

The lungs, heart, stomach, and intestines, for example, can expand and contract without distorting other tissues or disrupting the activity of nearby organs.

Subdivisions of the Posterior (Dorsal) and Anterior (Ventral) Cavities

The posterior (dorsal) and anterior (ventral) cavities are each subdivided into smaller cavities.

In the posterior (dorsal) cavity, the cranial cavity houses the brain, and the spinal cavity (or vertebral cavity) encloses the spinal cord.

The anterior (ventral) cavity has divided by the diaphragm muscle into 2 parts:

1. **A superior thoracic cavity,** containing the

A. **Pleural cavity (left and right, divided by the mediastinum) organs:** lungs membranes: visceral and parietal pleura

B. **Pericardial cavity organs: heart membranes:** visceral and parietal pericardium

2. **Inferior abdominopelvic cavity**, containing the

A. **Peritoneal cavity membranes:** visceral and parietal peritoneum

B. **Abdominal cavity (superior peritoneal) organs:** liver, stomach, spleen, intestine

C. **Pelvic cavity (inferior peritoneal) organs:** intestine, bladder, reproductive organs

Membranes of the Anterior (Ventral) Body Cavity:

The walls of the ventral body cavity and the outer surfaces of the organs are covered with a thin, double layered membrane – serosa or serous membranes.

Part of the membrane lining the cavity walls - parietal serosa -folds on itself to form the visceral serosa which covers the organs in the cavity.

– Parietal - "parie"- means wall

– Visceral - "viscus"- means an organ in a body cavity

BODY FLUIDS:

Water content of the body is divided into:

1. Intracellular compartment (67%) - Inside the cell

2. Extracellular compartment (33%) - Outside the cell

1. Intracellular Fluid (ICF)

- Comprises, 2/3 of the body water.
- If body has 60% water, ICF is about 40% of your weight.
- The ICF is primarily a solution of potassium and organic anions, proteins etc.
- The cell membranes and cellular metabolism control the constituents of this ICF.

2. Extracellular compartment (ECF):

It is the remaining 1/3 of your body's water.

ECF is about 20% of the body weight.

The ECF is primarily a NaCl and NaHCO3 solution.

The ECF is further subdivided into three sub-compartments:

A. Interstitial Fluid (ISF).

B. Plasma.

C. Transcellular fluid

A. Interstitial Fluid (ISF)

Interstitial Fluid (ISF) surrounds the cells, but does not circulate.

It is the main component of the extracellular fluid

It comprises about 3/4 of the ECF.

Interstitial fluid is found in the interstitial spaces, also known as the tissue spaces.

Composition of interstitial fluid:

- Water solvent amino acids
- Sugars
- Fatty acids
- Coenzymes
- Hormones
- Neurotransmitters
- Salts
- Waste products from the cells.
- Lymph is considered a part of the interstitial fluid

Function of interstitial fluid

- Intercellular communication.
- Interstitial fluid bathes the cells of the tissues.
- Removal of metabolic waste.

B. Plasma:

- It is the yellow liquid component of blood in which the blood cells in whole blood are normally suspended
- 55% of the total blood volume.
- It is the intravascular fluid part of extracellular fluid (all body fluid outside of cells)
- It makes up about 1/4 of the ECF.

Composition of plasma

- Water (90% by volume)
- Dissolved proteins
- Glucose
- Clotting factors
- Mineral ions
- Hormones
- Carbon dioxide.

Function of plasma

- Plasma is the main medium for excretory product transportation.
- Blood serum is blood plasma without fibrinogen or the other clotting factors (i.e., whole blood minus both the cells *and* the clotting factors).

C. Transcellular fluid

- Transcellular fluid is the portion of total body water contained within epithelial lined spaces.
- Smallest compartment.
- It is about 2.5% of the total body water.

Examples

- Cerebrospinal fluid
- Ocular fluid (Aqueous humor)
- Joint fluid (Synovial fluid)
- Urine

Composition of transcellular fluid:

1. Cerebrospinal fluid:

– The CSF is mainly produced by the choroid plexus.

– The entire nervous system contains between 80-150 ml of CSF.

– It is a clear colourless liquid that contains White blood cells, glucose, protein, lactic acid, urea, cations (Na+, K+, Ca+ etc) and anions (Cl-, and HCO3-).

2. Ocular fluid (Aqueous humor):

– The aqueous humor is a transparent, gelatinous fluid similar to plasma.

– It is located in the anterior and posterior chambers of the eye, the space between the lens and the cornea.

– It contains Amino acids (transported by cilliary muscles), 98% water, Electrolytes, Ascorbic acid, Glutathione

3. Joint fluid (Synovial fluid):

– Synovial fluid is clear, pale yellow, viscid, and does not clot.

– The principal role of synovial fluid is to reduce friction between the articular cartilage of synovial joints during movement.

– It contains Normal 3–4 mg/ml hyaluronic acid, a polymer of disaccharides, WBC, RBC and proteins

4. Urine:

– Urine is a typically sterile liquid by product of the body secreted by the kidneys through a process called urination and excreted through the urethra.

– It contains 95% water, Organic solutes like urea, creatinine, uric acid, and trace amounts of enzymes, carbohydrates, hormones, fatty acids, pigments, and mucins, and inorganic ions such as sodium (Na+), potassium (K+), chloride (Cl-), magnesium (Mg2+), calcium (Ca2+), ammonium (NH4+), sulfates (SO42-), and phosphates (e.g., PO43-).

SOME DEFINITIONS RELATED TO HAP

CELL: It is living structural and functional units of body enclosed by membrane.

CYTOLOGY: It is the branch of science concern with the study of cells.

TISSUE: It is a group of cells that usually have common embryonic origin and function together for special activities.

BLOOD: It is a liquid connective tissue.

LYMPH: It is a thin, watery, clear, modified tissue fluid formed by the passage of substance from the blood capillaries into the tissue space (interstitial space) and enters in to the closed system of lymphatic capillaries to lymphatic vessels and lymphatic sinus.

CARDIOVASCULAR SYSTEM: Cardiovascular is the system which includes the study of the heart, blood vessels and blood.

IMMUNE SYSTEM: It is the collection of cells, tissues and molecules that protects the body from numerous pathogenic microbes and toxins in our environment.

CELL ORGANELLES

- Cell organelle is a specialized entity present inside a particular type of cell that performs a specific function.

- There are various cell organelles, out if which, some are common in most types of cells like cell membranes, nucleus, and cytoplasm. However, some organelles are specific to one particular type of cell-like plastids and cell walls in plant cells.

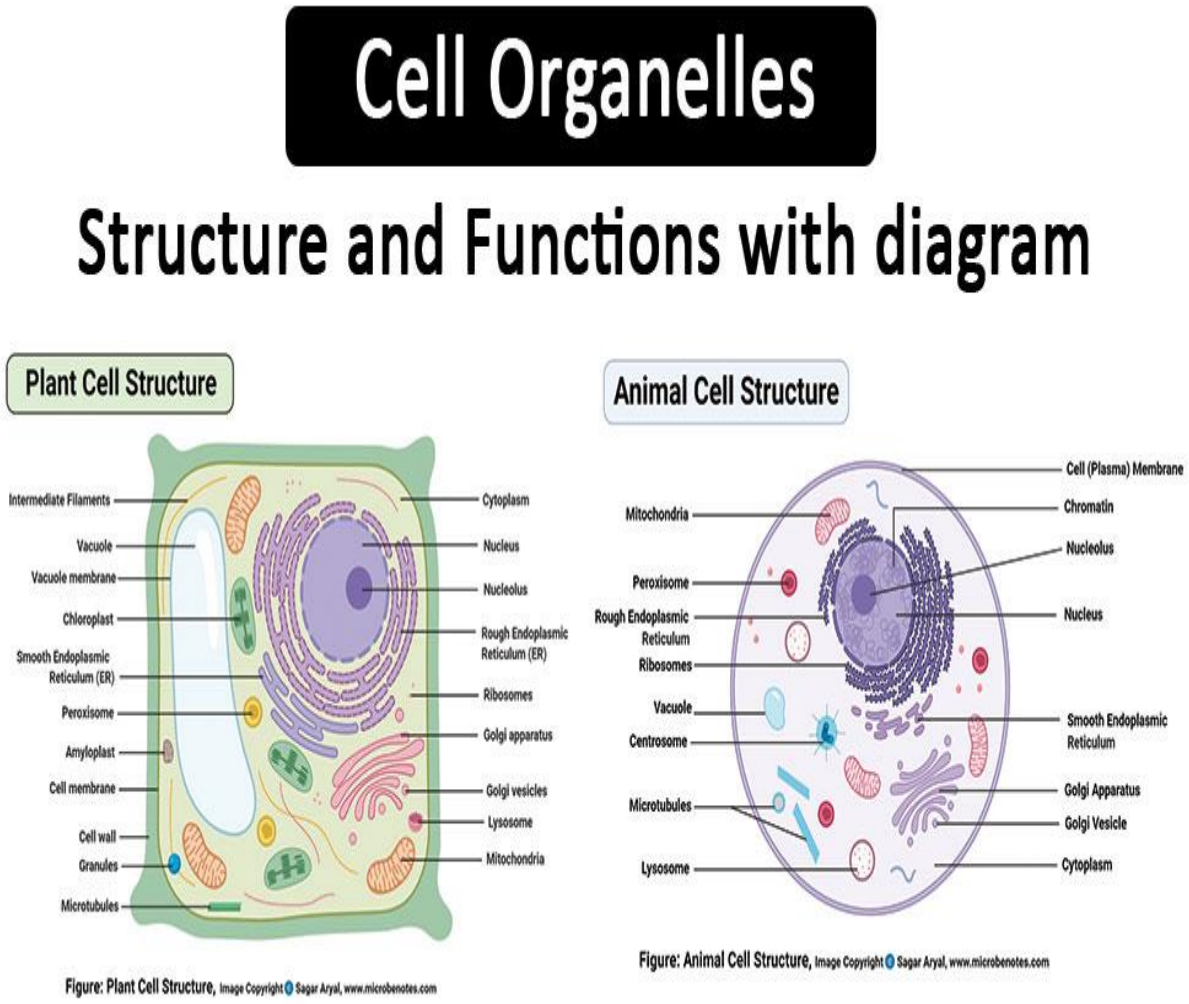


Figure: Plant Cell Structure, Image Copyright © Sagar Aryal, www.microbenotes.com

Figure: Animal Cell Structure, Image Copyright © Sagar Aryal, www.microbenotes.com

Cell membrane (Plasma membrane/ Plasmalemma)

- A plasma membrane is composed of lipids and proteins where the composition might fluctuate based on fluidity, external environment, and the different stages of development of the cell.

Structure

- Structurally, it consists of a phospholipid bilayer along with two types of proteins viz. embedded proteins and peripheral proteins that function in providing shape and allowing the movement of particles in and out of the cell.
- The most abundant lipid which is present in the cell membrane is a phospholipid which contains a polar head group attached to two hydrophobic fatty acid tails.
- The embedded proteins act as channels for the transfer of particles across the cell with some proteins acting as receptors for the binding of various components.
- The peripheral proteins function as to provide fluidity as well as mechanical support to the structure of the cell.

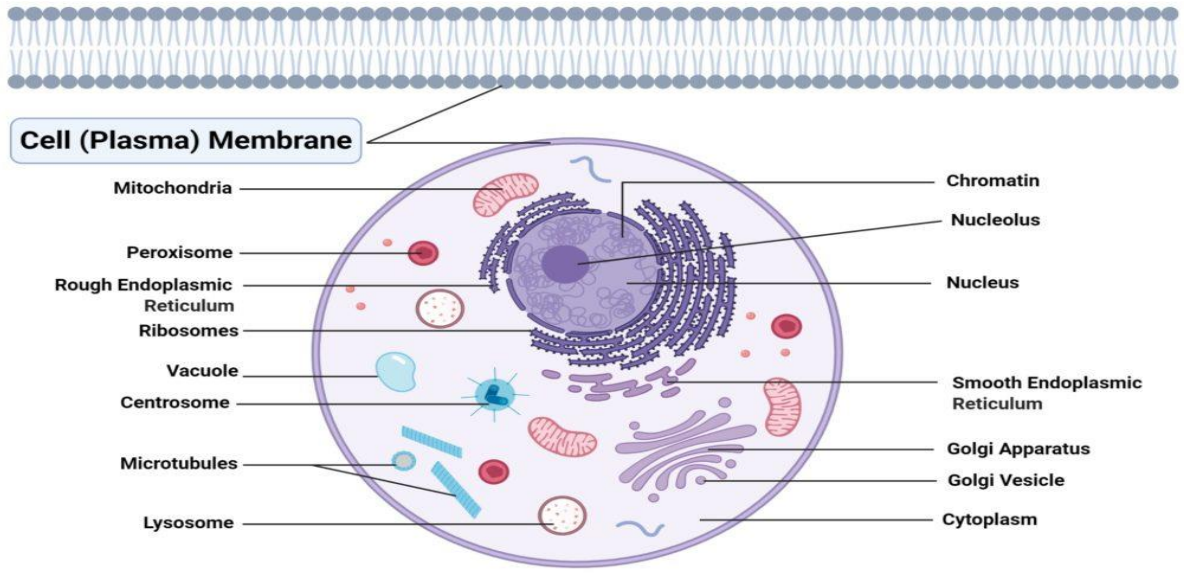


Figure: Animal Cell Structure with Cell (Plasma) Membrane, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- The cell membrane provides mechanical support that facilities the shape of the cell while enclosing the cell and its components from the external environment.
- It regulates what can be allowed to enter and exit the cell through channels, acting as a semi-permeable membrane, which facilities the exchange of essential compounds required for the survival of the cell.
- It generates and distributes signals in and outside of the cell for the proper functioning of the cell and all the organelles.
- It allows the interaction between cells required during tissue formation and cell fusion.

Centriole

- Centrioles are tubular structures mostly found in eukaryotic cells which are composed mainly of the protein tubulin.

Structure

- A centriole consists of a cylindrical structure made with nine triplets microtubules that surround the periphery of the centriole while the center has a Y-shaped linker and a barrel-like structure that stabilizes the centriole.
- Another structure called cartwheel is present in a centriole which is made up of a central hub with nine spokes/filaments radiating from it. Each of these filaments/spokes is connected to the microtubules through a pinhead.

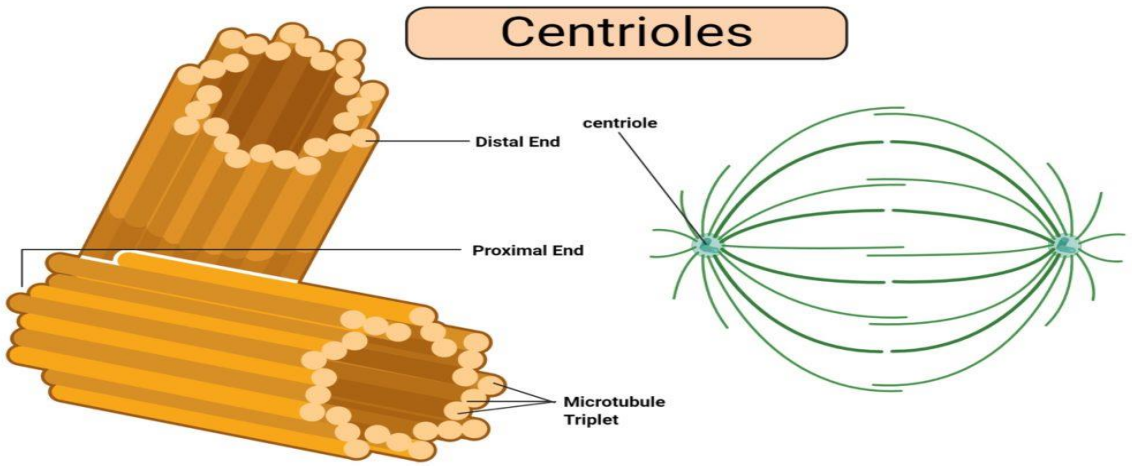


Figure: Centrioles, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- During cell division, centrioles have a crucial role in forming spindle fibers which assist the movement of chromatids towards their respective sides.
- They are involved in the formation of cilia and flagella.

Cilia and Flagella

- Cilia and Flagella are tiny hair-like projections from the cell made of microtubules and covered by the plasma membrane.

Structure

- Cilia are hair-like projections that have a 9+2 arrangement of microtubules with a radial pattern of 9 outer microtubule doublet that surrounds two singlet microtubules. This arrangement is attached to the bottom with a basal body.
- Flagella is a filamentous organelle, the structure of which, is different in prokaryotes and eukaryotes.
- In prokaryotes, it is made up of the protein called flagellin wrapped around in a helical manner creating a hollow structure at the center throughout the length.

- In eukaryotes, however, the protein is absent and the structure is replaced with microtubules.

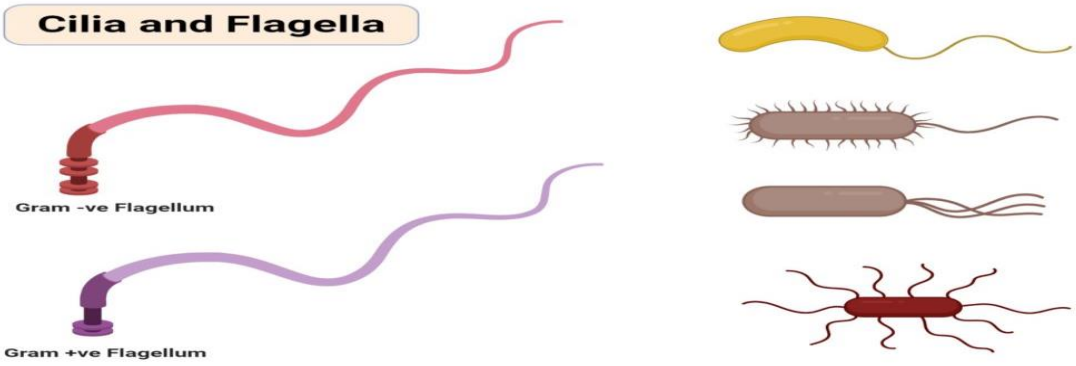


Figure: Cilia and Flagella, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- The most critical role of cilia and flagella is movement. These are responsible for the movement of the organisms as well as for the movement of various particles present around the organisms.
- Some cilia present in some particular organs may have the function of sense. The cilium in the blood vessels, which helps in controlling the flow of blood is an example.

CYTOPLASM

- Cytoplasm refers to everything present inside the cell except the nucleus.

Structure

- The cytoplasm consists of a cytosol; a gel-like substance that contains other matter; cell organelles; smaller cell-like bodies bound by separate membranes; and cytoplasmic inclusions; insoluble molecules that store energy and are not surrounded by any layer.
- The cytoplasm is colorless and has about 80% water along with various nutrients required for the cell.

- It is known to have the properties of both viscous matters as well as elastic matter. Under its elasticity, cytoplasm helps in the movement of materials inside the cell by a process termed cytoplasmic streaming.

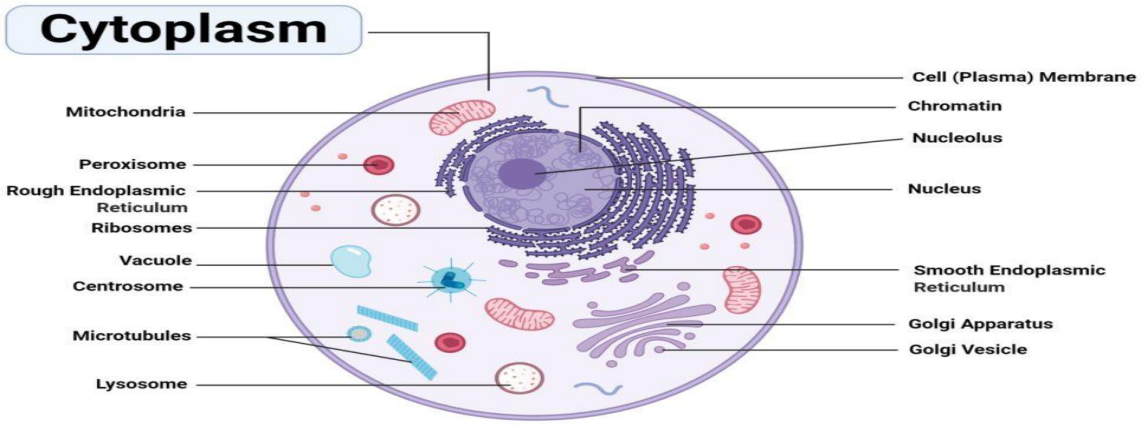


Figure: Animal Cell Structure with Cytoplasm, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- Most of the vital cellular and enzymatic reactions like cellular respiration and translation of mRNA into proteins occur in the cytoplasm.
- It acts as a buffer and protects genetic materials as well as other organelles from damage due to collision or change in the pH of the cytosol.
- The process called cytoplasmic streaming helps in the distribution of various nutrients and facilitates the movement of cell organelles within the cell.

CYTOSKELETON

- A number of fibrous structures are present in the cytosol that helps give shape to the cell while supporting cellular transport.

Structure

- Around three different classes of fibers make up the cytoskeleton which is: microtubules, microfilaments, and intermediate filaments.
- These are separated based on a protein present in them.

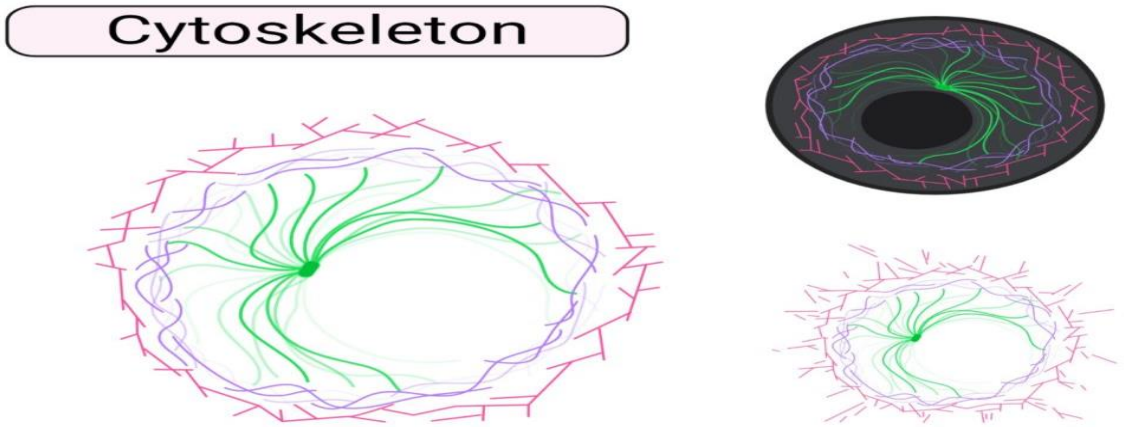


Figure: Cytoskeleton, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- The critical function of the cytoskeleton is to provide shape and mechanical support to the cell against deformation.
- It allows the expansion and contraction of the cell which assists in the movement of the cell.
- It is also involved in intracellular and extracellular transport of materials.

Endoplasmic Reticulum (ER)

- Endoplasmic Reticulum (ER) is present as an interconnection of tubules that are connected to the nuclear membrane in eukaryotic cells.
- There are two types of ER based on the presence or absence of ribosomes on them:
  - Rough ER (RER) with ribosomes attached on the cytosolic face of Endoplasmic Reticulum and thus is involved in protein synthesis
  - Smooth ER (SER) which lacks ribosomes and has a function during lipid synthesis.

Structure

- Endoplasmic Reticulum exists in three forms viz. cisternae, vesicles, and tubules.

- Cisternae are sac-like flattened, unbranched structures that remain stacked one on top of another.
- Vesicles are spherical structures that carry proteins throughout the cell.
- Tubules are tubular branched structures forming a connection between cisternae and vesicles.

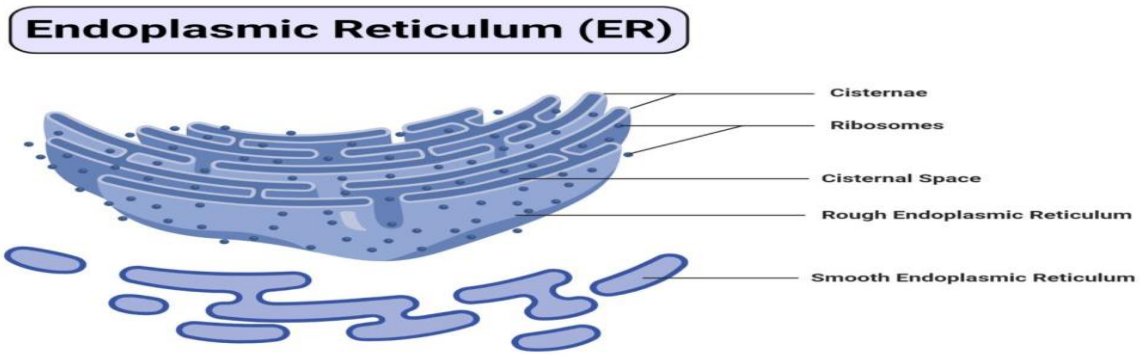


Figure: Endoplasmic Reticulum (ER), Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- ER contains many of the enzymes required for several metabolic processes, and the surface of the ER is essential for other operations like diffusion, osmosis, and active transport.
- One of the crucial functions of ER is the synthesis of lipids like cholesterol and steroids.
- Rough ER allows for the modification of polypeptides emerging out of the ribosomes to prepare secondary and tertiary structures of the protein.
- ER also synthesizes various membrane proteins and has a crucial role in preparing the nuclear envelope after cell division.

Endosomes

- Endosomes are membrane-bound compartments within a cell originating from the Golgi network

Structure

- There are different types of endosomes based on morphology and the time it takes for the endocytosed materials to reach them.
- The early endosomes are made with the tubular-vesicular network while the late endosomes lack tubules but contain many close-packed intraluminal vesicles. The recycling endosomes are found with microtubules and are mainly composed of tubular structures.

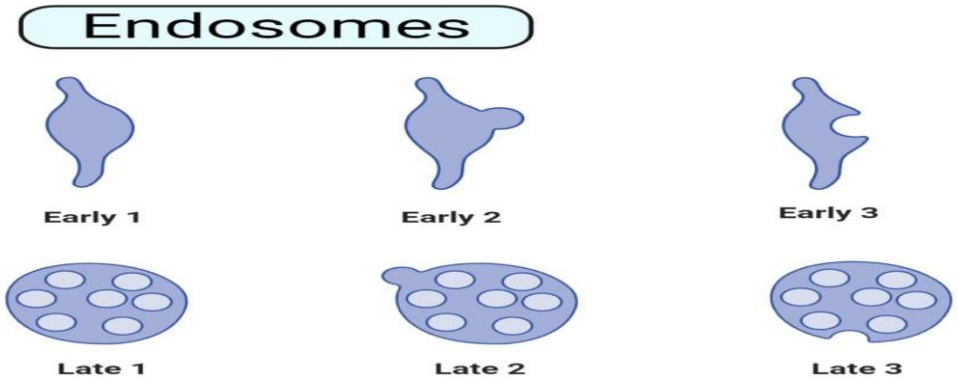


Figure: Endosomes, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- Endosomes allow the sorting and delivery of internalized materials from the cell surface and transport of materials to the Golgi or the lysosomes.

GOLGI APPARATUS/ GOLGI COMPLEX/ GOLGI BODY

- The Golgi apparatus is the cell organelle mostly present in eukaryotic cells which is responsible for the packaging of macromolecules into vesicles so that they can be sent out to their site of action.

Structure

- The structure of the Golgi Complex is pleomorphic; however, it typically exists in three forms, i.e. cisternae, vesicles, and tubules.

- The cisternae, which is the smallest unit of Golgi Complex, has a flattened sac-like structure which is arranged in bundles in a parallel fashion.
- Tubules are present as tubular and branched structures that radiate from the cisternae and are fenestrated at the periphery.
- Vesicles are spherical bodies that are divided into three groups as transitional vesicles, secretory vesicles, and clathrin-coated vesicles.

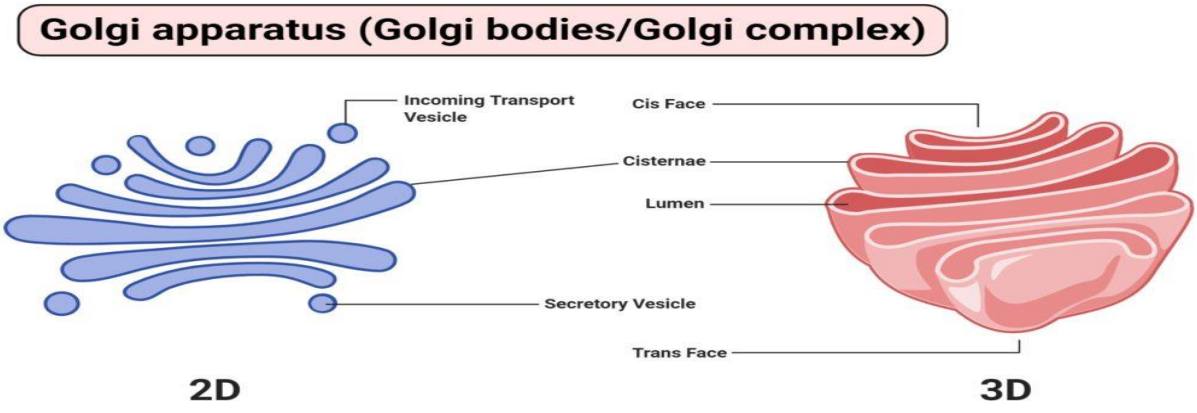


Figure: Golgi apparatus (Golgi bodies/Golgi complex), Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- Golgi Complex has an essential purpose of directing proteins and lipids to their destination and thus, act as the "traffic police" of the cell.
- They are involved in the exocytosis of various products and proteins like zymogen, mucus, lactoprotein, and parts of the thyroid hormone.
- Golgi Complex is involved in the synthesis of other cell organelles like a cell membrane, lysozymes, among others.
- They are also involved in the sulfation of various molecules.

INTERMEDIATE FILAMENTS

- The third class of filament that makes up the cytoskeleton are the intermediate filaments.

- They are designated at intermediate filaments because of the intermediate diameter of the filaments as compared to microfilaments and myosin proteins.

Structure

- Intermediate filaments contain a family of related proteins.
- The individual filaments are coiled around each other in a helical structure called coiled-coil structure.

Functions

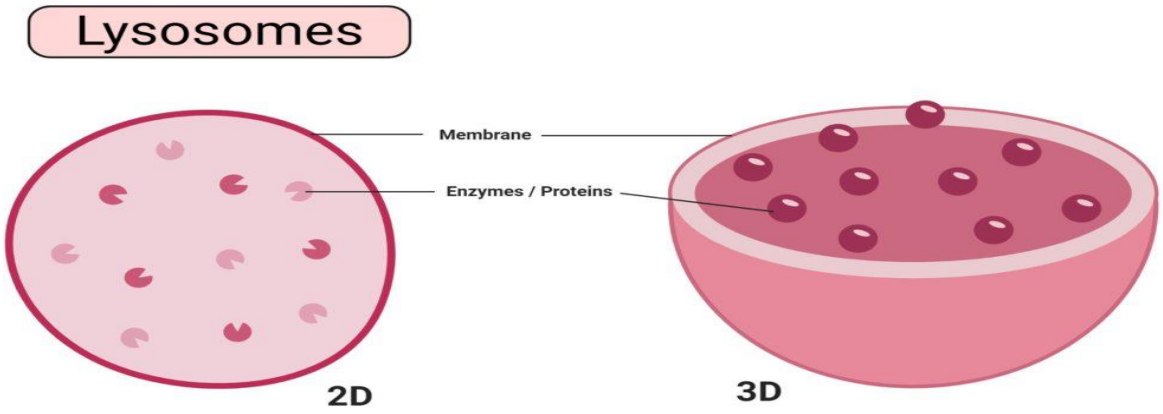
- Intermediate filaments contribute to the structural integrity of a cell while playing a crucial role in holding tissues of various organs like the skin.

LYSOZYME

- Lysozymes are membrane-bound organelles that occur in the cytoplasm of animal cells.
- These organelles contain an array of hydrolytic enzymes required for the degradation of various macromolecules.
- There are two types of lysozymes:
  - Primary lysosome containing hydrolytic enzymes like lipases, amylases, proteases, and nucleases.
  - Secondary lysozyme formed by the fusion of primary lysozymes containing engulfed molecules or organelles.

Structure

- The shape of lysozymes is irregular or pleomorphic; however, mostly, they are found in the spherical or granular structure.
- Lysozymes are surrounded by a lysosomal membrane that contains the enzymes within the lysosome and protects the cytosol with the rest of the cell from the harmful action of the enzymes.



Functions

- These organelles are responsible for intracellular digestion where the larger macromolecules are degraded into smaller molecules with the help of enzymes present in them.
- Lysozymes also perform the critical function of the autolysis of unwanted organelles within the cytoplasm.
- Besides these, the lysosome is involved in various cellular processes, including secretion, plasma membrane repair, cell signaling, and energy metabolism.

MICROFILAMENTS

- Microfilaments are a part of the cytoskeleton of a cell made up of actin protein in the form of parallel polymers.
- These are the smallest filaments of the cytoskeleton with high rigidity and flexibility, providing strength and movement to the cell.

Structure

- The filaments are present either in cross-linked forming networks or as bundles. The chains of protein remain twisted around each other in a helical arrangement.

- One of the polar ends of the filament is positively charged and barbed, whereas the other end is negatively charged and pointed.

Functions

- It generates the strength for the structure and movement of the cell in association with myosin protein.
- They help in cell division and are involved in the products of various cell surface projections.

MICROTUBULES

- Microtubules are also a part of the cytoskeleton differing from microfilaments in the presence of tubulin protein

Structure

- They are long hollow, beaded tubular structure of diameter of about 24nm.
- The wall of the microtubules consists of globular subunits present at a helical array of a and b tubulin.
- Similar to microfilaments, the ends of microtubules also have a defined polarity with one end being positively charged while the other being negatively charged.

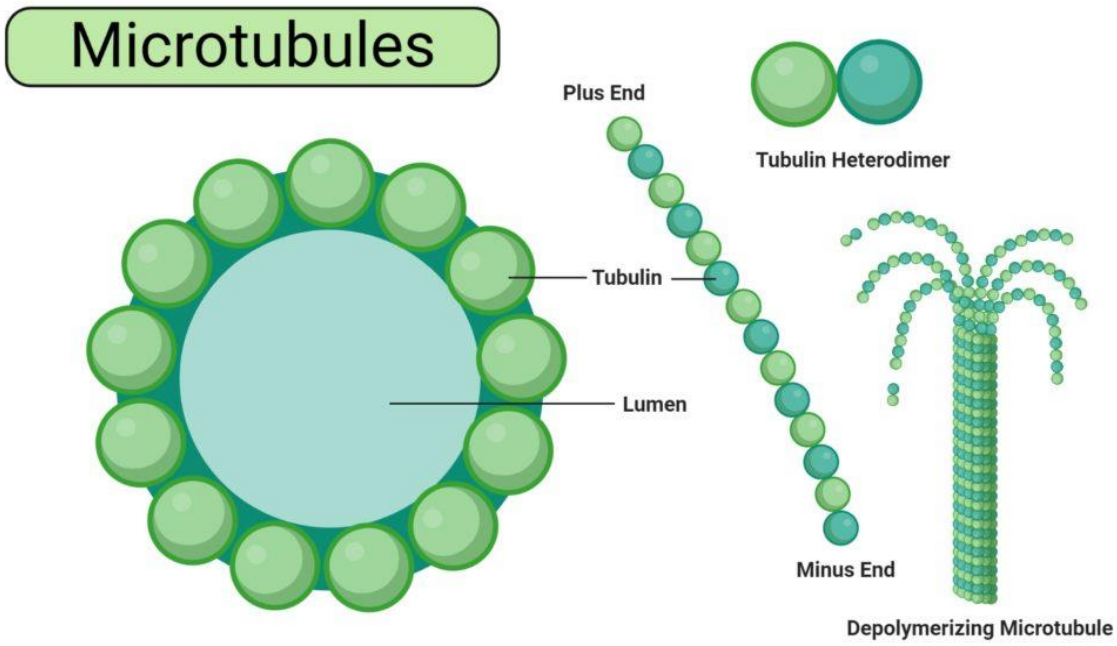


Figure: Microtubules, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- As a part of the cytoskeleton, they provide shape and movement to the cell.
- Microtubules facilitate the movement of other cell organelles within the cell through binding proteins.

MICROVILLI

- Microvilli are tiny finger-like structures that project on or out of the cells. These exist either on their own or in conjunction with villi.

Structure

- Microvilli are bundles of protuberances loosely arranged on the surface of the cell with little or no cellular organelles.
- These are surrounded by a plasma membrane enclosing cytoplasm and microfilaments.
- These are bundles of actin filaments bound by fimbrin, villin, and epsin.

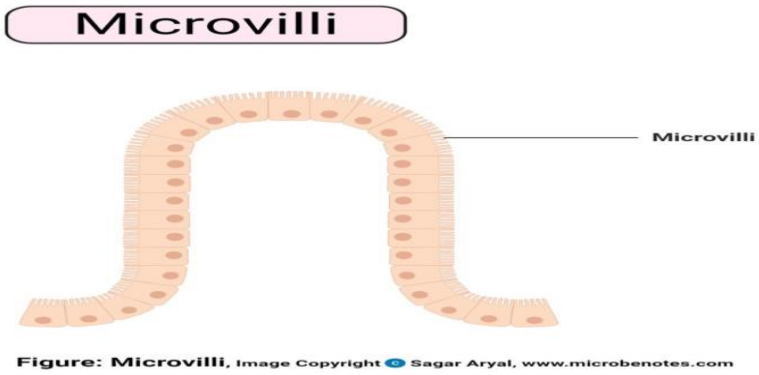


Figure: Microvilli, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- Microvilli increase the surface area of the cell, thus, enhancing the absorption and secretion functions.
- The membrane of microvilli is packed with enzymes that allow the break down of larger molecules into smaller allowing more effective absorption.
- Microvilli act as an anchoring agent in white blood cells and in sperms during fertilization.

MITOCHONDRIA

- Mitochondria are double membrane-bound cell organelles responsible for the supply and storage of energy for the cell.
- The oxidation of various substrates in the cell to release energy in the form of ATP (Adenosine Triphosphate) is the primary purpose of mitochondria.

Structure

- A mitochondrion contains two membranes with the outer layer being smooth while the inner layer is marked with folding and finger-like structures called cristae.
- The inner mitochondrial membrane contains various enzymes, coenzymes, and components of multiple cycles along with pores for the transport of substrates, ATP, and phosphate molecules.

- Within the membranes is a matrix that contains various enzymes of metabolic processes like Kreb's cycle.
- In addition to these enzymes, mitochondria are also home to single or double-stranded DNA called mtDNA that is capable of producing 10% of the proteins present in the mitochondria.

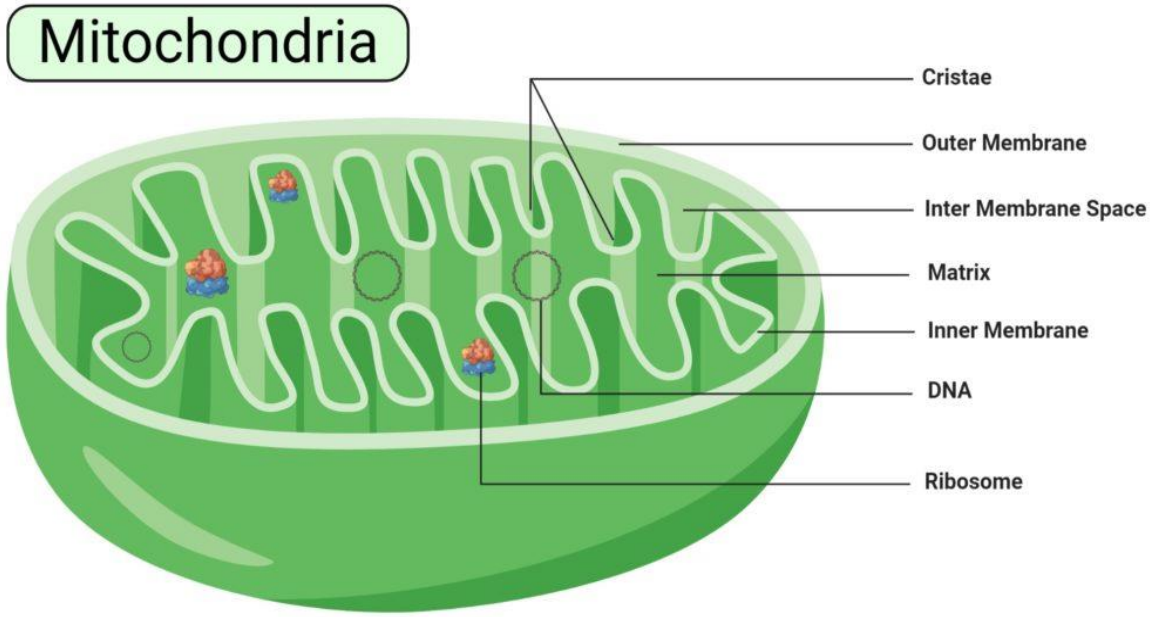


Figure: Mitochondria, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- The primary function of mitochondria is the synthesis of energy in the form of ATP required for the proper functioning of all the cell organelles.
- Mitochondria also help in balancing the amount of Ca+ ions within the cell and assists the process of apoptosis.
- Different segments of hormones and components of blood are built within mitochondria.
- Mitochondria in the liver have the ability to detoxify ammonia.

NUCLEUS

- The nucleus is a double membrane-bound structure responsible for controlling all cellular activities as well as a center for genetic materials, and it's transferring.
- It is one of the large cell organelles occupying 10% of total space in the cell.
- It is often termed the "brain of the cell" as it provides commands for the proper functioning of other cell organelles.
- A nucleus is clearly defined in the case of a eukaryotic cell; however, it is absent in prokaryotic organisms with the genetic material distributed in the cytoplasm.

Structure

- Structurally, the nucleus consists of a nuclear envelope, chromatin, and nucleolus.
- The nuclear envelope is similar to the cell membrane in structure and composition. It has pores that allow the movement of proteins and RNA in and outside the nucleus. It enables the interaction with other cell organelles while keeping nucleoplasm and chromatin within the envelope.
- The chromatin in the nucleus contains RNA or DNA along with nuclear proteins, as genetic material that is responsible for carrying the genetic information from one generation to another. It is present in a sense and compact structure which might be visible as chromosome under powerful magnification.
- The nucleolus is like a nucleus within the nucleus. It is a membrane-less organelle that is responsible for the synthesis of rRNA and assembly of ribosomes required for protein synthesis.

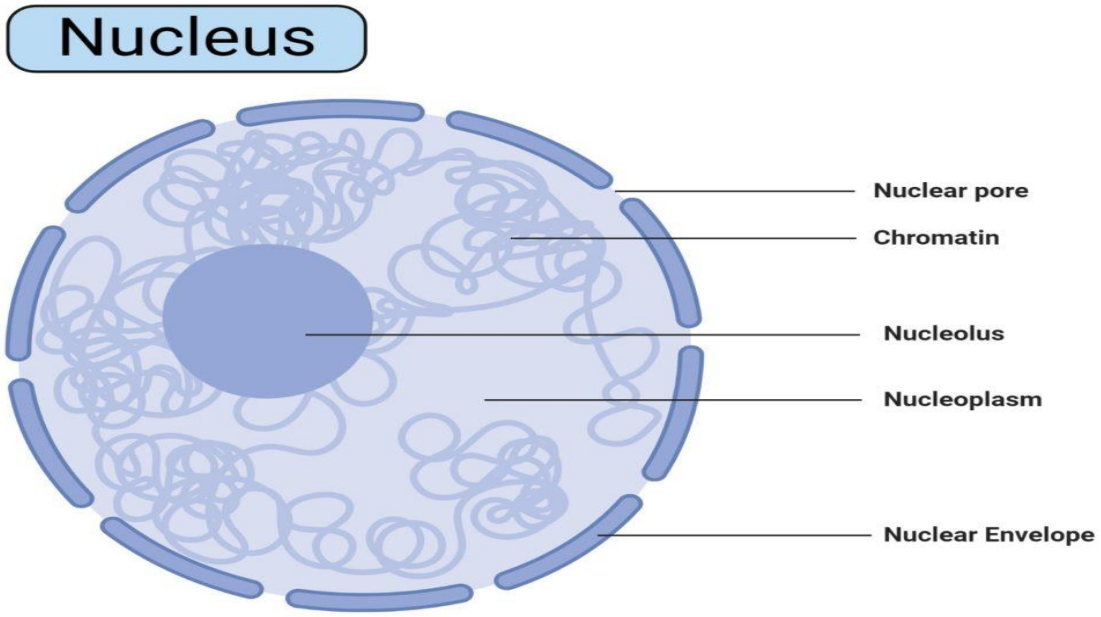


Figure: Nucleus, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- The nucleus is responsible for storage as well as the transfer of genetic materials in the form of DNA or RNA.
- It aids in the process of transcription by the synthesis of mRNA molecules.
- The nucleus controls the activity of all other organelles while facilitating processes like cell growth, cell division and synthesis of proteins.

PEROXISOMES

- Peroxisomes are oxidative membrane-bound organelles found in the cytoplasm of all eukaryotes.
- The name is accredited due to their hydrogen peroxide generating and removing activities.

Structure

- Peroxisome consists of a single membrane and granular matrix scattered in the cytoplasm.

- They exist either in the form of interconnected tubules or as individual peroxisomes.
- The compartments within every peroxisome allow the creation of optimized conditions for different metabolic activities.
- They consist of several types of enzymes with major groups being urate oxidase, D-amino acid oxidase, and catalase.

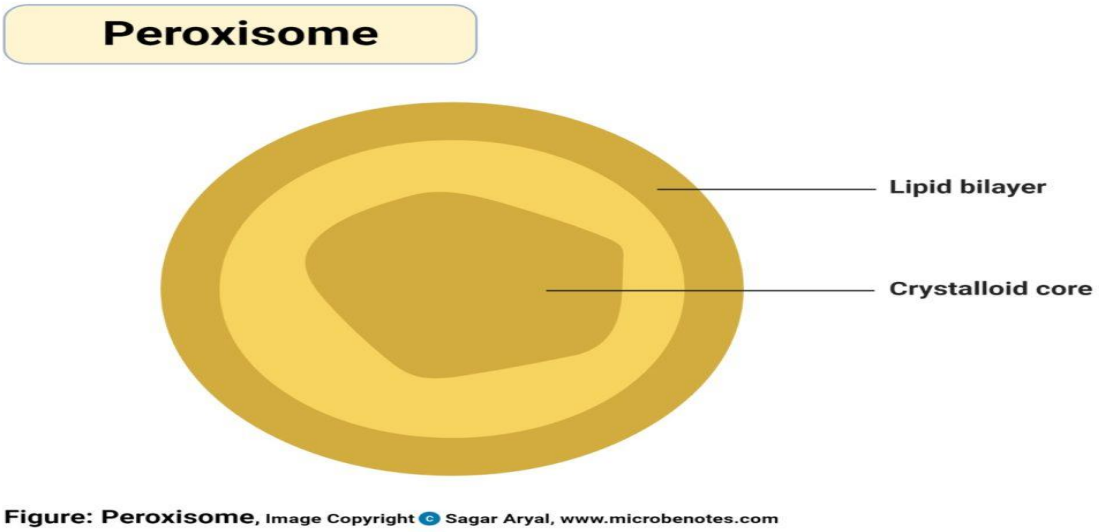


Figure: Peroxisome, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- Peroxisomes are involved in the production and elimination of hydrogen peroxide during biochemical processes.
- Oxidation of fatty acids takes place within peroxisomes.
- Additionally, peroxisomes are also involved in the synthesis of lipid-like cholesterol and plasmalogens.

PLASMODESMATA

- Plasmodesmata are tiny passages or channels that allow the transfer of material and communication between different cells.

Structure

- There are 103 – 105 number of plasmodesmata connecting two adjacent cells with 50-60 nm in diameter.
- A plasmodesma has three layers:
  - The plasma membrane is continuous with the plasma membrane of the cell and has the same phospholipid bilayer.
  - The cytoplasmic sleeve that is continuous with the cytosol that allows the exchange of materials between two cells.
  - Desmotubule which is a part of the endoplasmic reticulum that provides a network between two cells and allows the transport of some molecules.

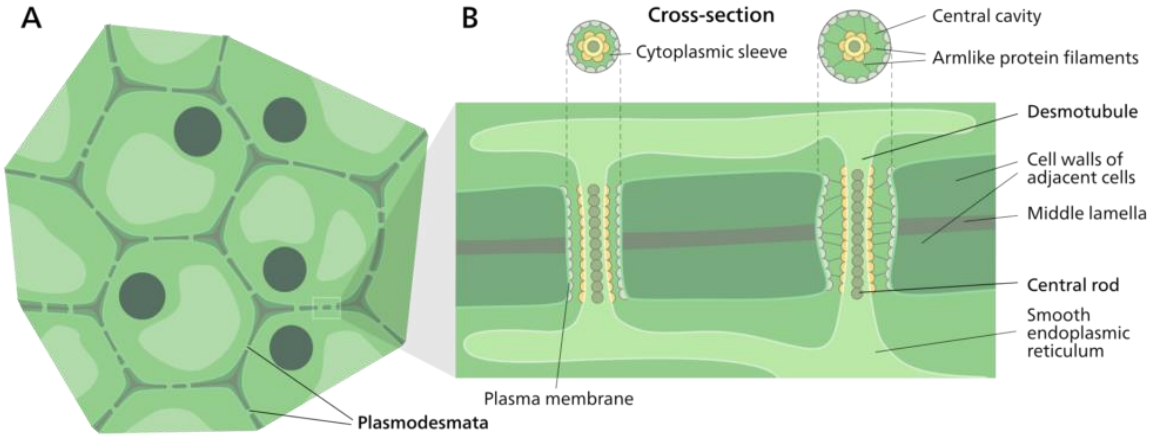


Figure: Diagram of Plasmodesmata.

Functions

- Plasmodesmata are the primary site for the communication of two cells. It allows the transfer of molecules like proteins, RNA, and viral genomes.

PLASTIDS

- Plastids are double membrane-bound structures present in plants and other eukaryotes involved in the synthesis and storage of food.

Structure

- Plastids are usually oval or spherical with an outer and an inner membrane between which lies the intermembrane space.

- The inner membrane enclosed a matrix called stroma that contains small structures called grana.
- Each granum consists of several sac-like thylakoids piled one on the other and connected by stroma lamellae.
- Plastids contain DNA and RNA that allows it to synthesize necessary proteins for different processes.

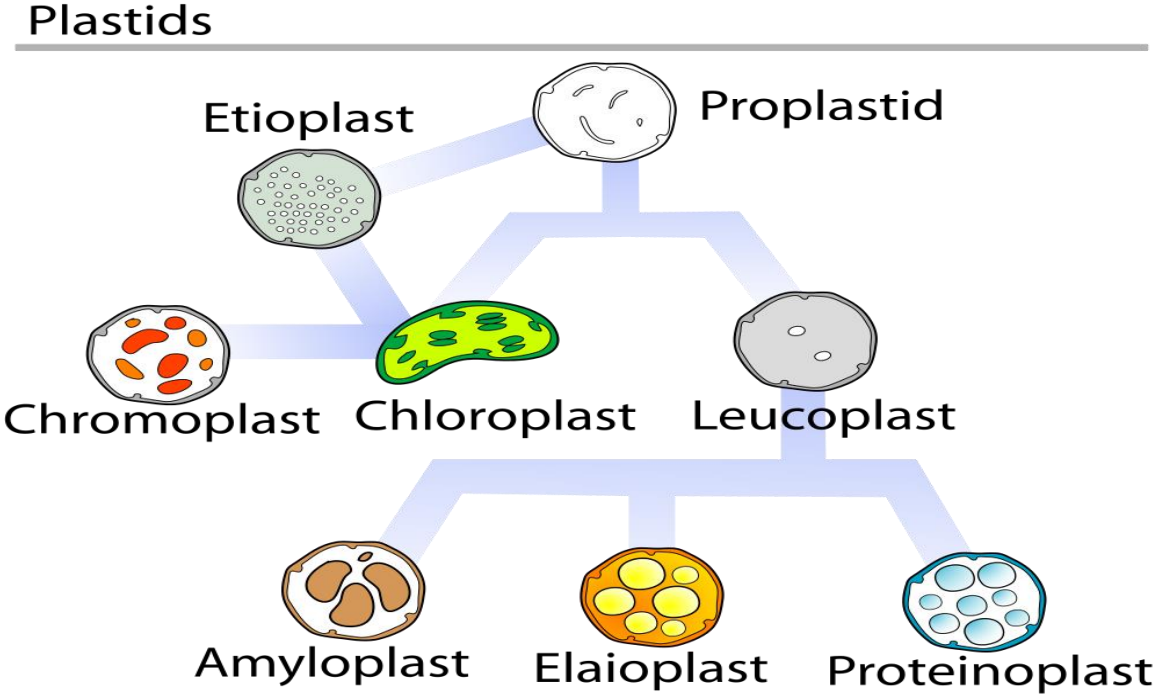


Figure: Diagram of types of plastids.

Functions

- Chloroplasts are the center for many metabolic activities, including photosynthesis as it contains enzymes and other components required for it.
- They are also involved in the storage of food, primarily starch.

RIBOSOMES

- Ribosomes are ribonucleoprotein containing equal parts RNA and proteins along with an array of other essential components required for protein synthesis.

- In prokaryotes, they exist freely while in eukaryotes, they are found either free or attached to the endoplasmic reticulum.

Structure

- The ribonucleoprotein consists of two subunits.
- In the case of prokaryotic cells, the ribosomes are of the 70S with the larger subunit of 50S and the smaller one of 30S.
- Eukaryotic cells have 80S ribosomes with 60S larger subunit and 40S smaller subunit.
- Ribosomes are short-lived as after the protein synthesis, the subunits split up and can be either reused or remain broken up.

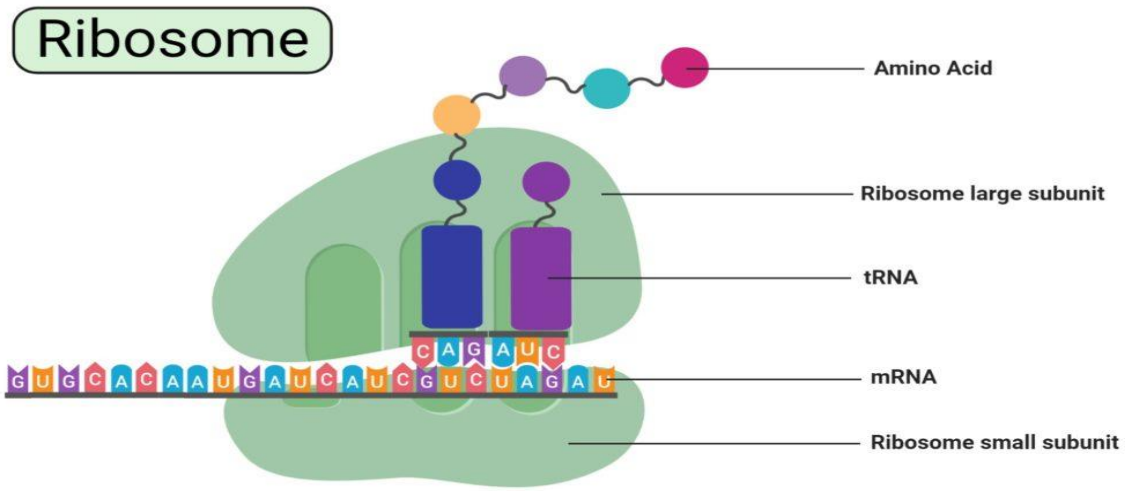


Figure: Ribosome, Image Copyright © Sagar Aryal, www.microbenotes.com

Functions

- Ribosomes are the site of biological protein synthesis in all living organisms.
- They arrange the amino acids in the order indicated by tRNA and assist in protein synthesis.

STORAGE GRANULES

- Storage granules are membrane-bound organelles, also called zymogen granules storing cell's energy reserve and other metabolites.

Structure

- These granules are surrounded by a lipid bilayer and are composed mostly of phosphorus and oxygen.
- The components inside these storage granules depend on their location in the body with some even containing degradative enzymes yet to participate in digestive activities.

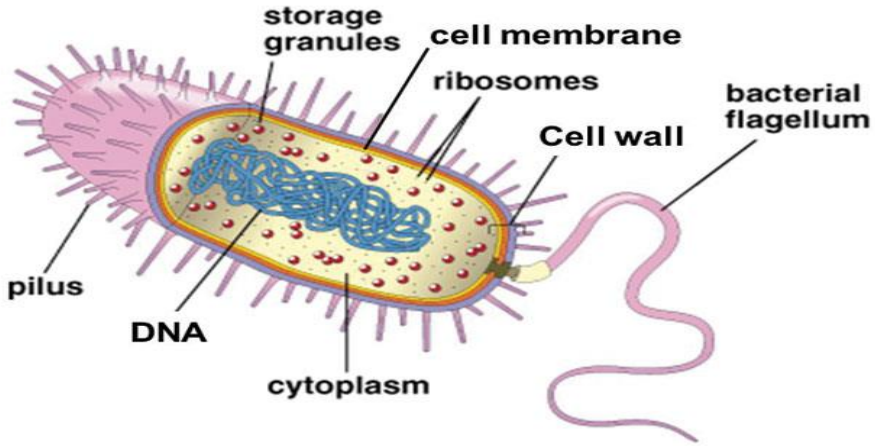


Figure: Diagram of Storage Granules.

Functions

- Many prokaryotes and eukaryotes store nutrients and reserves in the form of storage granules in the cytoplasm.
- Sulfur granules are characteristic of prokaryotes that utilize hydrogen sulfide as a source of energy.

VESICLES

- Vesicles are structures present inside the cell which are either formed naturally during processes like exocytosis, endocytosis or transport of materials throughout the cell, or they might form artificially, which are called liposomes.
- There are different types of vesicles like vacuoles, secretory and transport vesicles based on their function

Structure

- A vesicle is a structure containing liquid or cytosol which is enclosed by a lipid bilayer.
- The outer layer enclosing the liquid is called a lamellar phase which is similar to the plasma membrane. One end of the lipid bilayer it hydrophobic whereas the other end is hydrophilic.

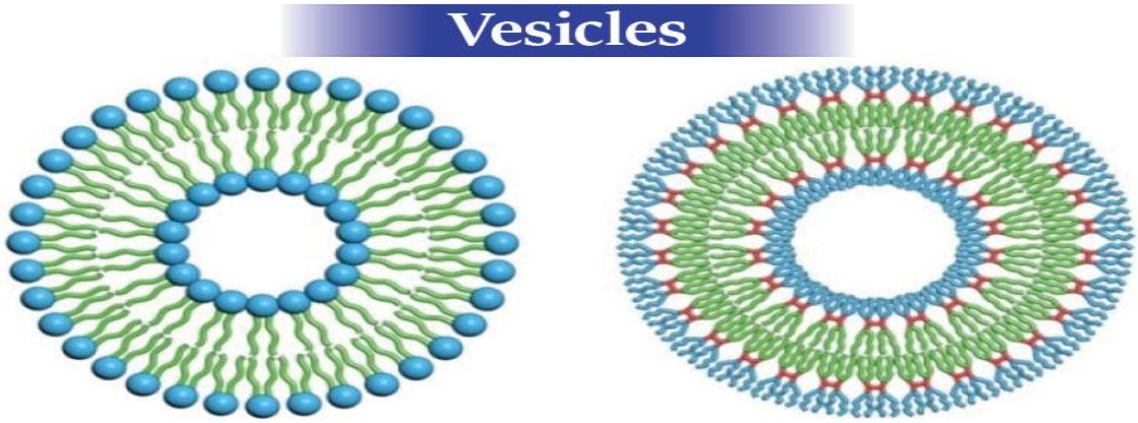


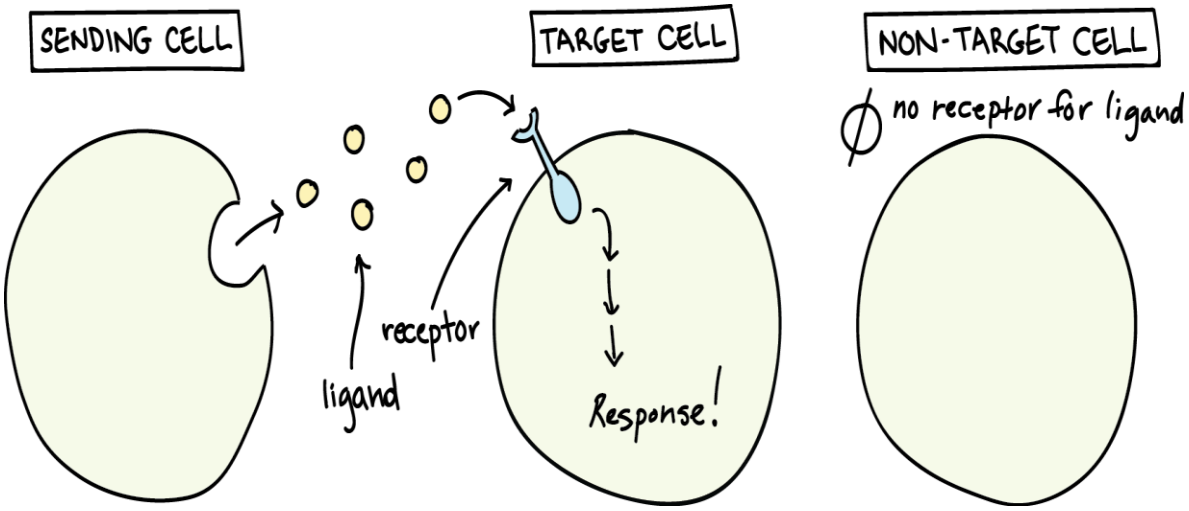
Figure: A liposome (left) and dendrimersome. The blue parts of their molecules are hydrophilic, the green parts are hydrophobic. Credit: Image courtesy of University of Pennsylvania

Functions

- Vesicles facilitate the storage and transport of materials in and outside the cell. It even allows the exchange of molecules between two cells.
- Because vesicles are enclosed inside a lipid bilayer, vesicles also function in metabolism and enzyme storage.
- They allow temporary storage of food and also control the buoyancy of the cell.

Overview of cell signalling

Cells typically communicate using chemical signals. These chemical signals, which are proteins or other molecules produced by a **sending cell**, are often secreted from the cell and released into the extracellular space. There, they can float – like messages in a bottle – over to neighboring cells.



Sending cell: this cell secretes a ligand.

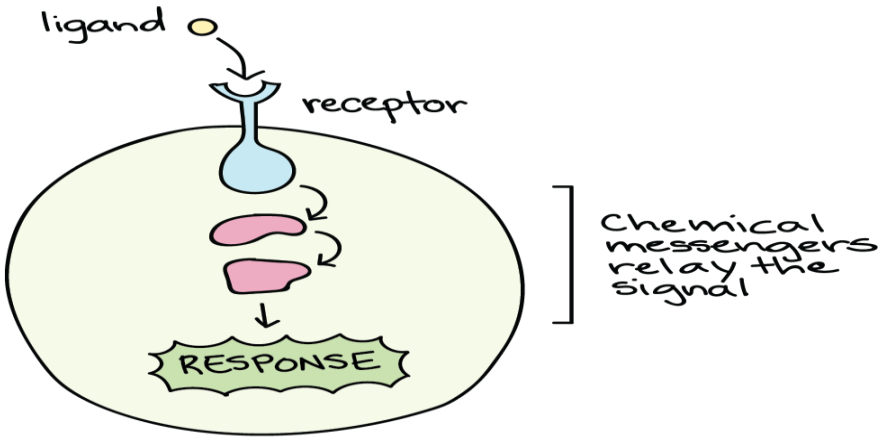
Target cell: this cell has a receptor that can bind the ligand. The ligand binds to the receptor and triggers a signaling cascade inside the cell, leading to a response.

Nontarget cell: this cell does not have a receptor for the ligand (though it may have other kinds of receptors). The cell does not perceive the ligand and thus does not respond to it.

Not all cells can "hear" a particular chemical message. In order to detect a signal (that is, to be a **target cell**), a neighbour cell must have the right **receptor** for that signal. When a signalling molecule binds to its receptor, it alters the shape or activity of the receptor, triggering a change inside of the cell. Signalling molecules are often called **ligands**, a general term for molecules that bind specifically to other molecules (such as receptors).

The message carried by a ligand is often relayed through a chain of chemical messengers inside the cell. Ultimately, it leads to a change in the cell, such as alteration in the activity of a gene or even the induction of a whole process, such

as cell division. Thus, the original **intercellular** (between-cells) signal is converted into an **intracellular** (within-cell) signal that triggers a response.



Forms of signalling

Cell-cell signalling involves the transmission of a signal from a sending cell to a receiving cell. However, not all sending and receiving cells are next-door neighbors, nor do all cell pairs exchange signals in the same way.

There are four basic categories of chemical signaling found in multicellular organisms: paracrine signaling, autocrine signaling, endocrine signaling, and signaling by direct contact. The main difference between the different categories of signaling is the distance that the signal travels through the organism to reach the target cell.

Paracrine signalling

Often, cells that are near one another communicate through the release of chemical messengers (ligands that can diffuse through the space between the cells). This type of signaling, in which cells communicate over relatively short distances, is known as **paracrine signaling**.

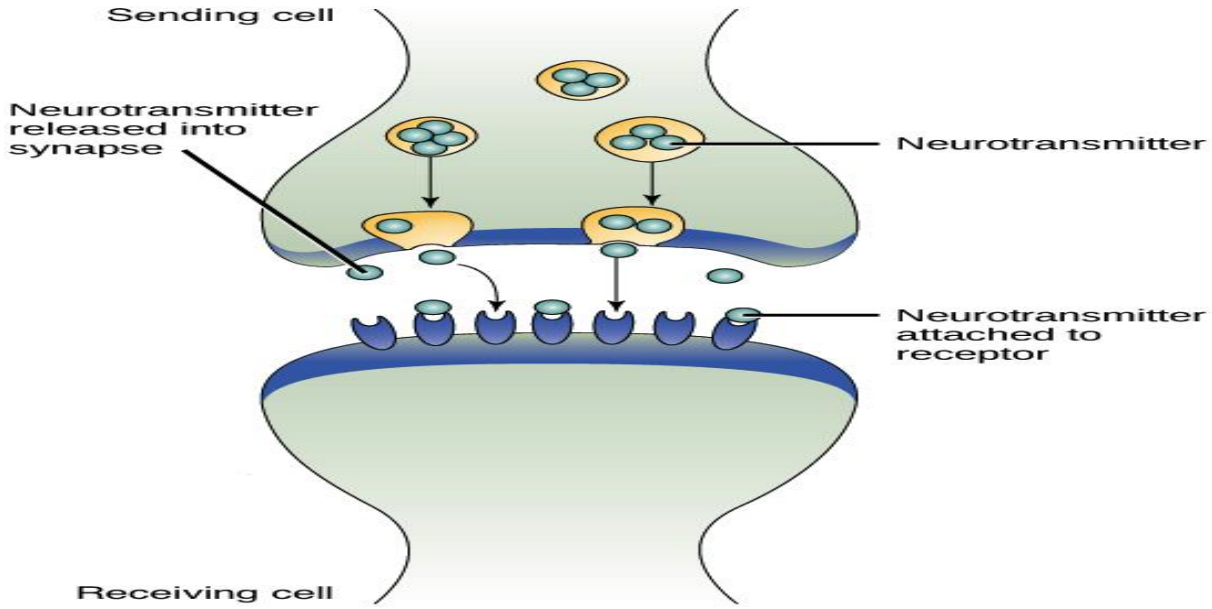
Paracrine signaling allows cells to locally coordinate activities with their neighbors. Although they're used in many different tissues and contexts, paracrine signals are especially important during development, when they allow

one group of cells to tell a neighbouring group of cells what cellular identity to take on.

Synaptic signaling

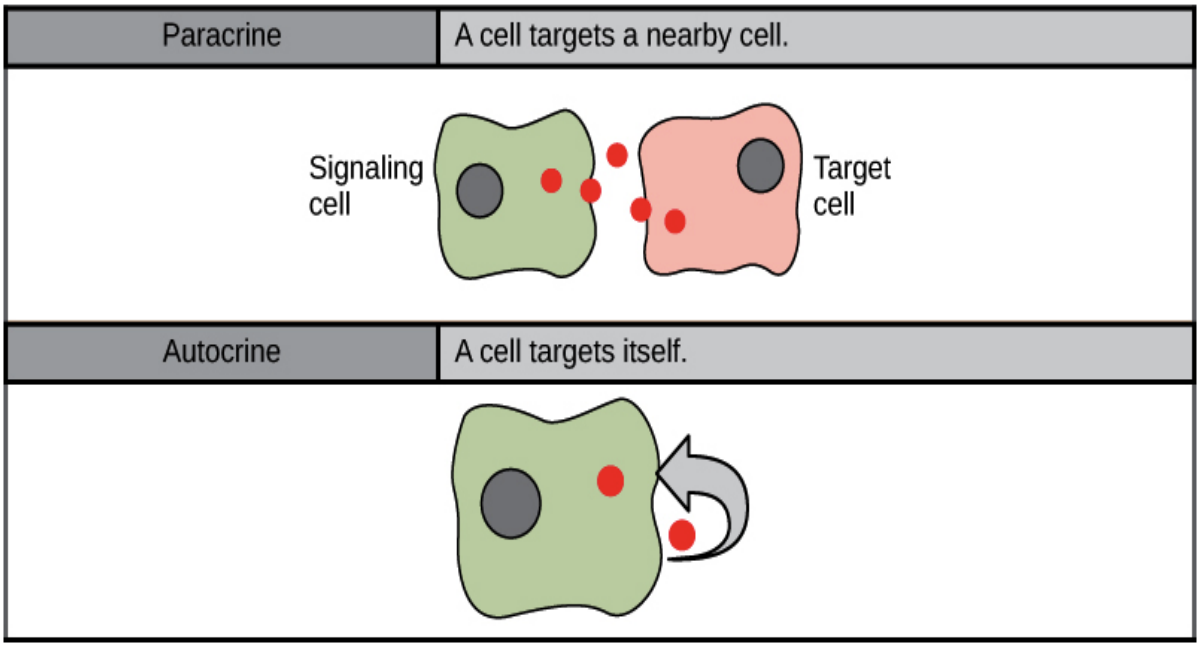
One unique example of paracrine signalling is **synaptic signaling**, in which nerve cells transmit signals. This process is named for the **synapse**, the junction between two nerve cells where signal transmission occurs.

When the sending neuron fires, an electrical impulse moves rapidly through the cell, traveling down a long, fiber-like extension called an axon. When the impulse reaches the synapse, it triggers the release of ligands called **neurotransmitters**, which quickly cross the small gap between the nerve cells. When the neurotransmitters arrive at the receiving cell, they bind to receptors and cause a chemical change inside of the cell (often, opening ion channels and changing the electrical potential across the membrane).



Synaptic signaling. Neurotransmitter is released from vesicles at the end of the axon of the sending cell. It diffuses across the small gap between sending and target neurons and binds to receptors on the target neuron.

The neurotransmitters that are released into the chemical synapse are quickly degraded or taken back up by the sending cell. This "resets" the system so they synapse is prepared to respond quickly to the next signal.



Paracrine signaling: a cell targets a nearby cell (one not attached by gap junctions). The image shows a signaling molecule produced by one cell diffusing a short distance to a neighbouring cell.

Autocrine signaling: a cell targets itself, releasing a signal that can bind to receptors on its own surface.

Autocrine signaling

In **autocrine signaling**, a cell signals to itself, releasing a ligand that binds to receptors on its own surface (or, depending on the type of signal, to receptors inside of the cell). This may seem like an odd thing for a cell to do, but autocrine signaling plays an important role in many processes.

For instance, autocrine signaling is important during development, helping cells take on and reinforce their correct identities. From a medical standpoint, autocrine signaling is important in cancer and is thought to play a key role in

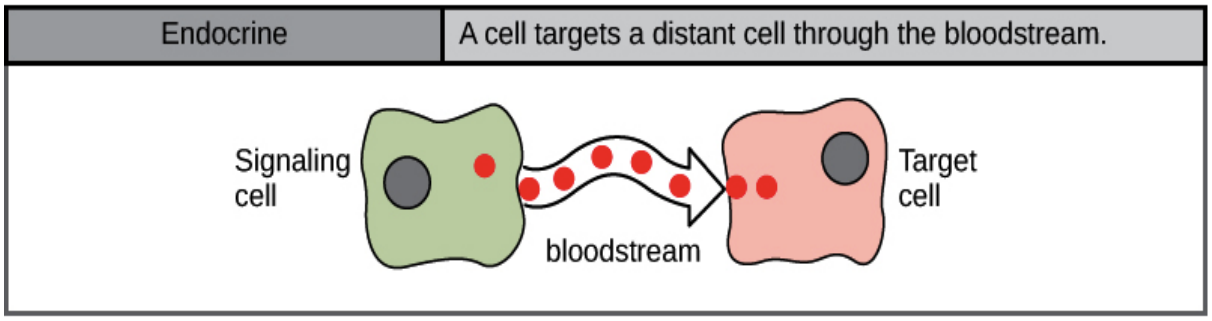
metastasis (the spread of cancer from its original site to other parts of the body. In many cases, a signal may have both autocrine and paracrine effects, binding to the sending cell as well as other similar cells in the area.

Endocrine signaling

When cells need to transmit signals over long distances, they often use the circulatory system as a distribution network for the messages they send. In long-distance **endocrine signaling**, signals are produced by specialized cells and released into the bloodstream, which carries them to target cells in distant parts of the body. Signals that are produced in one part of the body and travel through the circulation to reach far-away targets are known as **hormones**.

In humans, endocrine glands that release hormones include the thyroid, the hypothalamus, and the pituitary, as well as the gonads (testes and ovaries) and the pancreas. Each endocrine gland releases one or more types of hormones, many of which are master regulators of development and physiology.

For example, the pituitary releases **growth hormone** (**GH**), which promotes growth, particularly of the skeleton and cartilage. Like most hormones, GH affects many different types of cells throughout the body. However, cartilage cells provide one example of how GH functions: it binds to receptors on the surface of these cells and encourages them to divide^7 7start superscript, 7, end superscript.

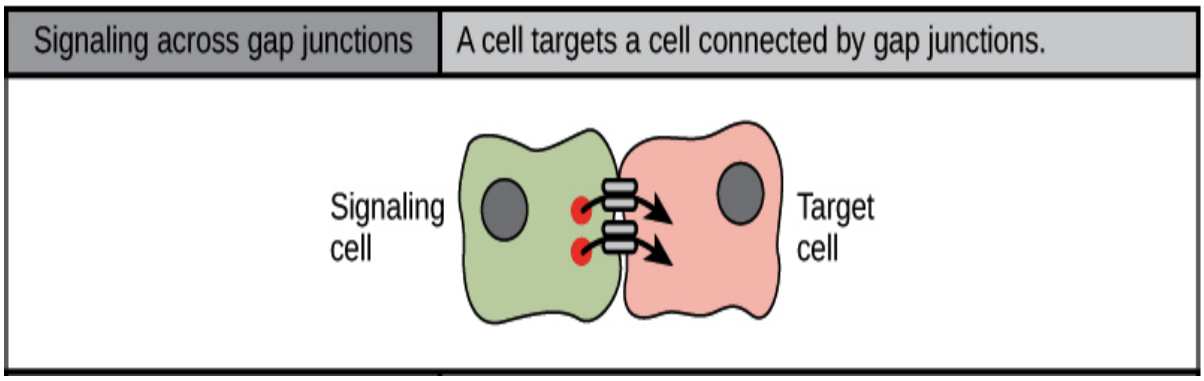


Endocrine signaling: a cell targets a distant cell through the bloodstream. A signaling molecule is released by one cell, then travels through the bloodstream to bind to receptors on a distant target cell elsewhere in the body.

Signaling through cell-cell contact

Gap junctions in animals and plasmodesmata in plants are tiny channels that directly connect neighboring cells. These water-filled channels allow small signaling molecules, called **intracellular mediators**, to diffuse between the two cells. Small molecules and ions are able to move between cells, but large molecules like proteins and DNA cannot fit through the channels without special assistance.

The transfer of signaling molecules transmits the current state of one cell to its neighbor. This allows a group of cells to coordinate their response to a signal that only one of them may have received. In plants, there are plasmodesmata between almost all cells, making the entire plant into one giant network.

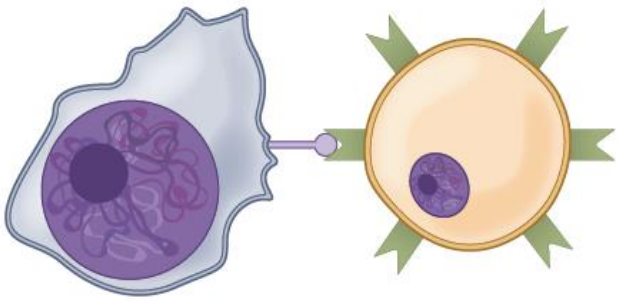


Signaling across gap junctions. A cell targets a neighboring cell connected via gap junctions. Signals travel from one cell to the other by passing through the gap junctions.

In another form of direct signaling, two cells may bind to one another because they carry complementary proteins on their surfaces. When the proteins bind to one another, this interaction changes the shape of one or both proteins, transmitting a signal. This kind of signaling is especially important in the immune

system, where immune cells use cell-surface markers to recognize “self” cells (the body's own cells) and cells infected by pathogens^{9}9start superscript, 9, end superscript.

A natural killer (NK) immune cell recognizes a healthy cell of the body by binding to a "self" marker on the cell's surface.



NK cell Healthy cell

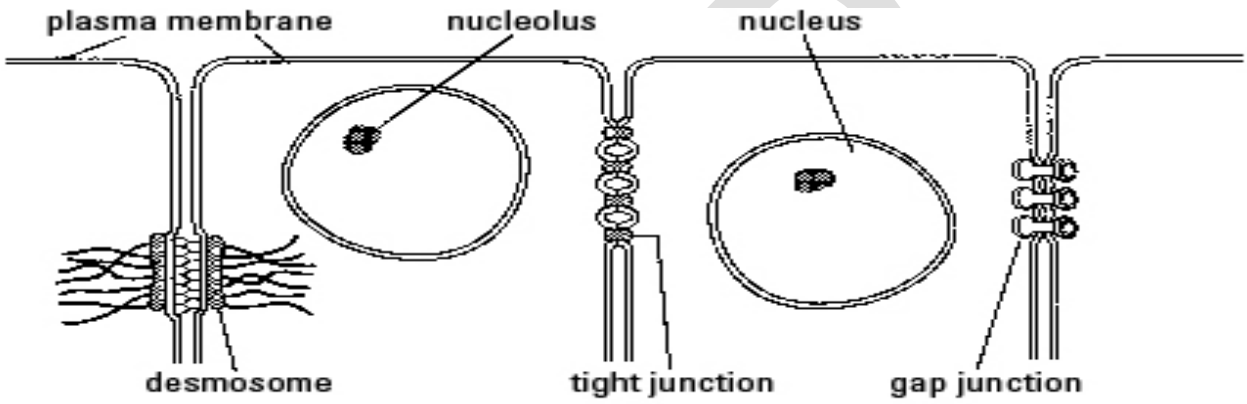
Cell Junctions

The plasma membranes of adjacent cells are usually separated by extracellular fluids that allow transport of nutrients and wastes to and from the bloodstream. In certain tissues, however, the membranes of adjacent cells may join and form a junction. As shown in Figure 1, three kinds of cell junctions are recognized:

- **Desmosomes** are protein attachments between adjacent cells. Inside the plasma membrane, a desmosome bears a disk-shaped structure from which protein fibers extend into the cytoplasm. Desmosomes act like spot welds to hold together tissues that undergo considerable stress (such as skin or heart muscle).
- **Tight junctions** are tightly stitched seams between cells. The junction completely encircles each cell, preventing the movement of material between the cells. Tight junctions are characteristic of cells lining the digestive tract, where materials are required to pass through cells (rather than intercellular spaces) to penetrate the bloodstream.

- **Gap junctions** are narrow tunnels between cells that consist of proteins called connexons. The proteins allow only the passage of ions and small molecules. In this manner, gap junctions allow communication between cells through the exchange of materials or the transmission of electrical impulses.

The three types of cell junctions.



Cell Junctions

CELL CYCLE

The cell cycle is the sequence of events occurring in an ordered fashion which results in cell growth and cell division.

- The cycle begins at the end of each nuclear division and ends with the beginning of the next.
- A cell cycle acts as a unit of biological time that defines the life history of the cell.
- The cell cycle is a continuous process that includes all significant events of the cell, ranging from duplication of DNA and cell organelles to subsequent partitioning of the cytoplasm.
- In addition, the process of cell growth where the cell absorbs nutrients and prepares for its cell division is also a part of the cell cycle.

- The process of the cell cycle occurs in various phases, all of which are specialized for a particular stage of the cell.
- The overall process and steps of the cell cycle might differ in eukaryotic and prokaryotic organisms as a result of the differences in their cell complexity.
- Three main cycles are involved in the cell cycle; chromosome cycle, cytoplasmic cycle, and centrosome cycle.
- The chromosome cycle involves DNA synthesis that alternates with mitosis. During this cycle, the double-helical DNA of the cell replicates to form two identical daughter DNA molecules. This is followed by mitosis to separate the cell into two daughter cells.
- The cytoplasmic cycle involves cell growth that alternates with cytokinesis. During growth, the cell accumulates nutrients and growth factors and doubles the contents of the cytoplasm. Eventually, the cytoplasm divides via cytokinesis to equally divide the cytoplasmic contents into two cells.
- The final cycle is the centrosome cycle where the centrosome is divided so that it can be inherited reliably and duplicated accordingly to form two poles of the mitotic spindle fibers.
- The cell cycle is regulated by various stimulatory and inhibitory factors that decide whether the cell needs to divide or grow.
- The cell cycle is divided into different phases (according to Howard and Pelc), each of which is defined by various processes.
- Phases of the Cell Cycle
- 1. Gap 0 Phase (G0)
    - Gap 0 phase or G0 phase of the cell cycle is a period of time where the cell is present in a quiescent stage or resting phase, as it neither divides nor grows.

- The G0 phase can be considered either an extended G1 phase or a separate phase-out of the cell cycle.
- Usually, cells enter the G0 phase when they reach maturity like in the case of muscle cells and nerve cells, but the cells continue to perform their function throughout their life.
- In some cases, however, cells might enter the G0 phase from the checkpoint in the G1 phase due to the lack of growth factors or nutrients.
- In the G0 phase, the cell cycle machinery of the cell is dismantled, and the cell continues to remain in the G0 phase until there is a reason for the cell to divide.
- There are some cells like the parenchymal cells of the liver and kidneys that enter the G0 phase semi-permanently and can be induced to divide.
- Even though the G0 phase is often associated as senescence, the G0 phase is a reversible stage where a cell can enter the cell cycle again to divide.
- The cells in the G0 phase have different regulators that ensure the proper functioning of the cell.

2. Gap 1 Phase(G1)

- The G1 phase of the cell cycle is a part of the interphase where the cell begins to prepare for cell division.
- A cell enters the G1 phase after the M phase of the previous cycle, and thus, it is termed as the first gap phase of the first growth phase.
- In this phase, no DNA synthesis takes place, but RNA synthesis occurs in order to produce proteins required for proper cell growth.
- G1 phase is considered a time of resumption where the cell finally picks up normal cell metabolism that had slowed down during the M phase of the previous cycle.

- The process and steps of the G1 phase are highly variable, even within the cells of the same species.
- The most important event of the G1 phase, however, is the transcription of all three types of RNAs which then undergo translation to form proteins and enzymes necessary for other events in the cell cycle.
- The duration of the G1 phase is also highly variable among cells. In some cells, it occupies about 50% of the total cell cycle time, whereas, in rapidly dividing cells, the phase is entirely omitted.
- An important in the G1 phase is the G1/S checkpoint that determines if the cell is ready enough to proceed into the division phase.
- At this point, events like the detection of DNA damage and nutrient concentration are performed to ensure that the cell has enough machinery to undergo cell division.

3. Synthesis Phase (S)

- The S phase or synthesis phase of the cell cycle is a part of the interphase where important events like DNA replication and formation of histone proteins take place.
- The processes of the S phase are tightly regulated as the synthesis of proteins and replication of DNA require utmost precision.
- The production of histone proteins and other proteins are crucial in this phase as the newly replicated DNA molecules require histone proteins to form nucleosomes.
- The entry into the S phase is regulated by the G1/S checkpoint that only allows cells with enough nutrients and healthy DNA to enter the next phase.
- The phase is moderately long, occupying about 30% of the total cell cycle time.

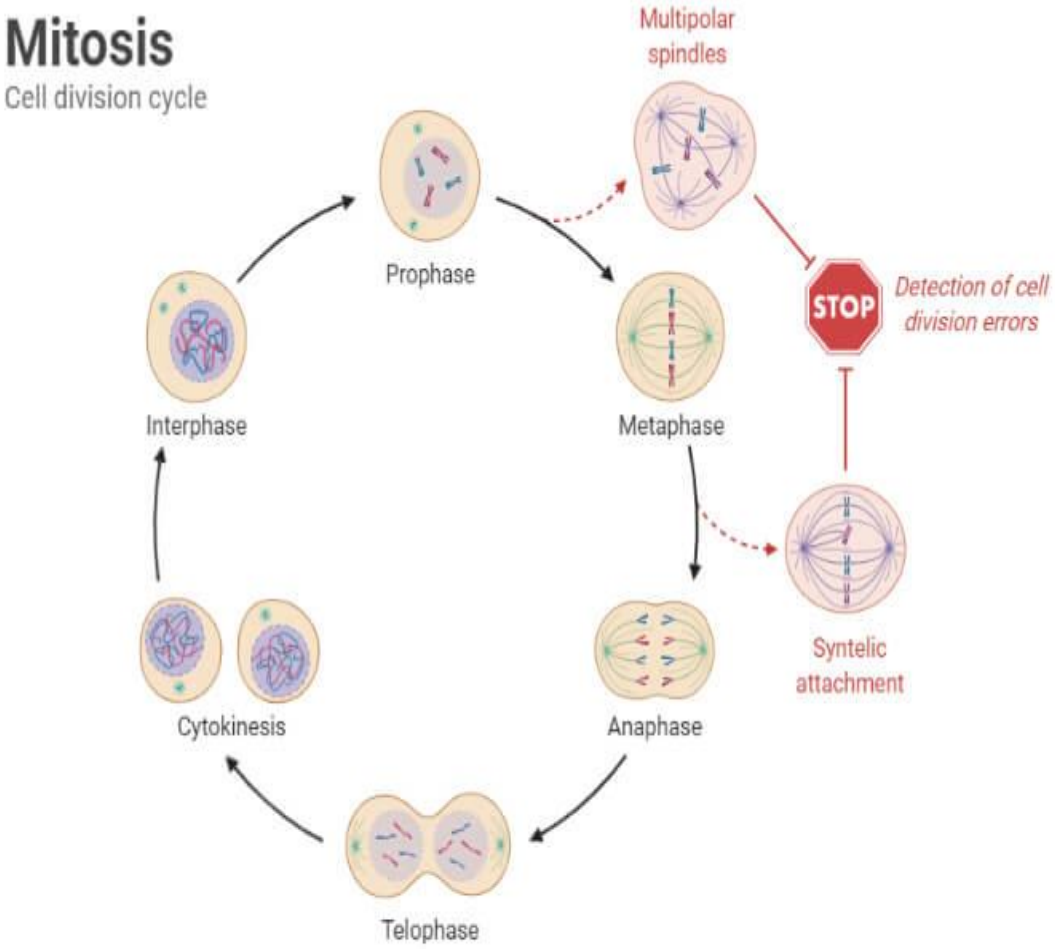
- During this phase, the content of DNA doubles in the cell, but the number of chromosomes remain the same as the division of chromosome doesn't take place just yet.
- The regulatory mechanism of the S phase also ensures that the process of DNA synthesis takes place before the M phase and with precision.
- In order to preserve the epigenetic information, different regions of the DNA are replicated at different times.
- Similarly, actively expressed genes tend to replicate during the first half of the S phase, whereas inactive genes and structural DNA tend to replicate during the latter half.
- Therefore, at the end of the S phase, each chromosome of the cell has double the amount of DNA with a double set of genes.

4. Gap 2 Phase (G2)

- The G2 phase or Gap Phase 2 or Growth Phase 2 is a phase of the cell cycle where the cell collects nutrients and releases proteins in order to prepare the cell for the M phase.
- The G2 phase is also a part of the interphase when the cell is still in the resting phase while preparing for cell division.
- The G2 phase is also important as it checks for DNA damage (during replication) to ensure that the cell is in proper condition to undergo division.
- The phase might be skipped in some rapidly dividing cells that directly enter the mitotic phase after DNA replication.
- It is, however, an essential phase that checks for mutations and DNA damage to prevent excessive cell proliferation.

- Even though information on the regulation and working of the G2 phase has been studied, its role in cancer initiation and development is yet to be determined.
- DNA repair is a crucial step in the G2 phase as it repairs breaks that might be present in the DNA strand after replication.
- The entry of the cell from the G2 phase to the M phase is regulated by the G2 checkpoint, where different proteins and complexes are involved.
- In the case of DNA damage or insufficient nutrients, the cell remains in the G2 phase and is not passed for cell division.

5. Mitosis Phase (M)



- The M phase or Mitotic phase of the cell cycle is the most crucial and dramatic phase of the entire cycle where the cell divides to form identical daughter cells.
- The most important event of this phase is the karyokinesis (nuclear division) where the chromosomes separate into form two distinct cells.
- The process of mitosis might differ from one organism to another and even from one cell to another.

- Mitosis begins with the condensation of chromosomes which then separate and move towards opposite poles.
- A cell entering the M phase has a 4N concentration of genetic material and ends with two cells, each containing a 2N concentration of DNA.
- Mitotic cell division occurs via four distinct steps; prophase, metaphase, anaphase, and telophase.
- Prophase is the first stage of mitosis where the chromosome of the cell divides into two chromatids held together by a unique DNA region called the centromere. As the prophase progresses, the chromatids become shorter and thicker. Prophase also includes the division of centriole that move toward the two opposite ends of the cell.
- Metaphase is the second and the longest stage of cell division where the chromatids are lined up on the metaphase plate. The chromatids are shorter and thicker and are still held together by a centromere.
- Anaphase is the next stage of mitosis involving the splitting of each chromosome into sister chromatids to form daughter chromosomes. After splitting, the chromatids are moved towards the pole due to the shortening of the microtubules.
- Telophase is the final stage of mitosis which involves the reorganization of two nuclei and the entry of the cell into the next phase. During this phase, a nuclear envelope is formed around the chromosomes to form two distinct daughter nuclei.
- Telophase indicates the end of the M phase, which initiates the division of cell organelles and separation of cytoplasm into two cells (cytokinesis).

Read More: Mitosis- definition, purpose, stages, applications with diagram

6. Cytokinesis

- Cytokinesis is the division of cytoplasm into two halves, indicating the end of cell division.
- Cytokinesis occurs immediately after the M phase to separate the nucleus, cell membrane and the rest of the cytoplasm into two halves to form two distinct and complete cells.
- The phase begins with the constriction of the cell membrane, which ultimately leads to cleavage and division.
- The constriction is first observed during anaphase, which continues to grow deeper to finally cause cleavage.
- The process and mechanism of cytokinesis might be different in different cells.
- In some cases, cytokinesis is often considered to be a part of the M phase, but in the case of animal cells, cytokinesis and mitosis might occur independently.
- The contraction of the cell membrane during cytokinesis is brought about by the contraction of actin fibres that form a bundle, called a contractile ring.
- In the case of a plant cell, however, a distinct cell plate is formed at the middle of the dividing cell which separates the cytoplasm and cell organelles into equal halves.
- Cytokinesis, like the rest of the cell cycle, is also regulated by several factors that are responsible for the initiation of division as well as the termination.

Read More: Cytokinesis- Definition and Process (in animal and plant cells)

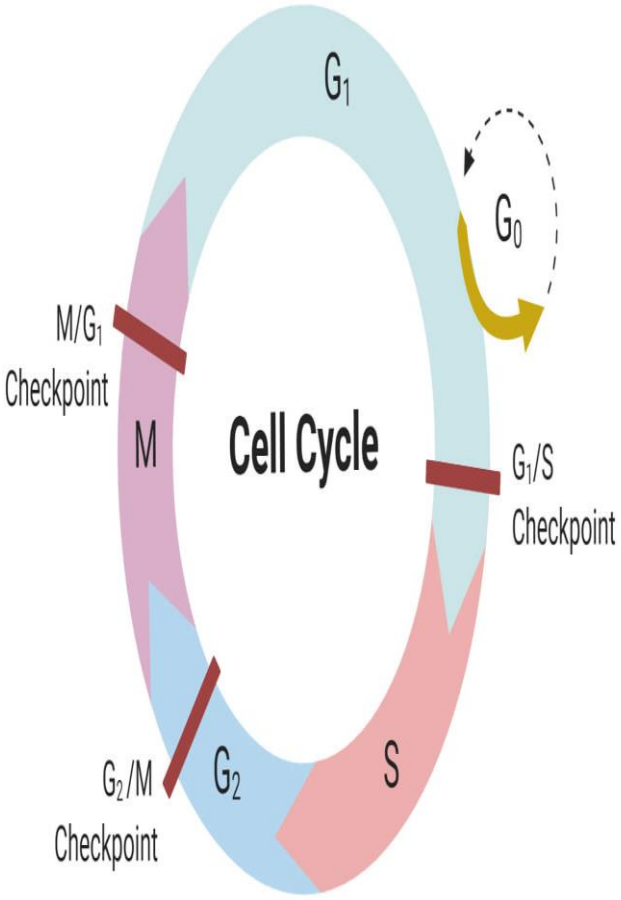
Cell Cycle Regulation

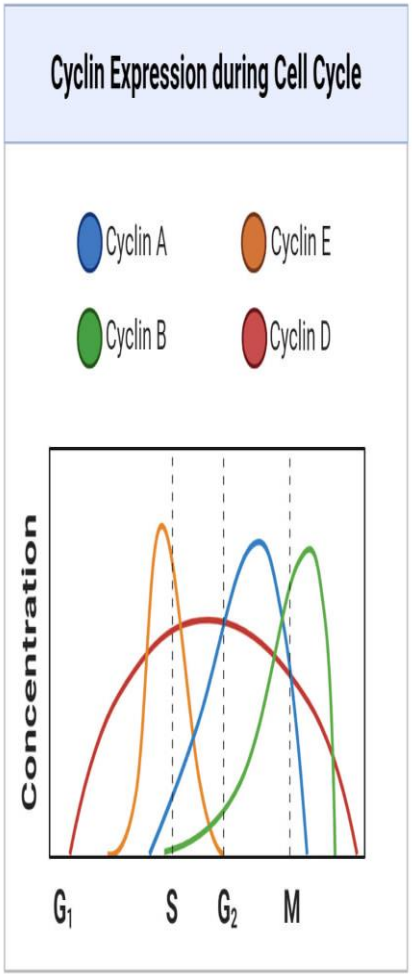
1. Cyclins

- Cyclins are a group of proteins that together work to regulate different phases of the cell cycle as core regulators.

- These proteins regulate the various phases of the cell cycle by either activating the cyclin-dependent kinases or by activating some other enzymes or complexes.
- Cyclins are specific to different phases as work to regulate different phases of the cycle.
- In humans, four different cyclins are known, G1 cyclins, G1/S cyclins, S cyclins, and M cyclins. These cyclins, as the name suggests, regulate different phases.
- The term 'cyclin' was given to this class of proteins because of the varying concentration of these proteins in the cell during the cell cycle.

Cyclins: cell cycle regulators





Mechanism

- The concentration of these cyclins usually remains low for the most part but peaks dramatically if they are needed during the cycle.
- The activation of the cyclin proteins is stimulated by the binding of the growth factors to the receptors on the cell, which activate the transcription of the cyclin genes.
- Most of the cyclin proteins act by binding themselves to the cyclin-dependent kinases, which form a complex. The complex is then responsible for the regulation of the cell cycle.
- Some cyclin proteins like the cyclin D of the G1 phase (or G1 cyclin) act as rate-limiting proteins for cell cycle progression. G1 cyclins accelerate G1 transition by the overexpression of the cyclin genes.
- Even though cyclins do not have any enzymatic activity on their own, they induce different processes in the cell cycle by providing binding sites for other enzymes.

2. Cyclin-dependent kinases (CDKs)

- Cyclin-dependent kinases (CDKs) are a group of enzymes that work to regulate different processes in the cell cycle after activation by the binding of a cyclin molecule.
- CDKs are a part of the CMGC group of enzymes consisting of serine or threonine units that are characterized by their dependency on protein subunits.
- The activity of these enzymes is only observed after the binding of a cyclin molecule followed by the phosphorylation of the threonine unit.

Mechanism

- The cyclin molecules that bind to these kinases provide additional sequences to the enzymes that are required for their enzymatic activity.

- The CDKs usually have specificity towards different cyclin molecules, and the binding of cyclin to the CDK molecule determines the specificity of the enzyme towards its substrate.
- The mechanism of action of these enzymes might differ among different kinases regulation different phases of the cell cycle.
- The activated CDKs in the interphase undergo phosphorylation and cause inactivation of the retinoblastoma protein (Rb).
- The inactivation of Rb causes depression of multiple genes encoding proteins that are necessary for DNA synthesis.
- The regulation of the cell cycle is also brought by the inhibition of the CDKs in which case, CDK inhibitors are involved.
- CDK regulating the cell cycle is negatively regulated by the binding of other smaller proteins of the Cip/Kip families of inhibitors.
- These are also specific to the enzymes and act by distorting the cyclin interface and the ATP-binding pocket of the enzyme.
- These prevent the activation of CDKs, which causes a negative regulation of the cell cycle.

3. Maturation-promoting factor (MPF)

- Maturation-promoting factor or M-phase promoting factor (MPF) is a large-sized diffusible protein that regulates the M-phase of a cell cycle.
- The protein consists of two subunits; an inert subunit and a kinase subunit. The kinase subunit is capable of activating the inert subunit as well as other molecules.
- MPF is the regulator of the G2/M transition where it activates activities like nuclear envelope breakdown and chromosome condensation.

Mechanism

- During the interphase, the inert subunit of MPF is inactive due to the presence of an enzyme, Wee1.
- The activation of the MPF unit is brought about by CDC25, which results in the binding of the cyclin molecule to the kinase subunit.
- After the binding of cyclin to cyclin-dependent kinase, and the activation of CDK, transition into the M phase begins.
- The MPF molecules then act by adding phosphate molecules to the nuclear envelope, which causes the breakdown of the membrane.
- Besides, it also triggers the formation of spindle fibers as a result of microtubule instability.
- The MPF kinase also phosphorylases several substances like histone H1, which then promotes chromosome condensation.
- The activity of MPF is further regulated by other components like p34. The phosphorylation of p34 regulates the activity of MPF.

4. Anaphase-promoting complex/cyclosome (APC/C)

- Anaphase-promoting complex (APC) is a protein that regulates the M phase of the cell cycle by inhibiting the action of MPF and causes the destruction of cyclin molecules.
- This molecule is important during the transition of a cell from metaphase to anaphase of the M phase.
- The APC is an enzyme that functions in the cell cycle by a different mechanism than CDKs.

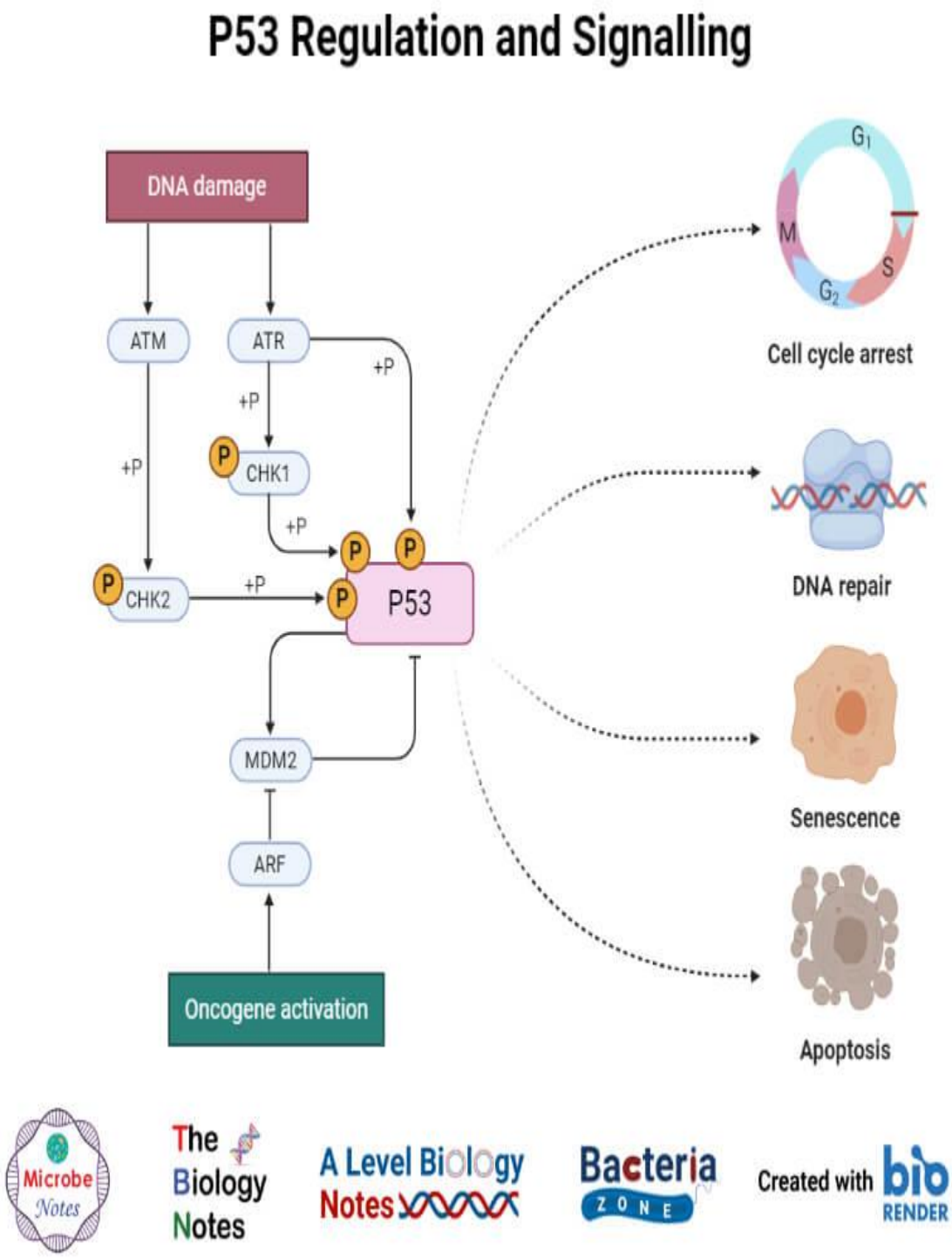
Mechanism

- Instead of activation by phosphorylation and addition of phosphate group to the targets, APC adds ubiquitin on the target molecules. The target molecules are either S and M cyclins or securing.

- In the case of cyclins, the binding of ubiquitin on the surface causes the movement of the cell to the proteasome. In the proteasome, the cyclins are degraded, which allows the newly formed daughter cell to enter the G1 phase.
- Besides, it also triggers the separation of sister chromatids during the metaphase. It binds the ubiquitin tag to a protein, called securing.
- The binding of the tag causes the destruction of securin, which then releases the separase enzyme.
- The separase enzyme acts on the cohesion protein present at the site of connection between two sister chromatids. The separation of sister chromatids indicates anaphase.

5. p53

- p53, also called TP53 or tumor protein, is a gene that encodes for the protein that regulates cell proliferation and also acts as a tumor suppressor.
- The p53 gene is often termed the 'guardian of the genome' as it helps in conserving stability of the genome by preventing genome mutation.
- In eukaryotic organisms, it is important as it suppresses cancer.
- It also stimulates apoptosis if DNA damage is detected that is irreparable.



Mechanism

- The presence of p53 ensures proper cell cycle as it prevents the division of cells with damaged DNA.

- The concentration of p53 in a normal cell is quite low; however, it increases due to DNA damage or stress signals.
- The p53 gene can perform one of three functions, cell cycle arrest, DNA repair, and apoptosis.
- The cell cycle arrest by p53 is mediated by the activation of p21/WAF1. The p21 binds to the G1 cyclin which arrests the cell in the G1 phase as the cyclin can no longer bind to its CDK.
- The p21 also interacts with proliferating cell nuclear antigen that inhibits DNA replication, causing cell-cycle arrest.
- Further, it also regulates the G2/M transition as p21 inhibits cyclin B, which is responsible for the activation of CDK in the G2/M checkpoint.
- In the case of DNA damage, the cell cycle arrest by p53 activates the transcription of proteins involved in DNA repair.

6. Retinoblastoma protein (Rb)

- Retinoblastoma protein is a nuclear phosphoprotein that helps in cell cycle regulation while also acting as a tumor suppression protein.
- The primary function of Rb is to prevent excessive cell growth during the cell cycle progression.
- It acts as a negative regulator of the cell cycle as inhibiting the process.
- The protein is expressed in both cycling and resting cells which functions by inhibiting a variety of nuclear proteins involved in the cell cycle.
- It regulates the transition of a cell from the G1 phase to the S phase by inhibiting DNA replication.

Mechanism

- The family of transcription factors, E2F is the primary target of Rb. These factors regulate the timing and levels of expression of different genes involved in the cell-cycle process.

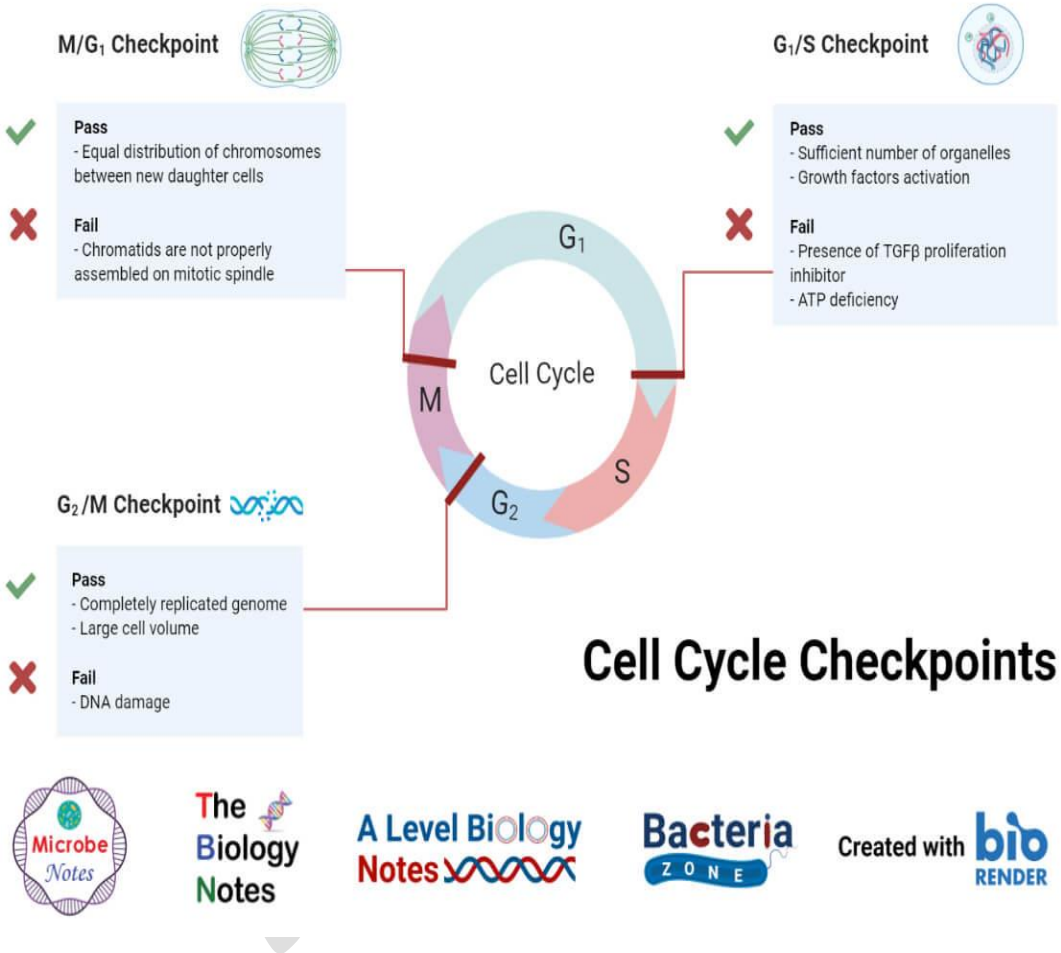
- E2F factors target the proteins involved in replication like DNA polymerase and thymidine kinase.
- In the G0/G1 phase hypophosphorylated Rb binds to E2F which inactivates and prevents cell-cycle progression,
- Similarly, in the S phase, the chronic activation of Rb leads to downregulation of the necessary DNA replication factors.

Cell cycle checkpoints

1. G1 Checkpoint

- The G1 checkpoint is the first checkpoint in the cell cycle of a mammalian cell and the start point in the yeast cell that determines whether the cell enters the cell cycle or not.
- The checkpoint is present between the G1 phase and S phase and is responsible for the entry of the cell in the division phase.
- Depending on the external and internal factors and stimuli, the decision of whether the cell enters the cell cycle or undergoes the G0 phase is determined.
- The checkpoints are essential in the cell cycle as they limit the chances of genomic instability arising due to DNA damage during the cycle.
- The G1 checkpoint is regulated by p53 which aids in the downregulation of tumors and cell lines.
- In order to cause G1 checkpoint arrest, the p53 regulates the transcription of CDK inhibitor p21.
- The arrest is stimulated by factors like a break in the DNA double-strand, which prevents the proliferation of irreparably damaged cells.
- The G1 checkpoint arrest is a positive feedback mechanism where the presence of breaks in the DNA strand enhances the expression of the p53 gene.

- Because of the proteins involved in the checkpoint, the G1 checkpoint is an important checkpoint during tumor suppression and prevention of excessive cell proliferation.
- Cells with reparable DNA damage are held at the checkpoint to provide time for repair while others are either signaled for apoptosis or moved to the G0 phase.



2. G2 Checkpoint

- The G2 checkpoint is the second checkpoint in the cell cycle where is present at the transition between G2 and S phase.
- The checkpoint prevents the entry of cells into the S phase of the cycle by preventing the activation of regulators like cyclins and CDKs.

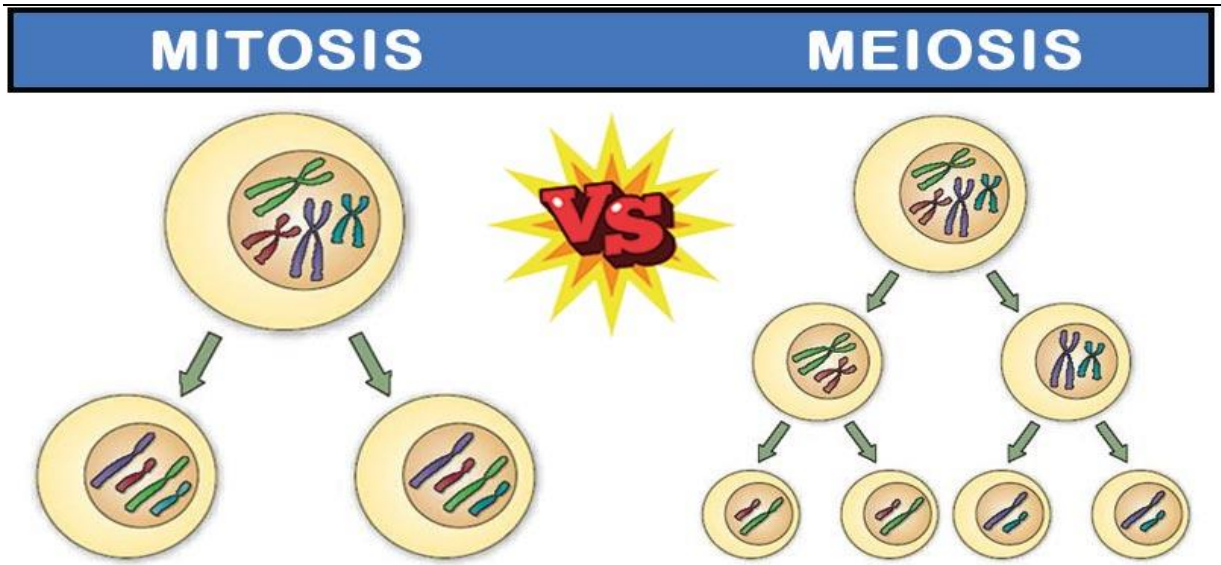
- This checkpoint, like the G1 checkpoint, looks for DNA damage and breaks to prevent the proliferation of mutated or damaged cells.
- As the checkpoint helps maintain genomic stability, studies on the checkpoint help to understand the molecular mechanism of cancer.
- The target of the G2 checkpoint arrest is the CDK2 that usually drives the transition from G2 to the S phase.
- In the checkpoint, DNA damage triggers the activation of the ATM pathway, which causes phosphorylation of ATM and inactivation of checkpoint kinases.
- The checkpoint also involves the p53 genes which inactivate enzymes by the expression of p21 proteins.
- Additional pathways in the G2 checkpoint ensure the stability of the arrest by the expression of proteins like Rb and downregulation of several genes that code for proteins required for the S phase.

3. Metaphase Checkpoint (Spindle checkpoint)

- The metaphase checkpoint or M phase checkpoint or Spindle checkpoint is the checkpoint during mitosis which checks if all the sister chromatids are correctly attached to the spindle fibers.
- The checkpoint ensures that all the chromosomes of cells entering the anaphase are firmly attached to at least two spindle fibers from opposite poles of the cell.
- The separation of chromosomes in anaphase is an irreversible process, which is why this checkpoint is crucial in mitosis.
- The proteins in the checkpoint look for straggler chromosomes that can be detected in the cytoplasm.
- The checkpoint acts by negative regulation of CDC20 which prevents the activation of ubiquitin tag by the anaphase-promoting complex.

- There are different mechanisms to deactivate the checkpoint once all chromosomes are correctly attached.
- One of the important mechanisms is by transporting the motor complex proteins away from the kinetochores. The proteins are then redistributed to the spindle poles.

DIFFERENCES BETWEEN MITOSIS AND MEIOSIS



Here are some of the differences:

S.N.	Character	Mitosis	Meiosis
1.	Alternate Name	Equational Division	Reduction Division
2.	Discovered by	Walther Flemming	Oscar Hertwig
3.	Type of Cells Involved	Somatic cells.	Sex cells/germ cells or gametes.

4.	Type of Reproduction	Asexual division	Sexual division
5.	Mother Cells	Can be either haploid or diploid	Always diploid
6.	Number of Divisions	Mitosis involves only one cell division.	Involves two successive divisions.
7.	Duration	Comparatively shorter.	Longer.
8.	Number of daughter cells	Two	Four
9.	Result into	Diploid (2n) offspring	Haploid (n) offspring
10.	Reduction in Chromosome Number	No reduction in chromosome number.	Results in the reduction in chromosome number by half.
11.	Genetical Identity	Daughter cells are genetically the same.	Daughter cells are genetically different due to recombination.
12.	Recombination or Crossing over	No recombination or crossing over occurs.	Crossing over occurs.

13.	Leads to formation of	Everything other than sex cells.	Sex cells only: female egg cells or male sperm cells.
14.	Steps Involved	Prophase, Metaphase, Anaphase, Telophase.	(Meiosis 1) Prophase I, Metaphase I, Anaphase I, Telophase I; (Meiosis 2) Prophase II, Metaphase II, Anaphase II and Telophase II.
15.	Interphase	Interphase occurs prior to each division.	Interphase precedes in only Meiosis I. It does not occur prior to Meiosis II.
16.	DNA replication during Interphase	Takes place during Interphase.	Takes place during Interphase I but not during Interphase II.
17.	DNA replication	Occurs once for one cell division.	Occurs once for two cell divisions.
18.	Steps and Length of Prophase	A cell spends less time in prophase of mitosis than a cell in prophase I of meiosis. No sub stages occur in mitosis.	Prophase I consist of five stages and lasts longer than prophase of mitosis. The five stages of meiotic prophase I are leptotene,

			zygotene, pachytene, diplotene, and diakinesis.
19.	Prophase	Simple	Complicated
20.	Synapsis	No synapsis	Synapsis of homologous chromosomes takes place during prophase.
21.	Tetrad Formation	Tetrad formation does not occur.	A tetrad consisting of four chromatids (two sets of sister chromatids) lined up closely together is formed.
22.	Centromere	Each chromosome consists of two chromatids united by a centromere.	The two homologous chromosomes form bivalents or tetrads. Each bivalents has four chromatids and two centromeres.
23.	Metaphase	Sister chromatids align at the metaphase plate (a plane that is equally distant from the two cell poles).	Tetrads (homologous chromosome pairs) align at the metaphase plate in metaphase I.

24.	Chromosome Alignment in Metaphase	In the metaphase plate, all the centromeres line up in same plate.	In metaphase I, the centromeres are lined up in two planes which are parallel to one another.
25.	Chiasmata	Absent	Observed during prophase I and metaphase I.
26.	Anaphase	Sister chromatids separate and begin migrating centromere first toward opposite poles of the cell. A separated sister chromatid becomes known as daughter chromosome and is considered a full chromosome.	During anaphase I, (double stranded) chromosomes are separated toward each cellular pole. Sister chromatids do not separate in anaphase I. On the other hand, (single stranded) chromosomes are the ones being segregated during anaphase II.
27.	Centromeres Split	The centromeres split during anaphase.	The centromeres do not separate during anaphase I, but during anaphase II.

28.	Spindle Fibres	Disappear completely in telophase.	Do not disappear completely in telophase I.
29.	Nucleoli	Reappear at telophase.	Do not reappear at telophase I.
30.	Karyokinesis	Occurs in Interphase.	Occurs in Interphase I.
31.	Cytokinesis (division of the cytoplasm)	Occurs at the end of telophase.	Cytokinesis happens at the end of telophase I and telophase II.
32.	Functions	• Facilitate growth, repair, and replacement. • To produce more cells especially during the early stages of development. • To regenerate damaged and lost cells. • Mitosis also occurs in **prokaryotes** as an essential form	• Takes part in the formation of gametes. • To maintain the chromosome number of the offspring. • For maintenance of genetic diversity on which the process of natural selection acts upon.

		of asexual reproduction.	

TISSUE

EPITHELIAL TISSUE DEFINITION

- **Epithelial Tissue** is one of the four types of tissue (epithelial, muscular, connective, and nervous) in animals which consists of closely aggregated polyhedral cells adhering firmly to one another, forming cellular sheets that line the interior of hollow organs and cover the body surface.
- An epithelial tissue or epithelium (plural is epithelia) consists of cells arranged in continuous sheets, in either single or multiple layers.

CHARACTERISTICS OF EPITHELIAL TISSUE

- Even though epithelial tissue present in different parts of the body might differ in structure and function, they all have some common characteristics.
- Some of these characteristics are given below:

1. **Shape and Size**

- The shapes and sizes of epithelial cells are variable, ranging from tall columnar to cuboidal to low squamous.
- The cell's size and morphology are generally based on their function.

2. **Polarity**

- Epithelial cells generally show polarity, with organelles and membrane proteins distributed unevenly within the cell.
- The apical (free) surface of an epithelial cell is present towards the body surface, the body cavity, the lumen of an internal organ, or a gland duct that receives cell secretions. Apical surfaces may contain cilia or microvilli.
- The lateral surfaces of an epithelial cell, facing the adjacent cells on either side, may contain intercellular adhesion and other junctions.
- The basal surface of an epithelial cell adheres to extracellular materials such as the basement membrane, which is an inert connective tissue made by the epithelial cells themselves.

3. **Basement Membrane**

- The basement membrane is a thin extracellular layer that commonly consists of two layers, the basal lamina, and the reticular lamina.
- The basal lamina is closer to and secreted by the epithelial cells and contains proteins like laminin and collagen as well as some glycoproteins and proteoglycans.
- The reticular lamina is closer to the connective tissue, present underneath, and contains collagen protein produced by connective tissue cells called fibroblasts.

4. **Intercellular Adhesion and Other Junctions**

- Several membrane-associated structures provide adhesion and communication between cells.
- Tight junctions, also called zonulae occludens, are the most apical of the junctions that form a band completely encircling each cell.
- The second type of junction is the adherens junction or zonula adherens, which also encircles the epithelial cell, usually immediately below the tight junction.

- Another anchoring junction is the desmosome or macula adherens which are disc-shaped structures at the surface of one cell that matches with identical structures at an adjacent cell surface.
- Gap junctions mediate intercellular communication rather than adhesion or occlusion between cells.

5. **Avascular**

- Epithelial tissue is avascular, relying on the blood vessels of the adjacent connective tissue to bring nutrients and remove wastes.
- The exchange of substances between epithelial tissue and connective tissue occurs by diffusion.

6. **Innervated**

- Epithelial tissue is innervated; that is, it has its own nerve supply.

7. **Renew and Repair**

- Epithelial cells have a high rate of cell division which allows the epithelial tissue to continually renew and repair itself by sloughing off dead or injured cells and replacing them with new ones.

FUNCTIONS OF EPITHELIAL TISSUE

Based on the location, epithelial tissue performs a bunch of functions. Some of which are:

Protection

- One of the most critical functions of epithelial tissue is protection. It protects the cells present below against radiation, desiccation, invasion by pathogens, toxins, and physical trauma.
- The absence of blood vessels in the epithelial tissue thus prevents bleeding in the tissue during abrasion.

Transportation

- Epithelial tissue also functions in the transportation of different molecules in and out of the cells with different pumps present in the epithelial tissue.
- Besides, in the digestive, respiratory, and urinary system, it allows the exchange of molecules between the underlying cells and the body cavity, capillaries, and ducts.

Secretion

- Glandular epithelium secretes various macromolecules like hormones responsible for multiple bodily functions.
- Many endocrine and exocrine glands also help maintain the body surfaces (skin) as well as support the functions of various organs (digestive system).

Absorption

- By the function of various specialized structures like cilia and microvilli on the surface of cells, epithelial tissue also aids in the absorption of multiple molecules by increasing the surface area.
- In the digestive system, columnar cells of the small intestine help in the absorption of water and various other nutrients.

Receptor function

- Some cells in the epithelial tissue are specialized to perform sensory functions that can detect the sensory information and convert them into neural signals.
- Cells in epithelial tissue like the pseudostratified columnar epithelium of the olfactory mucosa contain apical cilia that allow the sensation of odor.

CLASSIFICATION WITH EXAMPLES & LOCATION

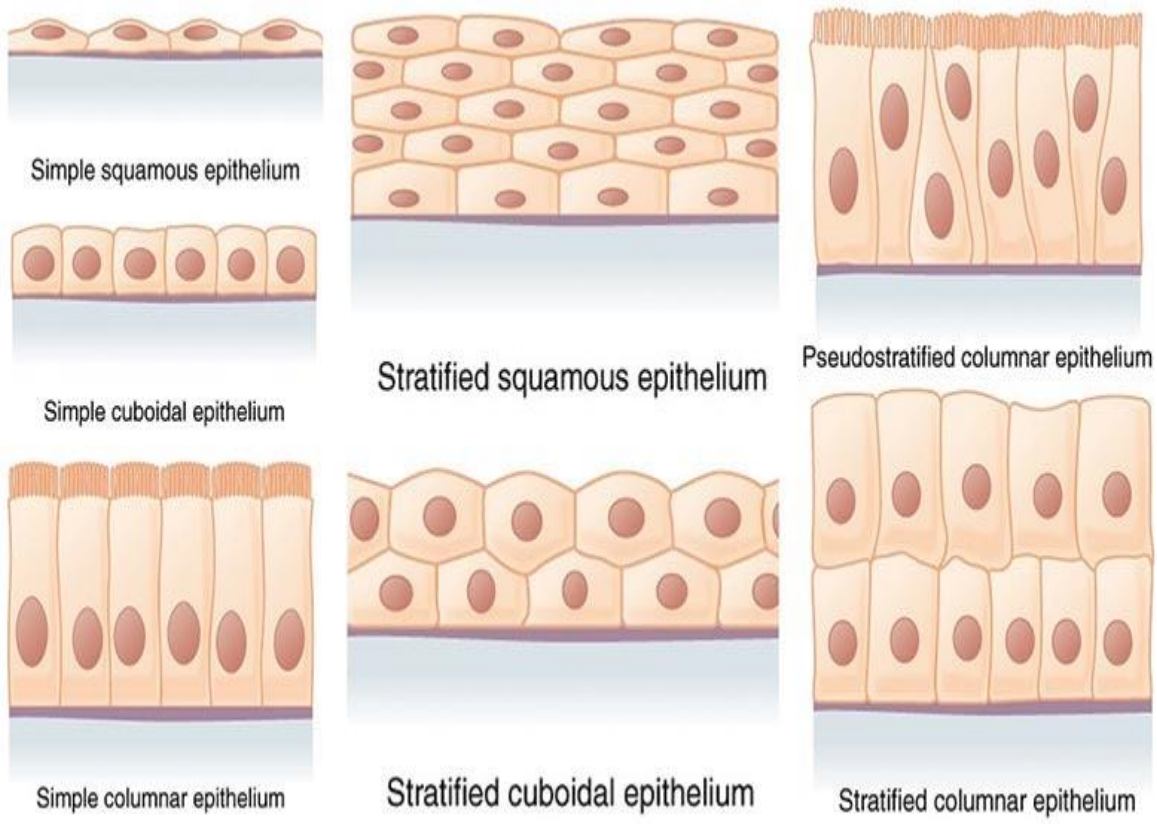
Epithelial tissue is divided into two types:

1. **Covering and lining epithelium**, also called the surface epithelium that forms the outer covering of the skin and some internal organs and also forms

the inner lining of blood vessels, ducts, body cavities, and the inner lining of the respiratory, digestive, urinary, and reproductive systems.

2. **Glandular epithelium** that makes up the secreting portion of glands such as the thyroid gland, adrenal glands, sweat glands, and digestive glands.

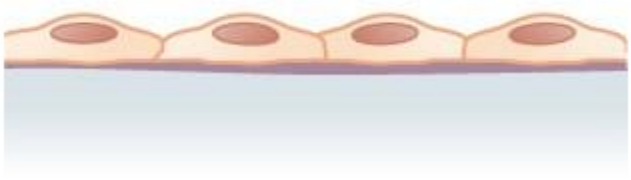
Further, types of covering and lining epithelial tissue are classified according to the arrangement of cells and the shapes of those cells.



Simple epithelium

- Simple epithelium is made up of a single layer of identical cells, which are usually found on secretory and absorptive surfaces, where the single layer enhances these processes.
- Simple epithelium is divided into three main types, and these are named according to the shape of the cells, which differ based on their functions.

a. Simple squamous epithelium



Simple squamous epithelium

- The simple squamous epithelium consists of a single layer of flat cells that resembles the tiles on a floor when viewed from the apical surface with a centrally located nucleus that is flattened and oval or spherical.
- This epithelium most commonly lines the cardiovascular and lymphatic system (heart, blood vessels, lymphatic vessels), where it is known as **endothelium** and forms the epithelial layer of serous membranes (peritoneum, pleura, pericardium), where it is called
- It is also found in air sacs of lungs, glomerular (Bowman's) capsule of kidneys, and the inner surface of the tympanic membrane (eardrum).

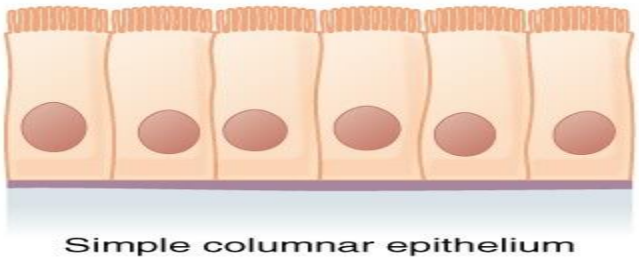
b. Simple cuboidal epithelium

Simple cuboidal epithelium

- Simple cuboidal epithelium is a single layer of cube-shaped cells that are round and have a centrally located nucleus.
- It covers the surface of the ovary, lines the anterior surface of the capsule of the lens of the eye, forms pigmented epithelium at the posterior surface of retina of the eye, lines kidney tubules and smaller ducts of various glands,

makes up secreting portion of some glands like the thyroid gland and ducts of some glands such as the pancreas.

c. Simple columnar epithelium



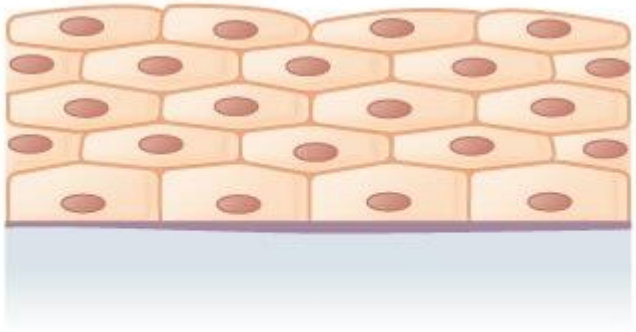
- The columnar epithelium is made by a single layer of cells, rectangular in shape, on a basement membrane.
- This epithelium lines many organs and is often derived to make it well suited for a specific function.
- Columnar epithelium lines the stomach without any surface structures. However, the free surface of the columnar epithelium lining the small intestine is covered with microvilli, which provide a vast surface area for the absorption of nutrients from the small intestine.
- In the trachea, the columnar epithelium is ciliated. Also, it contains goblet cells that secrete mucus, and in the uterine tubes, ova are propelled along by ciliary action towards the uterus.

Stratified epithelium

- A stratified epithelium consists of several layers of cells of various shapes, and basement membranes are usually absent.
- As basal cells divide, daughter cells arising from cell divisions are pushed older cells upward toward the apical layer.
- As they move toward the surface and away from blood supply in underlying connective tissue, they become dehydrated and less metabolically active.

- Tough proteins predominate as cytoplasm is reduced, and cells become tough, hard structures that eventually die.
- At the apical layer, after dead cells lose cell junctions, they are sloughed off, but they are continuously replaced as new cells emerge from basal cells.
- There are two main types of stratified epithelium: stratified squamous, stratified cuboidal, and stratified columnar epithelium.

a. Stratified squamous epithelium



Stratified squamous epithelium

The stratified squamous epithelium has two or more layers of cells. The cells in the apical layer and several layers deep to it are squamous while the cells in deeper layers vary from cuboidal to columnar.

i. Keratinized stratified squamous epithelium

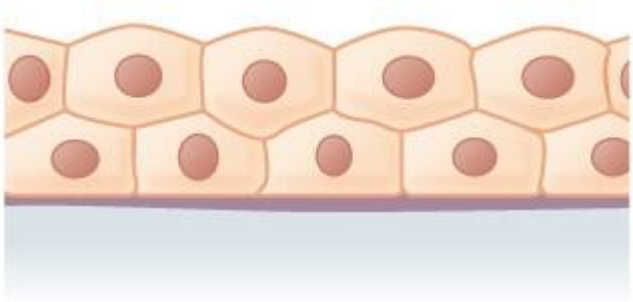
- This epithelium develops a tough layer of keratin in the apical segment of cells and several layers deep to it
- The relative amount of keratin increases in cells as they move away from the nutritive blood supply and the organelles eventually die.
- The keratin forms a tough, relatively waterproof protective layer that prevents drying of the live cells present underneath.

- Keratinized stratified squamous epithelium forms a superficial layer of skin.

ii. Non-keratinized stratified squamous epithelium

- This epithelium does not contain large amounts of keratin in the apical layer, and several layers deep and is moistened continuously by mucus from salivary and mucous glands.
- Nonkeratinized stratified squamous epithelium lines wet surfaces (lining of mouth, esophagus, part of the epiglottis, part of the pharynx, and vagina) and covers the tongue.

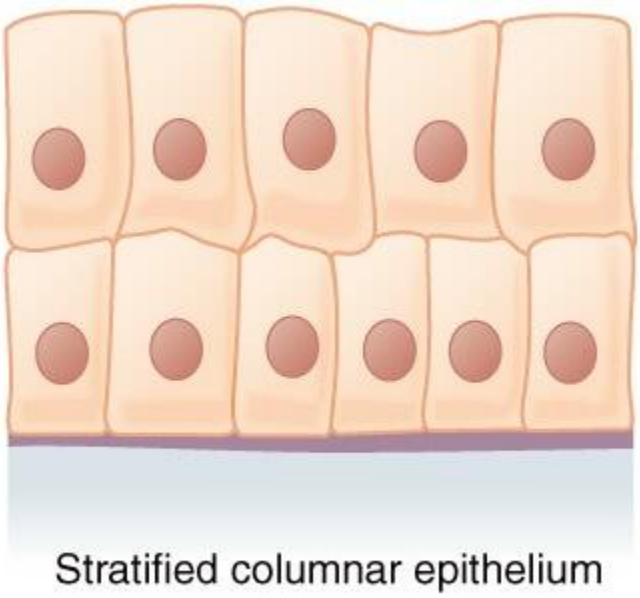
b. Stratified cuboidal epithelium



Stratified cuboidal epithelium

- Stratified cuboidal epithelium has multiple layers of cells in which the apical layer is made up of cuboidal cells while the deeper layer can be either cuboidal or columnar.
- Stratified cuboidal epithelium is seen in the excretory ducts of salivary and sweat glands.

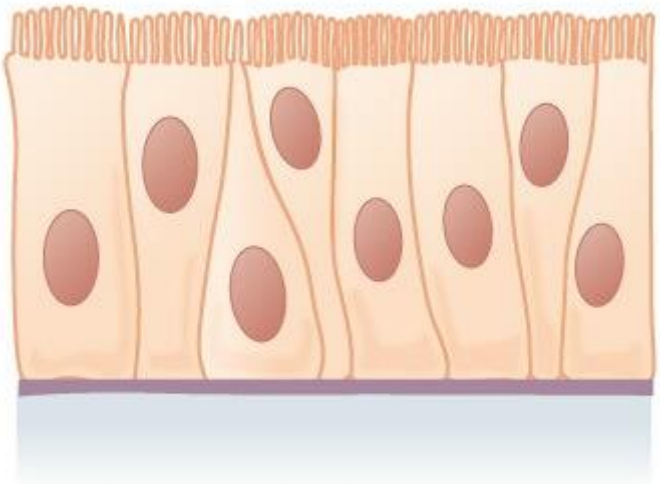
c. Stratified columnar epithelium



Stratified columnar epithelium

- The stratified columnar epithelium has multiple layers of cells in which the apical layer is made up of columnar cells while the deeper layer can be either cuboidal or columnar.
- This type of epithelium is present in the conjunctiva of the eyes, parts of the urethra, and the small area in the anal mucosa.

Pseudostratified columnar epithelium



Pseudostratified columnar epithelium

- Pseudostratified epithelium appears to have several layers because the nuclei of the cells are present at various levels.
- Although all the cells are attached to the basement membrane in a single layer, some cells do not reach the apical surface.
- As a result of these features, it appears as a multilayered tissue, but in fact, is the simple epithelium.
- This epithelium lines epididymis, larger ducts of many glands, and parts of male urethra and airways of most of the upper respiratory tract.

Transitional epithelium tissue

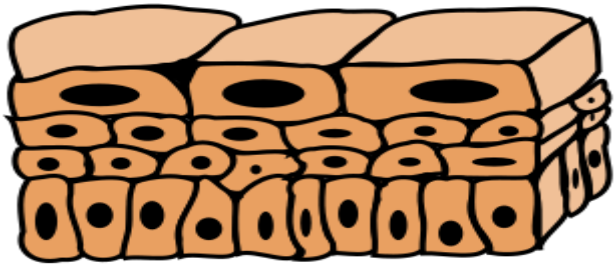


Figure: Transitional epithelium tissue.

- Transitional epithelium (urothelium) has a variable appearance (transitional).
- In a relaxed or unstretched state, looks like stratified cuboidal epithelium, except apical layer cells tend to be broad and rounded.
- As tissue is stretched, cells become flatter, giving the appearance of stratified squamous epithelium. Multiple layers and elasticity make it ideal for lining hollow structures (urinary bladder) subject to expansion from within.

Glandular Epithelium

- Epithelial cells that function mainly to produce and secrete various macromolecules may occur in epithelia with other significant functions or comprise specialized organs called glands.

- Scattered secretory cells, sometimes called unicellular glands, are common in simple cuboidal, simple columnar, and pseudostratified epithelia.
- Glands develop from covering epithelia in the fetus by cell proliferation and growth into the underlying connective tissue, followed by further differentiation.

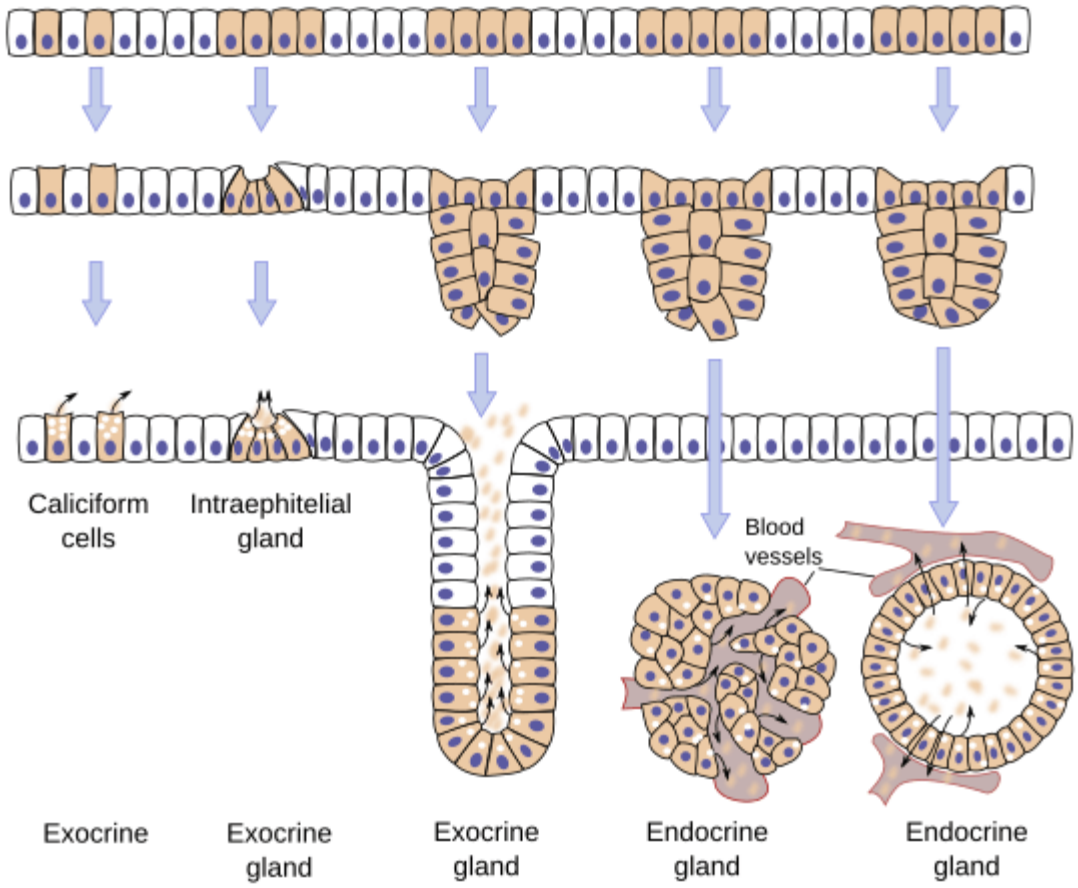


Figure: Main types of glands. Glands differentiate from epithelial tissues during embryo development. Arrows point to the released substances.

Endocrine glands

- The secretions of endocrine glands, called hormones, enter the interstitial fluid and then diffuse into the bloodstream without flowing through a duct.
- Endocrine secretions have far-reaching effects because they are distributed throughout the body by the bloodstream.

- Examples of endocrine glands include pituitary gland at the base of the brain, the pineal gland in the brain, thyroid and parathyroid glands near larynx (voice box), adrenal glands superior to kidneys, pancreas near the stomach, ovaries in the pelvic cavity, testes in the scrotum, thymus in the thoracic cavity.

Exocrine glands

- Exocrine glands secrete their products into ducts that release the secretions onto the surface of organs such as the skin surface or the lumen of a hollow organ.
- The effects of exocrine gland secretions are limited, and some of them would be harmful if they entered the bloodstream.
- Sweat, oil, and earwax glands of the skin, digestive glands such as salivary glands (secrete into mouth cavity) and pancreas (secretes into the small intestine) are the examples of exocrine glands.

Connective Tissue Definition

- Connective tissue is one of the tissue systems in animals composed of different types of cells, all of which work together to provide internal support, adhesion, and cohesion between tissues to form organs and systems.
- The cells of connective tissue provide a matrix that gives metabolic support to cells as well as a medium for the transport of nutrient and waste products between organs.
- There are different types of connective tissues that vary in density, cellularity, and specialized variants.

Characteristics of Connective Tissue

Connective tissues are of different types and might have different characteristics that are unique to each type. However, there are some characteristics that are common in all connective tissues. Some of such characteristics are given below:

- Connective tissues are the group of cells that work together to provide support and adhesion in order to form organs.
- All connective tissues originate from the embryonic mesenchyme or mesoderm. The mesenchymal cells have large nuclei which later differentiate to form different cells of connective tissues.
- Connective tissues are composed of cells and an extracellular matrix. The extracellular matrix consists of protein fibers and ground substances.
- Connective tissues are found in and around body organs and help connect the organs or diffuse nutrients and waste materials between the organs.
- Connective tissues are classified into different types on the basis of differences in composition and the concentration of cells, fibers, and ground substance.
- Connective tissue is highly vascular, except for cartilage, as it is provided with a large number of blood vessels for the transport of nutrients, oxygen, water, and waste materials.

Structure of Connective Tissue

- Connective tissues are composed of cells and the extracellular matrix. The cells are of different types and determine the type of connective tissues.
- The extracellular matrix of the connective tissues is composed of ground substance and fibers.
- It is present between the widely spaced cells that are often suspended in the ground substance. The matrix is responsible for the specific structure and

function of the tissues as the matrix of bone is rigid and inflexible, but that of cartilage is firm but pliable.

- The extracellular fibers of the matrix are secreted by the connective tissue cells and are responsible for the functional properties of the tissue.
- The ground substance is a clear, colorless, and viscous fluid that fills the space between the cells and the fibers.
- The ground substance is composed of proteoglycans and cell adhesion proteins. The ground substance is responsible for the adhesion function of the connective tissue.
- The ground substance also served as a molecular sieve that can travel between blood capillaries and the cells, thus helping is the movement of nutrients, oxygen, and waste materials between the two.
- The cells and fibers of connective tissues are of different types and perform different functions.

Connective tissue fibres

- Connective tissue fibers are elongated proteins that polymerize to both fibrous components of the tissue after secretion from fibroblasts.
- These fibers remain embedded in the extracellular matrix between the connective tissue cells—these function to strengthen and support the connective tissues.
- There are three different types of connective tissue fibers; collagen, reticular and elastic fibers. The proportion of each fiber in different connective tissue might differ, and the predominant fiber determines the characteristics of the tissue.

1. Collagen fibers

Fig- Collagen fibers

- Collagen fibers are composed of collagen protein which is the most abundant protein in the human body.
- Collagen fibers are defined by their ability to form extracellular fibers, sheets, and networks with strong resistance to normal shearing and tearing forces.
- Collagens are secreted by fibroblasts and several other cell types distinguished by their molecular composition, morphological characteristics, and distribution.
- Collagen fibers occur in bundles that add to the great tensile strength and flexibility. In collagen fibers, fibrillar collagens are present that form large eosinophilic bundles.
- These fibers densely fill the connective tissue matrix, forming structures like tendons, organ capsules, ligaments, and even the dermis.
- During the synthesis of collagen fibers, initial procollagen α chains are formed which are then selected, aligned, and stabilized by disulfide bonds at the carboxyl terminals, folded as a triple helix structure.
- The triple helix is then cleaved to form rod-like procollagen molecules that form the basic subunit of the collagen fibers.
- Depending on the composition of procollagen α chains, different collagen has different structures and functions.

2. Elastic fibers

Fig- Elastins

- Elastic fibers are smaller than collagen fibers and form a sparse network in between collagen bundles in some tissues that are subject to regular stretching or bending.
- Elastic fibers have rubber-like properties that allow the fibers to be stretched and return to their original shape.
- Elastic fibers commonly occur in the stroma of the lungs, the walls of large blood vessels, mostly arteries, and skin.
- An elastic fiber consists of molecules of protein elastin which is surrounded by a glycoprotein named fibrillin.
- Both the proteins are secreted by fibroblasts beginning with the secretion of microfibrils onto which elastin protein is deposited.
- The elastic property of elastic fibers is due to the structure of the elastin subunits and the cross-links holding them together.
- The elastin molecules have lysine-rich regions that are interspersed with hydrophobic domains rich in lysine and proline which are responsible for extensible, random-coil conformations.

3. Reticular fibers

- Reticular fibers are composed of collagen proteins arranged in bundles with an outer coating of glycoprotein, commonly found in the wall of blood vessels and forms a network around the cells in some tissues.

- Reticular fibers consist of collagen Type III which forms an extensive network of thin fibers that supports various cells.
- These are also produced by fibroblasts and usually occur in the reticular lamina of the basement membranes and surround cells like adipocytes, smooth muscle cells, and nerve fibers.
- The reticular fibers are much thinner than collagen fibers and usually occur in the form of branching networks.
- Reticular networks are delicate and occur abundantly in the stroma of hemopoietic tissue, the spleen, and lymph nodes.

Connective Tissue Cells

- Connective tissue consists of cells that are often characteristic of a particular type of connective tissue.
- All of these cells are developed during the embryonic life from the mesenchyme of the mesodermal layer of the embryonic germ layers.
- The cells of the mesenchyme have the ability to differentiate along different lines depending on the local condition of the body.
- In adults, it is believed that some number of mesenchymal cells persist in the walls of blood vessels that retain the capacity to differentiate into different connective tissue cells as the need arises.
- The cells of connective tissues are of two types; fixed or stationary or resident cells and transient or motile or wandering cells.

A. Fixed cells (or resident cells)

- Fixed or resident connective tissue cells are the cells that originate from local mesenchyme and are permanent residents of connective tissues.
- The following are the two types of resident connective cells;

1. Fibroblasts

- Fibroblasts are the most abundant and common cells of connective tissue that is present in all the general connective tissues.
- Fibroblasts are large cells with irregular processes that produce most of the extracellular components of the connective tissues.
- Fibroblasts secrete essential proteins like collagen, elastin, as well as other glycoproteins that comprise the ground substance of the extracellular matrix.
- Fibroblasts are active cells, whereas the quiescent cells are termed fibrocytes, fibroblasts consist of irregularly branched cytoplasm with rough endoplasmic reticulum and well developed Golgi apparatus.
- Fibroblasts are mostly active in tissue repair where they bind cut surfaces by forming granulation tissue after tissue destruction.

2. Adipocytes

- Adipocytes, also called fat cells, are derived from large mesenchymal cells and are specialized for cytoplasmic storage of lipids.
- These cells occur in many types of connective tissue in small numbers but are most abundant in adipose tissues.
- Adipocytes receive glucose from the blood, which is then converted into lipid. The lipid is accumulated in the cytoplasm of the cell as a large oil droplet.
- Adipocytes are of different shapes and sizes according to the amount of fat they store, but they have major metabolic significance and considerable medical importance.

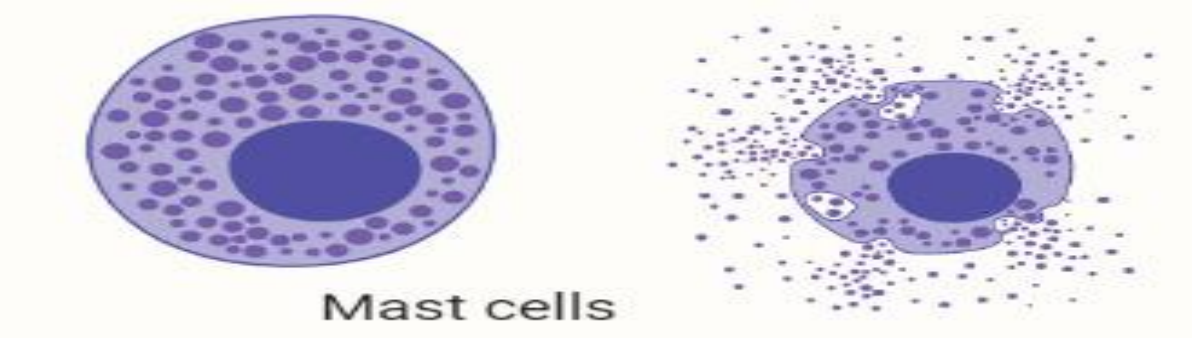
B. Transient cells (or wandering cells)

- Transient or wandering cells are free cells that are present in the interstices of loose connective tissues and can migrate through the extracellular spaces.
- The following are four transient cells found in connective tissues;

1. Macrophages

- Macrophages are irregularly shaped cells with granules in the cytoplasm that have the phagocytic ability and are specialized in the turnover of protein fibers and removal of dead cells and tissues.
- The shape and size of macrophages vary according to their state of functional activity, but they typically measure between 10 to 30 μm in diameter with a centrally placed kidney-shaped nucleus.
- These are found in the connective tissue of most organs and are often referred to as histiocytes.
- Macrophages are derived from bone marrow precursor cells called monocytes that cross the epithelial wall of blood vessels, reach the connective tissue, and differentiate to form phagocytic cells.
- Macrophages are important cells of the immune system as they play an important role in the early stages of repair and inflammation after tissue damage.

2. Mast cells



- Mast cells are oval cells that are between 7-20 μm in diameter with basophilic secretory granules in the cytoplasm.
- Mast cells usually occur in loose connective tissue in the fibrous capsule of organs like the liver and spleen.
- The granules in the cytoplasm contain heparin and histamine that are released when the cells are damaged by injury.

- Besides, these cells also release other bioactive substances that are essential in a local inflammatory response, innate immunity, and tissue repair.
- The origin of mast cells is similar to that of macrophages as these are also developed from the progenitor cells of the bone marrow.
- Mast cells occur in the connective tissue of small blood vessels, skin, and tissues of the digestive and respiratory tracts.

3. Plasma cells

- Plasma cells are antibody-producing cells that are derived from lymphocytes.
- The cells are large, ovoid with basophilic cytoplasm rich in the rough endoplasmic reticulum and large Golgi apparatus.
- Few plasma cells are present in almost all connective tissue, and they have an average lifespan of about 10-20 days.

4. Leukocytes

- Leukocytes or white blood cells are usually found in small numbers in healthy connective tissues, but the number is significantly higher during infection.
- These cells are derived from circulating blood cells where they leave the blood and migrate to endothelial cells to enter the connective tissues finally.
- Most leukocytes remain in connective tissues for a few hours, after which they undergo apoptosis.

Types of Connective Tissue

There are different types of connective tissues with varied histological structure as a result of different combinations and concentrations of cells, fibers, and other extracellular components. The name and classification designated to different types of connective tissues denote either the structural characteristics or a major component.

Connective tissue proper

- Connective tissue proper is a type of connective tissue that is flexible and has a viscous ground substance with large proportions of fibers.
- Connective tissue proper is broadly classified as loose or dense connective tissue which refers to the amount of collagen present in the tissue.

a. Loose connective tissue

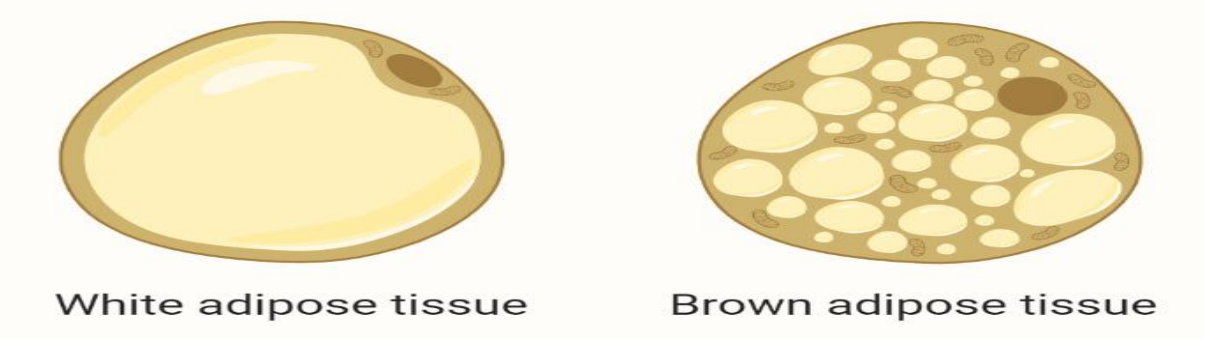
- Loose connective tissue is a common tissue that forms a layer beneath the epithelial lining of many organs and fills the spaces between the muscle and nerve fibers.
- The term loose connective tissue indicates the loose arrangement of fibers in the extracellular matrix of the tissue.
- Loose connective tissue is mostly delicate and flexible due to the limited amount of ground substance, and it is not very resistant to stress.
- Loose connective tissues are further classified into three different types;

i. Areolar connective tissue

- Areolar tissue is one of the most widely distributed connective tissues commonly found in nearly each body structure.
- This tissue consists of cells, fibers, and ground substances in roughly equal parts. The most abundant cells are fibroblasts, but other types of cells are also found in limited concentration.

- The predominant fibers in the extracellular matrix are the collagen fibers, but some amount of elastic and reticular fibers might also be present.
- Areolar tissue is distributed in areas like a subcutaneous layer of skin, the papillary region of the dermis of the skin, lamina propria of the mucous membrane, and around blood vessels.

ii. Adipose connective tissue



- Adipose tissue is a connective tissue composed of adipocytes that are specialized for the storage of fat in the form of oil droplets.
- Adipose tissue makes up about 15-20% of the total body weight in men and somewhat more in women.
- In addition to serving as storage deposits for fat, adipose tissue also functions as a key regulator of the body's energy metabolism. The tissue is also an excellent source of stem cells that are essential in the repair and replacement of damaged tissue.
- Adipose tissues have a rich supply of blood vessels and unlike other connective tissues, are surrounded by a thin external lamina containing type IV collagen.
- There are two types of adipose tissue with different structures, colors, and functions; white adipose tissue and brown adipose tissue.

- White adipose tissue is the more common type of adipose tissue that is specialized for fat storage. The tissue consists of adipocytes, each of which contains a large cytoplasmic droplet of whitish-yellow fat.
- The brown adipose tissue consists of adipocytes with multiple lipid droplets that are interspersed among the mitochondria of the cell. The presence of multiple droplets results in a darker appearance.
- The brown adipose tissue is involved in the release of heat and functions to maintain the temperature of the blood.

iii. Reticular connective tissue

- Reticular tissue is defined by the presence of abundant reticular or Type III collagen fibers that form a delicate network to support various cells.
- Reticular tissue consists of the protein reticulin produced by modified fibroblasts often termed as reticular cells.
- The extracellular matrix of the tissue consists of loose deposition of glycosylated reticular fibers that form a network of microenvironments for cells in hemopoietic tissue and lymphoid organs.
- Reticular tissues are found in the stroma of the liver, spleen, lymph nodes, bone marrow, and the reticular lamina of the basement membrane.

b. Dense connective tissue

- Dense connective tissue is another type of connective tissue proper that contains more fibers and the fibers are thicker and more densely packed with considerably fewer cells than in loose connective tissue.
- Dense connective tissue provides strength to the tissue, and the tissue is less flexible.
- Dense connective tissue is further classified into three types;

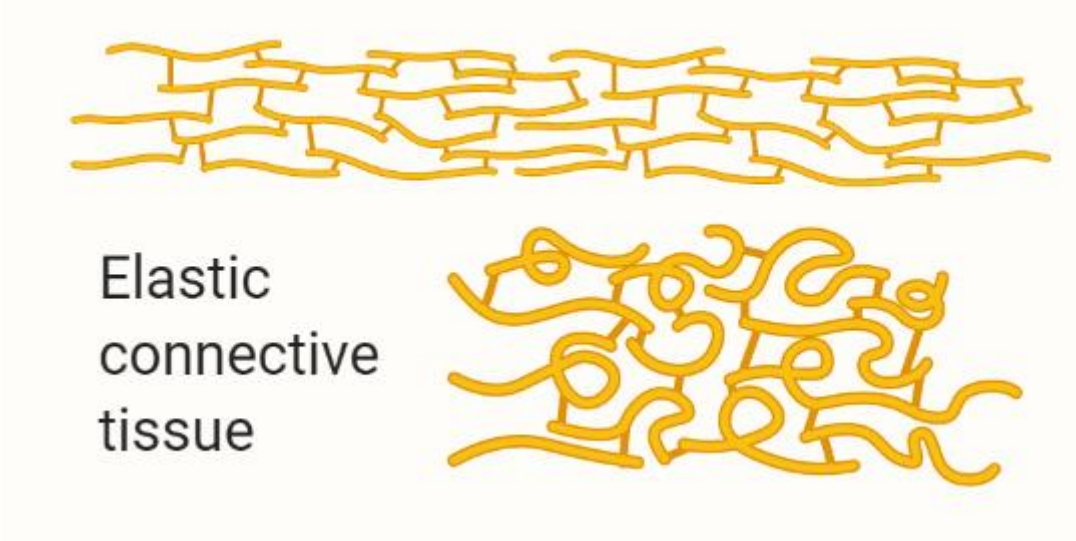
i. Dense regular connective tissue

- Dense regular connective tissue consists of Type I collagen bundles and fibroblasts arranged in parallel to provide resistance to repeated stresses from the same direction.
- The tissue consists of a shiny white extracellular matrix with dead fibroblast cells and fibers.
- As the cells are dead, damaged tendons and ligaments require a long period of time for healing.
- These tissues are found in tendons, most ligaments, and aponeuroses and have the primary function of providing strength and strong attachment between structures.

ii. Dense irregular connective tissue

- Dense irregular connective tissue consists of collagen fibers that are randomly interwoven with no definite orientation.
- The three-dimensional collagen network in the dense irregular connective tissue provides resistance against stress.
- The tissue is found in different areas like the deep dermis layer of skin and capsules of most organs.

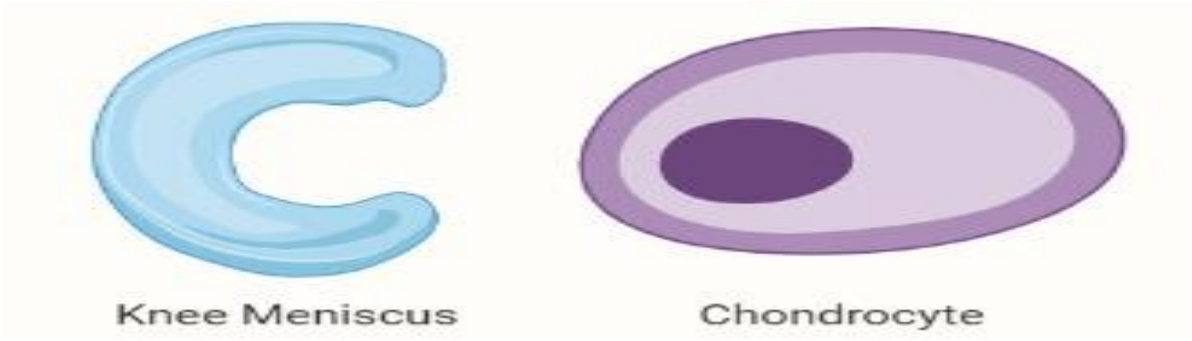
iii. Elastic connective tissue



- Elastic connective tissue consists mainly of elastic fibers in the extracellular matrix, which provides considerable extension and recoil to the tissue.
- The tissue is composed of few cells and a large number of elastic fibers secreted by fibroblasts.
- Elastic tissue is found in structures where stretching or change in shape is required, like the lungs and large blood vessels.

Special connective tissue

A. Cartilage



- Cartilage is a tough supporting connective tissue that is characterized by the extracellular matrix with a high concentration of proteins, proteoglycans, and fibers secreted by chondrocytes.

- Cartilage consists of a dense network of collagen fibers and elastic fibers embedded in the ground substance's gel-like component.
- The strength of cartilage is provided by the collagen fibers, and the resistance is due to the chondroitin sulfate extracellular matrix.
- Cartilage is stronger and more resilient than loose and dense connective tissues, but it doesn't have blood or nerve supply. Chondrocytes receive nutrients from the capillaries of the surrounding tissue by diffusion.
- The resilience and the smooth, lubricated surface of cartilage provide cushioning and sliding regions within skeletal joints that facilitate bone movement.
- Cartilage consists of cells called chondrocytes and no other cells. Chondrocytes alone synthesize and maintain all the components of the extracellular matrix in matrix cavities called lacunae.
- The semi-rigid consistency of cartilage is due to the water bound to the negatively charged hyaluronan and groups on proteoglycan chains. The water bound to the structure enables the cartilage to act as a shock absorber.
- Cartilage is further classified into three main groups on the basis of the composition of the matrix.

a. Hyaline Cartilage

- Hyaline cartilage is the most common cartilage found in animals that is homogenous and semitransparent when fresh.
- The extracellular matrix of hyaline cartilage is homogenous with type II collagen and aggrecan proteins.
- The primary connective tissue cell is chondroblasts and chondrocytes, which remain either isolated in the matrix or forms small isogenous groups.

- Collagen accounts for about 40% of the dry weight of hyaline cartilage and the collagen fibers are embedded in the hydrated gels of proteoglycans and glycoproteins.
- Hyaline cartilage is found in the articular surfaces of movable joints, in the walls of larger respiratory passages, and in the ventral ends of ribs.
- Hyaline cartilage forms the temporary skeleton in the embryonic stage which is then replaced by bone.
- Hyaline cartilage is covered with a perichondrium except at the epiphyses and articular cartilage.

b. Elastic Cartilage

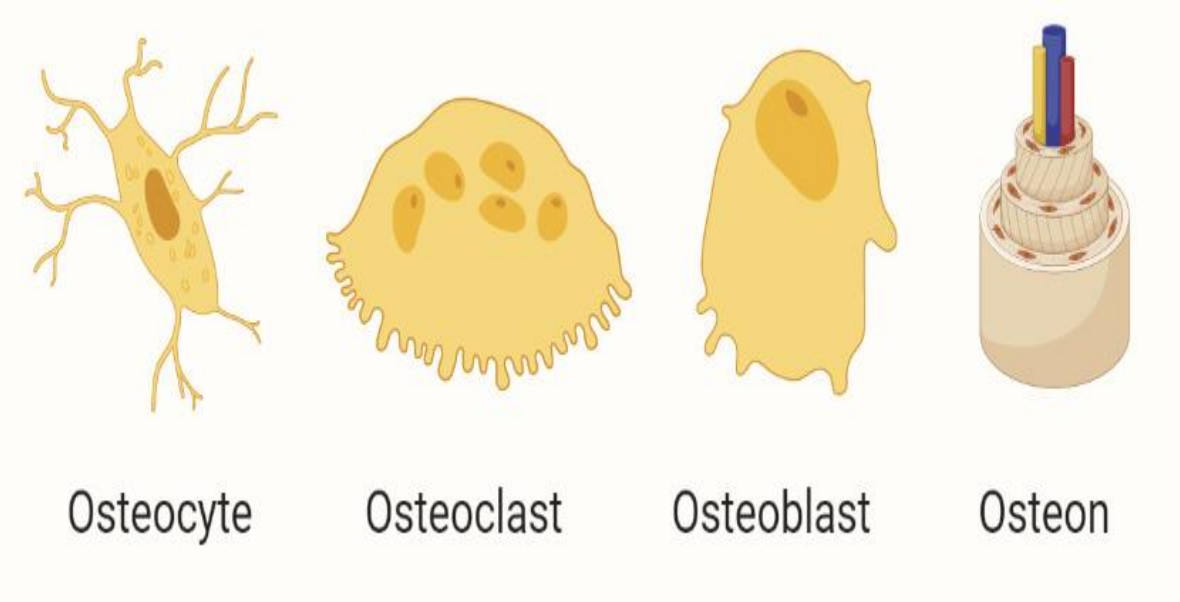
- Elastic cartilage is similar to hyaline cartilage in structure except for abundant networks of elastic fibers and collagen and aggrecan.
- The structure of elastic cartilage consists of elastic fibers lying in the solid matric with chondrocytes lying between the fibers.
- The chondrocytes are distributed in the matrix in the form of small isogenous groups.
- Elastic cartilage is more flexible than hyaline cartilage due to the presence of elastic fibers that provides flexibility in the movement of the cartilage.
- Elastic cartilage is found in different areas of the body like the auricle of the ear, walls of the external auditory canal, the epiglottis, and the upper respiratory tract.
- Like hyaline cartilage, elastic cartilage also contains an outer perichondrium.

c. Fibrocartilage

- Fibrocartilage is found in different forms in different structures, and its structure lies somewhere between the hyaline cartilage and the dense connective tissue.

- The extracellular matrix of fibrocartilage is composed of dense masses of white collagen fibers that are secreted by the chondrocytes.
- The chondrocytes occur either singly or in aligned isogenous aggregates in the matrix along with other extracellular matrix components.
- Fibrocartilage does not have an outer covering of the perichondrium, but the structure of fibrocartilage is essentially a mixture of hyaline and dense connective tissue.
- Fibrocartilage is found in the intervertebral discs of the spinal column, pubic symphysis, and portions of tendons.

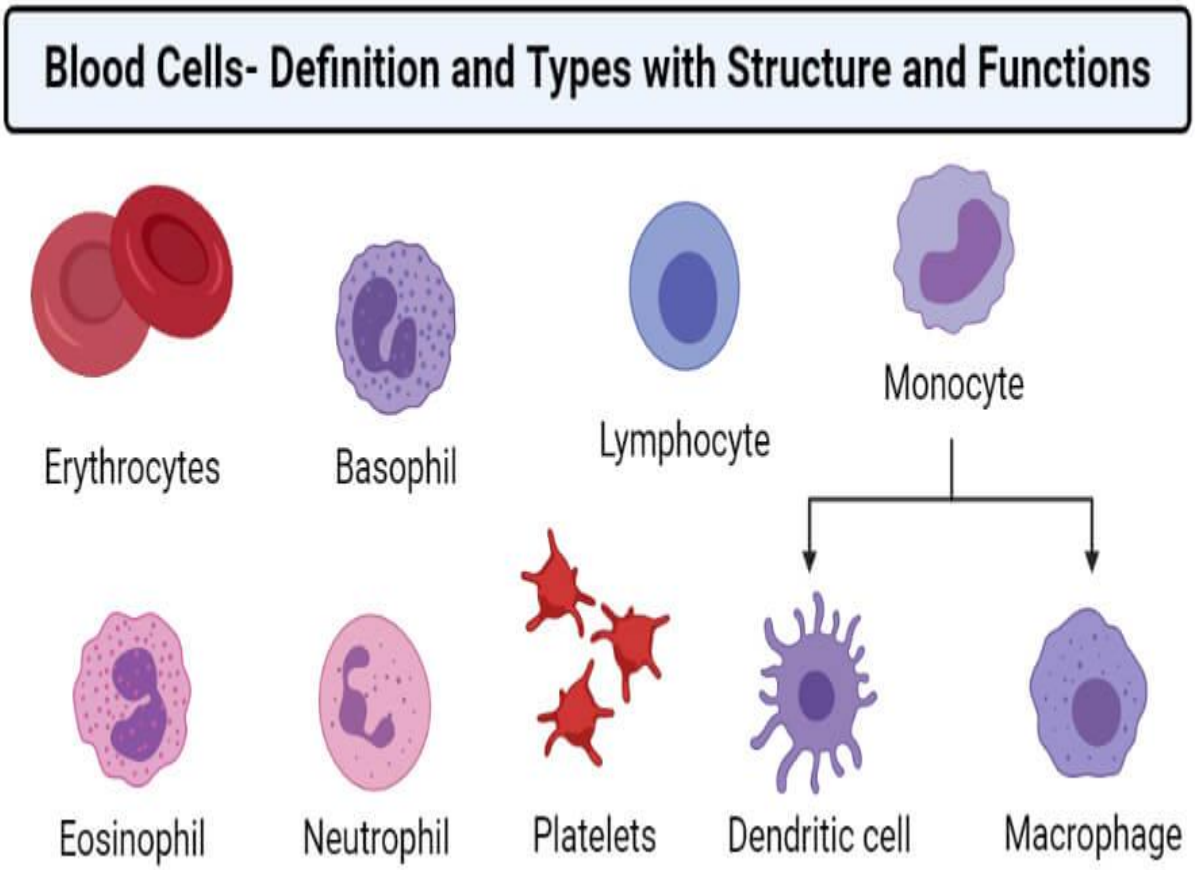
B. Bone



- Bone is a specialized connective tissue composed of a calcified extracellular matrix and osteocytes.
- The matrix of bone tissue is calcified and the movement of nutrients and other substances between osteocytes and blood capillaries through a thin cylindrical space of the canaliculi.

- The matrix is composed of about 15% water, 30% collagen fibers and 55% crystallized mineral salts. The most abundant mineral salt is calcium phosphate, followed by calcium hydroxide.
- The hardness of bone depends on the crystallized inorganic mineral salts, whereas the flexibility of the bone depends on the collagen fibers.
- The cells of the bone tissue are of three types; osteocytes, osteoblasts, and osteoclasts.
- Osteoblasts are found in lacunae between the bone matrix with cytoplasmic processes in small canaliculi.
- Osteoblasts are growing cells that synthesize and secrete the organic component of the matrix.
- Osteoclasts are giant, multinucleated cells that are involved in the removal of calcified bone matrix.
- The osteoblasts produce various components of the bone matrix, including Type I collagen fibers, proteoglycans, and matricellular glycoproteins.
- The activity of osteoblast is regulated by osteoclast cells which remove the calcified matric components.
- Depending on the size and distribution of the spaces in the matrix, regions of the bone can be either compact or spongy.
- Compact bone tissue contains few spaces and is the strongest form of bone tissue. Spongy bone tissue has numerous spaces with some spaces filled with red bone marrow.

C. BLOOD



- Blood is a specialized fluid connective tissue consisting of cells and extracellular fluid material called plasma.
- The plasma is an aqueous solution that makes up about 55% of the total volume of blood. It consists of water, nutrients, respiratory gases, nitrogenous waste products, and hormones.
- Important plasma proteins are albumin and globulins that are important in the maintenance of osmotic pressure of the blood and the transport of various materials.
- **Blood cells** comprise most of the composition of blood and are synthesized by the red bone marrow.

- Three different types of cells occur in the blood; red blood cells, white blood cells, and platelets.
- The cells are formed in the bone marrow, and these originate from stem cells followed by their maturation into different types of cells.
- The concentration of different blood cells in blood differs from the condition of the body and the individual's age.
- The primary function of blood is the transport of respiratory gases and nutrients from one cell to another.

Other Types

a. Fibrous connective tissue

- Fibrous tissue is mainly composed of closely packed bundles of collagen fibers, and the structure of the tissue is similar to that of dense connective tissue.
- Few fibrocytes are present in rows between the bundle of fibers, and the tissue is commonly found in ligaments, periosteum, and outer covering of other organs like the kidney and the brain.
- Fibrous tissue is also known as scar tissue as it is involved in the repair of damaged tissue mediated by the production of a large number of fibrocytes.
- Fibrous tissue is characterized by the presence of an interwoven network of collagen fibers in the matrix and fibrocytes.

b. Lymphoid connective tissue

- Lymphoid tissue is the tissue that makes up the lymphatic system of the body, consisting of white blood cells, bone marrow, thymus, spleen, and lymph nodes.
- Lymphoid or Lymphatic tissue is a specialized form of reticular connective tissue that contains a large number of lymphocytes.

- The extracellular matrix of lymphoid tissue is similar to loose connective tissue with scattered collagen and few elastin fibers.

Functions of Connective Tissue

1. Connective tissues provide adhesion as well as the connection between different tissues and organs of the body.
2. Connective tissues like bones and cartilage provide structure and internal support to different parts of the body. The skeletal system provides a framework for the body.
3. These tissues also protect important organs of the body like the lungs, heart, brains, and sense organs.
4. Cartilage, ligaments, and tendons help in the attachment between bones and muscles, which is important for movement.
5. Blood transports respiratory gases, nutrients, and water to different cells and tissues through the body.
6. Cells of connective tissue like lymphocytes, macrophages, and white blood cells are immune cells that protect the body against different forms of infections.
7. Connective tissues are involved in the repair and replacement of damaged tissues.
8. Adipose tissue stores a large number of fats which can then be metabolized later to produce energy.
9. The adipose tissue also provides insulation in the form of a layer underneath the skin, helping in maintaining the homeostasis of the body.

Examples of Connective Tissue

Tendons

- Tendon is a fibrous connective tissue that connects muscles to bone and can withstand certain tension.
- Tendon is composed of dense connective tissue with the extracellular matrix and connective tissue cells.
- Specialized fibroblasts are found in the tendon, which is called tenocytes. The tenocytes secrete collagen fibers forming the extracellular matrix of the tissue.
- The collagen fibers are densely packed and are arranged parallel to one another in the form of fascicles.
- The fascicles are surrounded by endotendineum, which is a layer of loose connective tissue.
- The structure of tendons is similar to that of muscles, but the protein fibers present in tendons are mostly collagen fibers with few elastic fibers.
- The most important function of tendons is to create a connection between muscle and bone, which helps in the movement of bones and provides additional stability.

Lymph

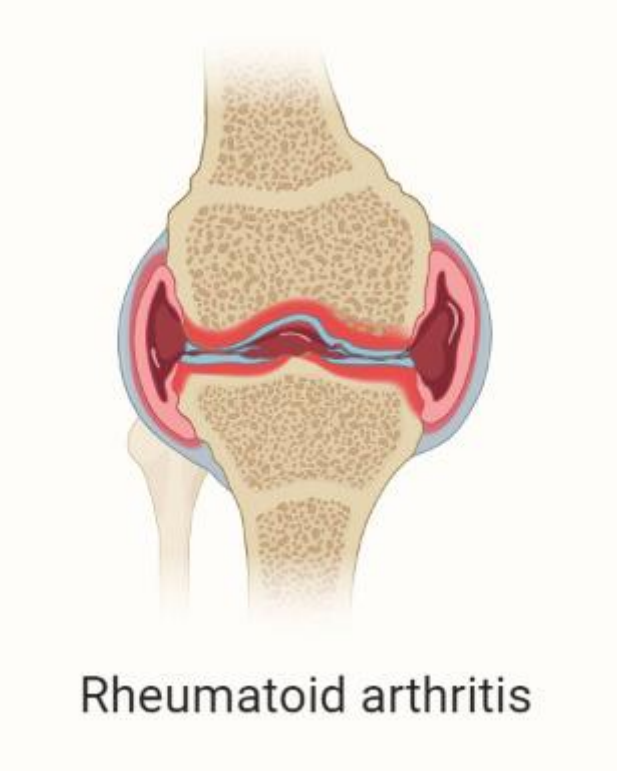
- Lymph is a fluid connective tissue that transports lymphocytes to different parts of the body.
- Lymph flows through the lymphatic system, which consists of lymph vessels and intervening lymph nodes.
- The lymph is derived from the interstitial fluid, and thus, its composition is similar to that of blood plasma.
- The lymph exchanges proteins and excess interstitial fluid with the bloodstream. It also moves the lymphocytes from the lymph nodes to other sites of the body.
- Lymph also contains chylomicrons that transport fats from the digestive system to the blood and then to other parts of the body.

Connective tissue diseases and disorders

Connective tissue disease is a condition that affects the tissue that is involved in the binding of different organs and tissues in the body. It is also known as collagenosis as the disease of connective tissue is often associated with the inflammation and weakness of collagen fibers. Many connective tissue diseases

occur as a result of inflammation in tissues as a result of an immune system response. The majority of these diseases and disorders are autoimmune in nature and might even be heritable. Some of the common connective tissue diseases and disorders can be explained as;

1. Rheumatoid arthritis



- Rheumatoid arthritis is one of the most common connective tissue diseases, which is an autoimmune disease and is heritable.
- During this disease, the immune cells attack the cells of the connective tissue, especially those present in the joints. However, it can affect other organs like the heart, lungs, and eyes.

2. Systemic Lupus Erythematosus

- Systemic Lupus Erythematosus is a disease of connective tissue that can cause inflammation of connective tissue present in every organ of the body.
- The most common site of inflammation during the disease include the brain, skin, blood, and lungs.

3. Scleroderma

- Scleroderma is also an autoimmune disease that causes scar tissue to form in the skin and internal organs like the gastrointestinal tract and blood vessels.
- Scleroderma is caused due to the inflammation of connective tissue cells present in the skin and epithelial tissue.

4. Mixed connective tissue disease

- Mixed connective tissue disease is a disorder where the features of various connective tissue diseases occur together or overlap.
- Some of the common diseases that make up the mixed connective tissue disease are systemic sclerosis, polymyositis, and dermatomyositis.
- The course of this disorder is chronic but milder than other connective tissue diseases. Mixed connective tissue disease is considered an intermediate stage of scleroderma or systemic lupus erythematosus.

5. Undifferentiated connective tissue disease

- Undifferentiated connective tissue disease is an autoimmune condition in which the immune system attacks its own tissues and cells.

- Undifferentiated connective tissue disease is diagnosed when the evidence of the existing autoimmune condition doesn't meet the criteria for a specific condition.

Frequently Asked Questions (FAQs)

Question 1. What is connective tissue?

Answer. Connective tissue is one of the tissue systems in animals composed of different types of cells, all of which work together to provide internal support, adhesion, and cohesion between tissues to form organs and systems.

Question 2. Is muscle a connective tissue?

Answer. No, muscle is not a connective tissue.

Question 3. Is cartilage a connective tissue?

Answer. Yes, cartilage is a specialized connective tissue.

Question 4. What are the three main components of connective tissue?

Answer. The three main components of connective tissue are cells, protein fibers, and the ground substance. The fibers and ground substance together form the extracellular matrix.

Question 5. What is connective tissue disease?

Answer. A connective tissue disease is a group of conditions that affect the protein-rich tissue supporting other organs and tissues of the body.

Question 6. What is the function of connective tissue?

Answer. The most important function of connective tissue is to provide internal support and adhesion to different organs and tissues of the body.

Question 7. What tissue connects muscles to bones?

Answer. A fibrous connective tissue called the tendon connects muscles to bones.

Question 8. Where are connective tissues found?

Answer. Connective tissues are found throughout the body and are present between different tissues and organs.

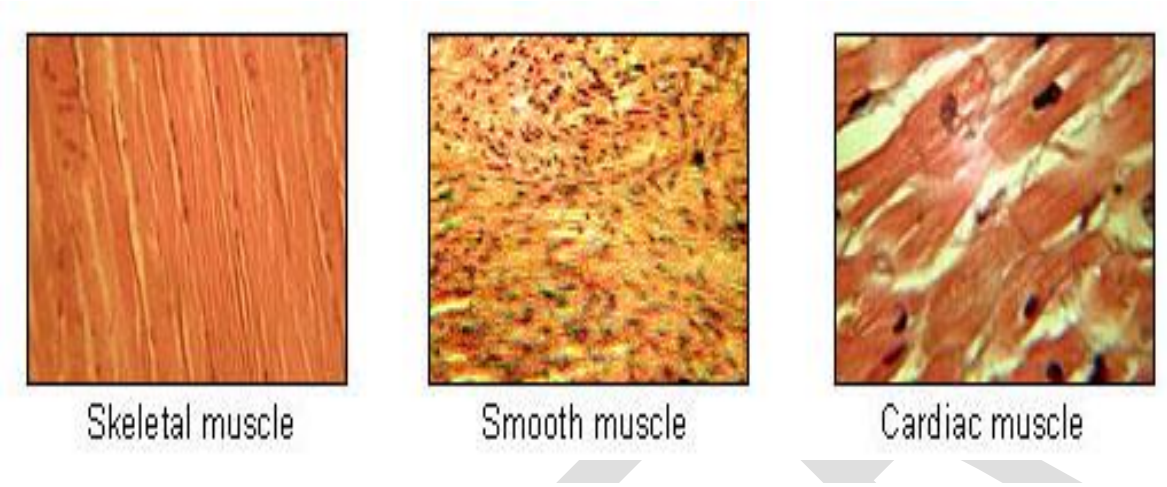
Question 9. Why is blood considered a connective tissue?

Answer. Blood is considered a connective tissue because it transports nutrients and other essential compounds throughout the body connecting different organs and systems of the body. Besides, structurally, blood consists of a closely packed extracellular matrix with blood cells.

MUSCLE TISSUE

- Muscle tissue is composed of cells that have the special ability to shorten or contract in order to produce movement of the body parts.
- The tissue is highly cellular and is well supplied with blood vessels.
- The cells are long and slender so they are sometimes called muscle fibers, and these are usually arranged in bundles or layers that are surrounded by connective tissue.
- Actin and myosin are contractile proteins in muscle tissue.

- Muscle tissue can be categorized into skeletal muscle tissue, smooth muscle tissue, and cardiac muscle tissue.



- Skeletal muscle fibers are cylindrical, multinucleated, striated, and under voluntary control.
- Smooth muscle cells are spindle shaped, have a single, centrally located nucleus, and lack striations.
- They are called involuntary muscles.
- Cardiac muscle has branching fibers, one nucleus per cell, striations, and intercalated disks.
- Its contraction is not under voluntary control.

NERVOUS TISSUE

- Nervous tissue is found in the brain, spinal cord, and nerves.
- It is responsible for coordinating and controlling many body activities.
- It stimulates muscle contraction, creates an awareness of the environment, and plays a major role in emotions, memory, and reasoning.
- To do all these things, cells in nervous tissue need to be able to communicate with each other by way of electrical nerve impulses.
- The cells in nervous tissue that generate and conduct impulses are called neurons or nerve cells.

- These cells have three principal parts: the dendrites, the cell body, and one axon.
- The main part of the cell, the part that carries on the general functions, is the cell body.
- Dendrites are extensions, or processes, of the cytoplasm that carry impulses to the cell body.
- An extension or process called an axon carries impulses away from the cell body.
- Nervous tissue also includes cells that do not transmit impulses, but instead support the activities of the neurons.
- These are the glial cells (neuroglial cells), together termed the neuroglia.
- Supporting, or glia, cells bind neurons together and insulate the neurons.
- Some are phagocytic and protect against bacterial invasion, while others provide nutrients by binding blood vessels to the neurons.

UNIT II

INTENGUMENTARY SYSTEM

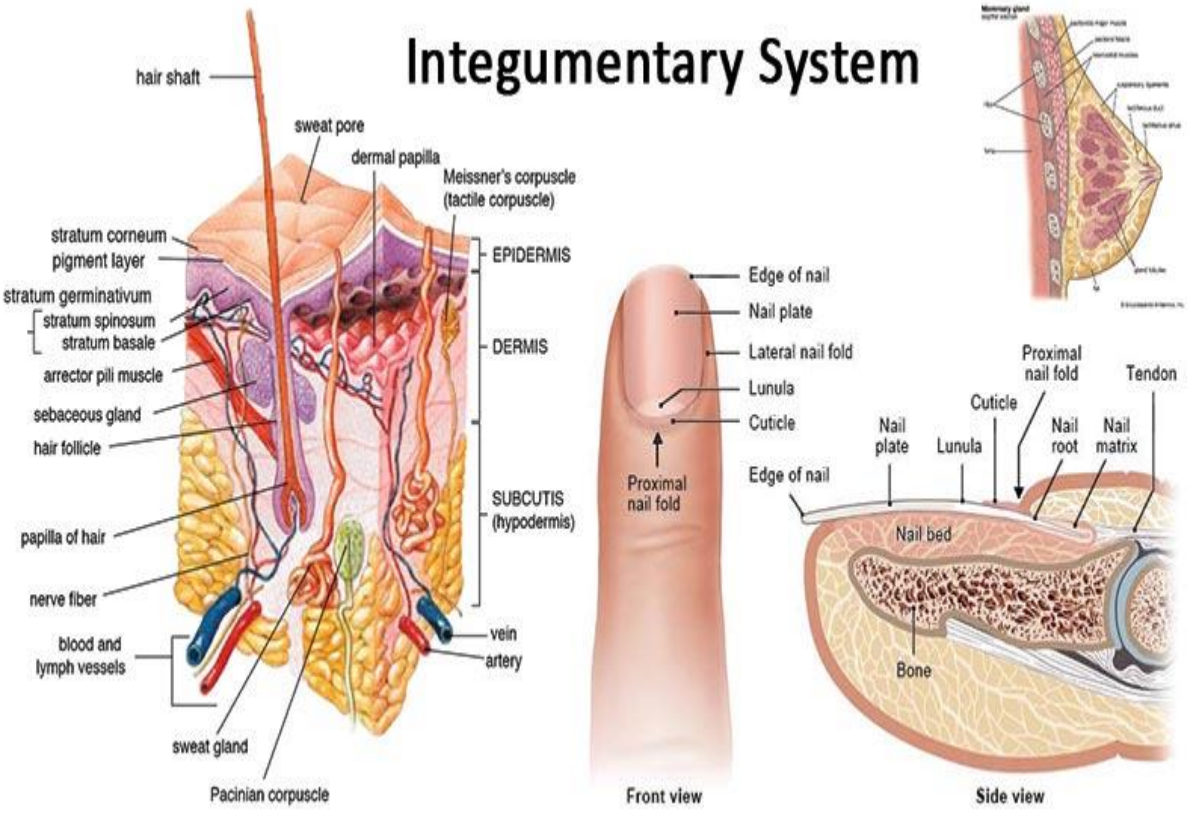


Figure: The Integumentary System.

Integumentary System definition

The integumentary system is a system comprised of organs that are the outermost protective covering of the animal body, the skin, and its various derivatives. The integumentary system protects against many threats such as infection, desiccation, abrasion, chemical assault, and radiation damage. In humans, the primary organ of the integumentary system is the skin. Along with skin, several other glands and different sensory units like somatosensory receptors and nociceptors are also a part of this organ system.

Organs of the Integumentary System (structure and functions)

The integumentary system is composed of skin and its appendages, subcutaneous tissue, deep fascia, mucocutaneous junctions, and breasts.

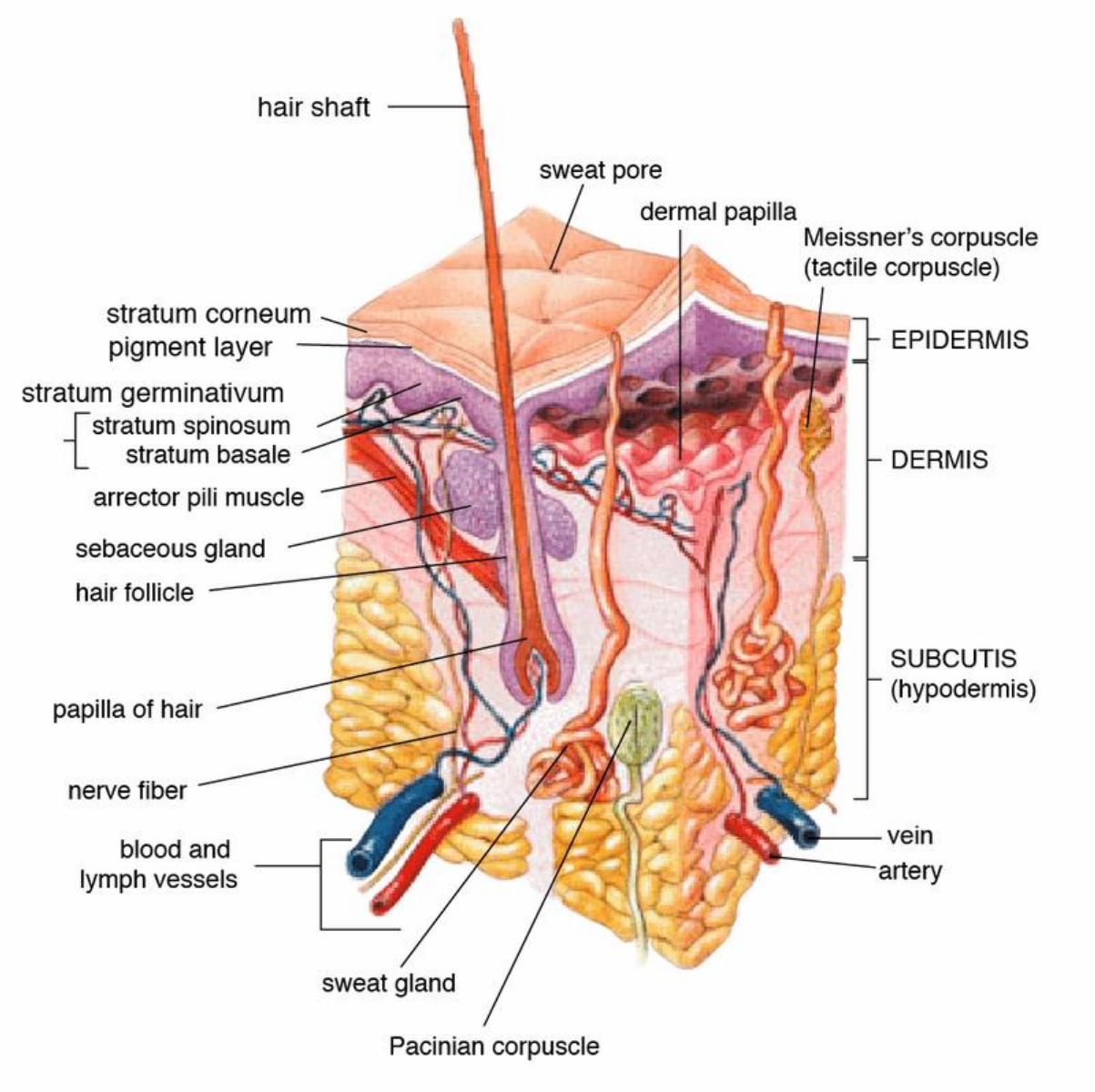


Figure: Anatomy of the human skin.

1. Skin

- Skin is the largest organ in our body.

- It covers up to $2m^2$ of the body surface area and contains numerous glands and sensory units.
- The skin is continuous but structurally different from the mucous membrane that lines the buccal cavity.

Structure

- Structurally, the skin is a multicellular organ composed of two distinct layers of tissues; an outer epidermis developed from ectoderm, and (ii) an inner dermis derived from the mesoderm.
- The related abundance of the two layers differs according to the environment.

a. Epidermis

- The epidermis is a stratified epithelium and usually quite thin in comparison to the dermis.
- It is the outer layer of skin that has no blood vessels supply, and the cells in the squamous epithelium receive blood via diffusion.
- It is further distinguished into two regions— The outermost region of many layers of dead usually flattened (squamous) cells forms a horny, resistant covering or stratum corneum on the skin surface.
- Its cells accumulate a horny protein, called keratin, gradually die and eventually wear off in the form of scurf or dandruff.
- The innermost or basal region of epidermis includes a single row of living columnar cells, the Malpighian layer, or stratum germinativum, which is separated from the underlying dermis by a basement membrane.
- Its cells actively divide and continually replace the worn-out cells of the cornified layer.
- Besides, the epithelium also contains few cells like melanocytes which are responsible for the pigmentation on the skin.

Functions

- Since keratin is tough and insoluble in water, the keratinized stratum corneum protects against mechanical injuries, fungal and bacterial attacks, and loss of body moisture.
- Melanin in the epidermis protects dermis and other internal organs against exposure to ultraviolet rays and its damaging effects.
- The epidermis is also responsible for the synthesis of Vitamin D under the exposure of UV rays from the sunlight.
- The Langerhans cells found in the epidermis are a part of the skin immune system and protect against foreign antigens.
- The sensory cells and receptors in the epidermis are responsible for sensation in the skin.

b. Dermis

- Dermis or corium, which is the inner layer of skin, is comparatively thicker than the epidermis.
- It is composed of fibrous connective tissue and contains many blood capillaries, lymph vessels, muscle fibers, nerve fibers, sense organs, and elastic fibers which bring the skin back to its normal shape.
- Pigment cells or melanocytes are mostly located in the dermis, although sometimes pigment granules are also found in the epidermis.
- Fat may accumulate as reserve food in specialized cells, called adipocytes, in deeper parts of the dermis and the subcutaneous tissue.
- Different glands like sweat glands and sebaceous glands are also present in the dermis.

Functions

- The blood vessels present in the dermis provide nourishment and waste removal from its cells as well as from the base of the epidermis.
- Dermis helps in thermoregulation as the sweat glands promote evaporation, resulting in a loss of excessive body heat.
- Dermis also provides support to the epidermis and allows the base for the cells.

c. Hypodermis

- The hypodermis is the innermost and thickest layer of the skin instead is the deeper subcutaneous tissue made of fat and connective tissue.
- This layer consists of cells like fibroblasts, fat cells, connective tissue, larger nerves and blood vessels, and macrophages.
- The purpose of hypodermis is to attach the skin to underlying bone and muscle as well as supplying the other layers of skin with blood vessels and nerves.
- The hypodermis is made up of loose connective tissue and elastin protein.
- The thickness of this layer differs in different parts of our body and is also significantly different in males and females.
- It is thickest in the shoulders and abdomen in men while in females, it is thicker in the hips and thighs.

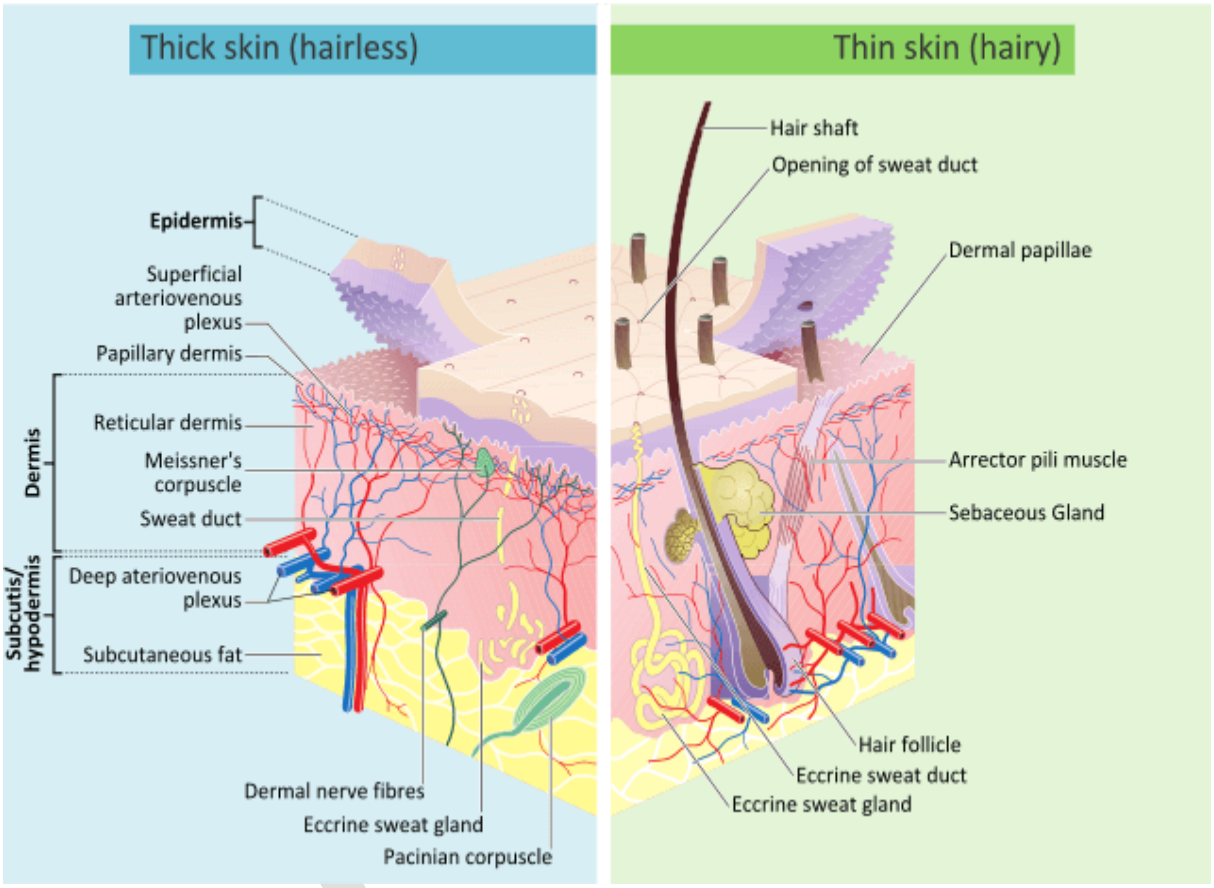
Functions

- Hypodermis contains a large amount of fat which function as energy storage.
- The thick layer protects the external agents and also acts as an insulator, protecting against cold.
- This layer provides attachment between the epidermis and dermis to the internal organs in the body.
- An appetite-regulating hormone called leptin is also synthesized by fat cells in the hypodermis layer.

Skin Anatomy and Physiology Video Animation

2. Appendages of the skin

- The skin itself is relatively simple, but its derivatives are numerous and complex.
- These derivatives are termed appendages of the skin and are formed form derived epidermal cells.



a. Epidermal glands

- Integumental or epidermal glands are formed by the Malpighian layer of epidermis that arise in the epidermis but often invade the dermis.
- They may be unicellular or multicellular, tubular or alveolar in shape, and simple, compound or branched.
- They are lined by cuboidal cells or columnar epithelium and are usually named after their nature or function.

Some of the common epidermal glands found in humans and other mammals are:

i. Sudoriferous Glands

- Sweat glands or sudoriferous glands (sudor = sweat) are abundant in the skin of most mammals.
- Sudoriferous glands are either of two types of secretory skin glands, eccrine or apocrine.
- Eccrine glands open directly onto the skin surface whereas apocrine glands open onto associated hair follicles.
- Eccrine glands can be found almost anywhere on the human body, with the highest concentration found on the palms and soles.
- However, apocrine glands are found in more restricted areas of the body including the axilla, anogenital region, external ear canal, and areola.

Structure

- They are slender coiled tubes embedded deep in the dermis, with their long ducts opening on the skin surface.
- The sweat glands consist of a secretory unit called a glomerulus and a long duct that takes the sweat to the target surfaces.
- These glands are embedded in the dermis or hypodermis, which are surrounded by adipose tissue.
- The secretory unit is surrounded by myoepithelial cells that facilitate the excretion of sweat.
- Ciliary glands in eyelashes and along margins of eyelids are modified sweat glands.

Function

- An essential function of the sweat gland is in the regulation of body temperature. Evaporation of watery perspiration also helps to cool and regulate body temperature in hot environments.

- Also, a little urea and some salts are eliminated dissolved in water in the sweat produced by these glands which help in excretion.

ii. Sebaceous gland

- The sebaceous gland consists of secretory epithelial cells derived from the same tissue as the hair follicles.
- These glands secrete an oily antimicrobial substance, sebum, into the hair follicles.
- Sebaceous glands are present in all parts of the body except the palms of the hands and the soles of the feet.
- The number of these glands is higher in the scalp, face, axillae, and groins.

Structure

- Most sebaceous glands are attached to hair follicles, and the size of the gland varies inversely with the diameter of the associated hair.
- A large-diameter hair has a small gland and vice versa.
- These are true holocrine glands, in that a gland in which the secretion is formed by the degeneration of the entire glandular cell.
- They open to the surface of the skin by way of the pilosebaceous canal.
- This holocrine type of gland has multiple acinar components. The acinus of each gland converges toward a common excretory duct.

Function

- Sebum helps to keep the hair soft and pliable and gives it a shiny appearance.
- It provides some waterproofing on the surface of the skin and acts as a bactericidal and fungicidal agent, preventing infection.
- The sebum also prevents drying and cracking of the skin, especially on exposure to heat and sunlight.

iii. Ceruminous Gland

- Ceruminous glands are modified apocrine glands, which together with sebaceous glands, produce the yellowish-brown wax secretion called cerumen or ear-wax.
- The ceruminous glands in humans are located in the cartilaginous section of the external auditory canal with the number ranging from 1,000 and 2,000 ceruminous glands in the normal ear.

Structure

- The ducts of the coiled tubules of the ceruminous gland pass through the dermis to empty into a hair follicle or onto the epidermal surface.
- The coiled ceruminous gland has a large lumen, and the cells are either cuboidal (inactive) or columnar (active).
- The gland is lined by a layer of secretory cells present on the myoepithelial cells.
- The secretion is first drained into respective ducts of the glandular cells which then flows into larger ducts and finally at the base of guard cells present in the auditory canal.

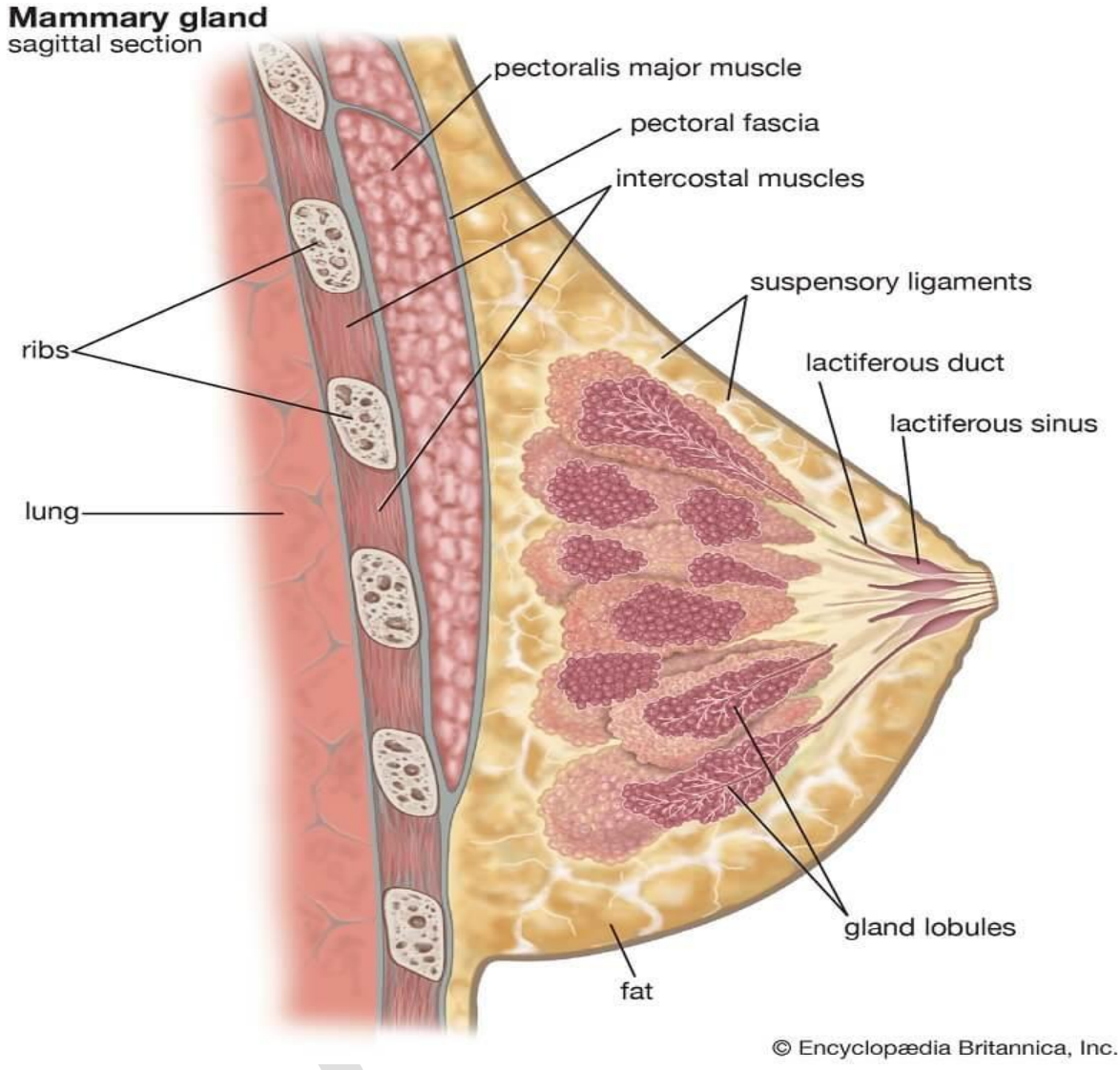
Function

- Cerumen plays an essential role in the protection of the ear canal against physical damage and microbial invasion.
- The pH of the ear canal is maintained by the secretions around 5.7 in the inner/medial aspects of the canal.

iv. Mammary glands

- Characteristic of mammals, these are compound tubular glands that produce milk during lactation period for feeding the young ones.
- These glands are present in all mammals and are rudimentary and non-functional in men.

- In humans, these glands develop at puberty by the action of growth hormone and estrogen; however, in other primates, breast development usually happens after the pregnancy.



Structure

- Mammary glands are, structurally, tear-shaped, and are composed of glandular tissue, fibrous tissue, fatty tissue, and blood supply.
- An adult female breast consists of around 20 lobes of glandular tissue where each lobe is made up of several lobules that radiate around the nipple.

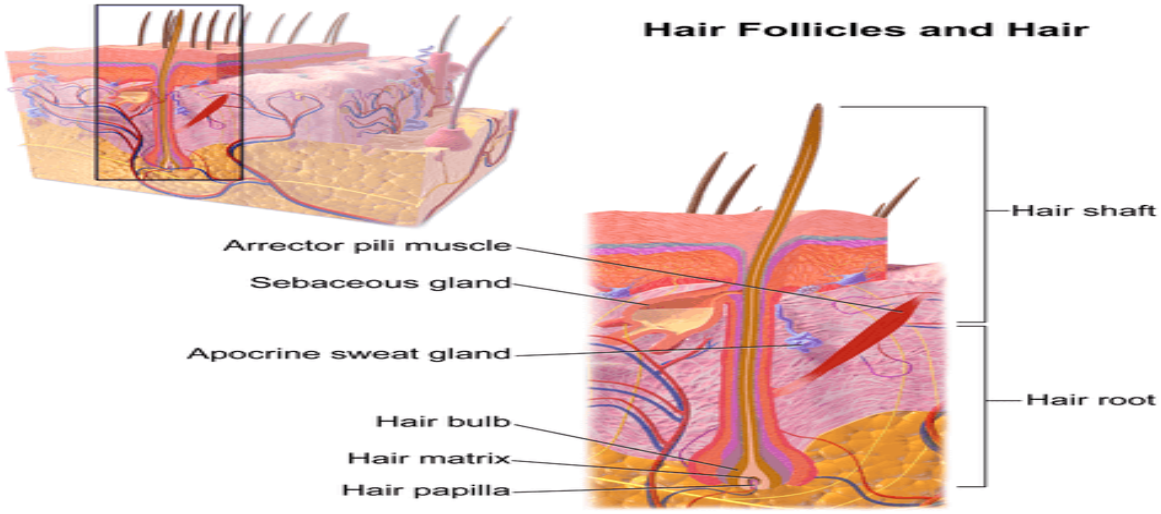
- Each of these lobules is composed of a group of alveoli that terminate into small ducts, which collectively form large excretory ducts called lactiferous ducts.
- These ducts, supported by the dense connective tissues, converge towards the center of the breasts to form reservoirs (also called lactiferous sinus) of milk. From each of these sinuses, a single duct arises that opens into the nipple.

Function

- The primary function of mammary glands is to provide nourishment to the infant through breastfeeding.
- In addition to their primary function of providing nutrients to the infant, breasts also have social and sexual prominence.
- Breasts, and especially the nipples, are an erogenous zone.

b. Hair and Hair follicles

- Hairs are characteristic of mammals. They may cover the entire body or may be reduced to patches or scattered hairs.
- Hairs are the cornified epidermal products of the integument.
- All the hairs on the surface of the skin are periodically lost by molting and are replaced by new sets of hairs.



Structure

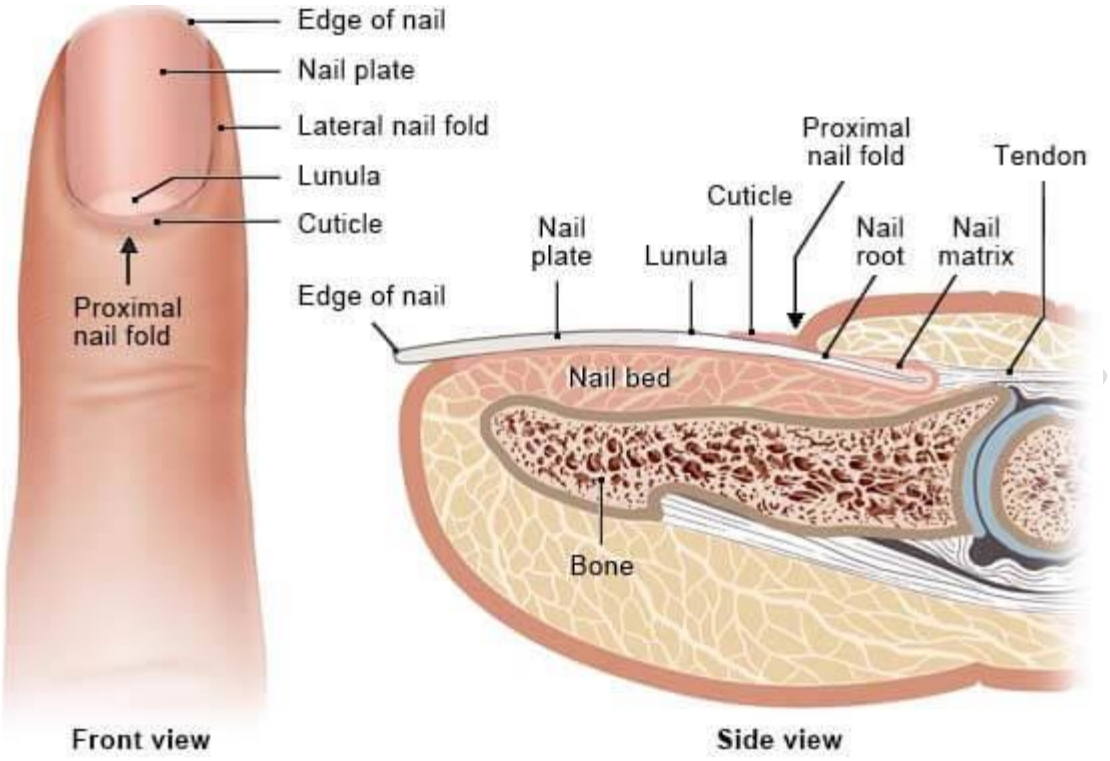
- Each hair originates from the bottom of a tubular invagination, or hair follicle, of the germinative layer of the epidermis into the dermis.
- A cluster of cells called the hair papilla or bulb is present at the base of the follicle.
- The hair is formed by the division of cells of the bulb, and they become keratinized when the old cells are push upwards, away from their source of nutrition.
- The part of the hair above the skin is called the shaft while the remainder is termed the root.
- Typically, the hair shaft consists of three layers: an external cuticle made up of overlapping microscopic scales, the middle cortex containing shriveled cells and pigments, and an inner medulla containing air spaces in larger hairs.

Functions

- The chief functions of hairs seem to serve for insulation of body and as sensitive tactile organs (e.g. vibrissae in rabbits).
- Hairs also function in the regulation of body temperature, and the facilitation of evaporation of perspiration.

c. Nails

- Human nails are equivalent to the claws, horns, and hooves of animals.
- Derived from the same cells as epidermis and hair these are hard, horny keratin plates that protect the tips of the fingers and toes.



Structure

- The nail organ consists of epithelial and connective tissue parts.
- The nail consists of the nail matrix that produces the nail plate and is mostly under the proximal nail wall and the nail bed epithelium, which ensures firm adhesion to the dermis of the nail bed.
- The root of the nail is embedded in the skin and covered by the cuticle, which forms the hemispherical pale area called the lunula.
- The nail plate is the exposed part that has grown out from the nail bed.

Functions

- The primary function of the nail is to protect the fingertip and the surrounding soft tissues from injuries.
- Nails also exert a counter-pressure that aids in the precise movement and touch sensitivity.

Structure and Functions of Nail Video Animation

Physiology of the Integumentary System

Development of skin color (Skin Pigmentation)

- The skin color in humans is determined by different pigments like melanin, carotene, and hemoglobin.
- Among all the pigments, melanin is the most crucial pigment for skin coloration and is formed only in the cytoplasm of the melanin-forming cell, the melanocyte.
- Melanin exists in two forms; eumelanin which gives the black and brown color and pheomelanin which gives red coloration.
- In general, there are more melanocytes per square millimeter on exposed skin than on covered areas. However, there is a high density of melanocytes about the genitalia and the nasal mucous membranes.
- Variations in skin color between racial groups and possibly between different individuals of the same race are a function of the rate and amount of melanin production by melanocytes rather than the number of melanocytes present.
- These are dendritic or branched cells that are found at the epidermal-dermal junction of the skin and mucous membranes.
- These dermal melanocytes reach the epidermis and become epidermal melanocytes. Melanocytes remaining down in the dermis in the human being gradually become inactive.

- On exposure to the UV radiation of the sun, the keratinocytes are stimulated to release chemicals which, in turn, stimulate the melanocytes to produce melanin.
- The melanin produced in the melanocytes is then transferred to the keratinocytes via a cell organelle called melanosome, which results in the accumulation of melanin in the keratinocytes.
- Melanosome contains a copper-containing enzyme called tyrosinase which catalyzes the synthesis of melanin from tyrosine.
- The accumulation of melanin results in the darkening of the skin. After the exposure to the sun, it takes about ten days for melanin synthesis to the peak.
- Similarly, as new skin is formed, epidermal cells move outward to become the stratum corneum, and the melanin granules contained within them are carried along and appear in the stratum corneum not as granules any longer but as fine irregular pigmented particles.

Hair Growth

- Hair is a component of the integumentary system and extends downward into the dermal layer where it sits in the hair follicle.
- Similar to the skin, hair forms by rapid division and differentiation of stem cells which form keratinocytes that migrate, flatten, and die, forming keratinized cells.
- The final hair product that is exposed on the surface of the skin will be composed entirely of keratin.
- The growth of the hair follicle is cyclical. This cycle can be divided into three phases: anagen(growth), catagen (transition), and telogen (rest).
- Anagengrowth is the active phase in which the hair follicle takes on its onion-like shape and works to produce the hair fiber. About 85–90% of all scalp hairs are in anagen.

- The synthesis of the hair shaft and pigmentation only takes place in the anagen phase. The axial symmetry within the hair bulb decides the curvature of the final hair structure.
- By the end of anagen, the mitotic activity of the matrix cells is reduced, and the follicle enters a highly controlled involuntary phase known as catagen.
- Catagen lasts approximately two weeks in humans, and during this phase, the proximal part of the hair shaft becomes keratinized and forms the club hair. In contrast, the distal portion of the follicle loses 1/6th of its diameter by apoptosis.
- The telogen stage is the duration between the completion of catagen and the onset of the next anagen phase.
- Telogen stage lasts for 2–3 months and approximately 10–15% of all hairs in the scalp are in this stage.
- In the telogen stage, the hair shaft is transformed into club hair and finally shed.
- This phase lasts until anagen initiating signals from the dermal papilla stimulates the hair germ to show enhanced proliferative and transcriptional activity, leading to the initiation of anagen.

Nail growth

- The nail is the most significant skin appendage. It grows continuously through life in a non-cyclical manner; its growth is not hormone-dependent.
- The nail of the middle finger of the dominant hand grows fastest with approximately 0.1 mm /day, whereas the big toenail grows only 0.03-0.05 mm /day.
- The nails' size and shape vary characteristically from finger to finger and from toe to toe, for which the size and shape of the bone of the terminal phalanx are responsible.

- The nail is a continuously and lifelong growing keratin plate that is biochemically identical to the hair shaft.
- The growth of nails occurs via extrusion, meaning that new growing cells are added to the base while the old cells are pushed outward to the fingertips.
- The keratin in the old cells becomes harder, and ultimately the cells become dead and just hardened structures.
- Some of the living cells are still present on the nail at the base in the form of the white moon-like lunula.
- The cell growth occurs mostly in the germinal matrix in the nail bed.
- The cells that provide shine to the nail surface are added on top of the nail fold.
- With the growth of the nail, it is forced into the concave structure.

Functions of the Integumentary System

The integumentary system of vertebrates is genuinely a 'jack-of-all-trades' since it performs several essential functions, some of which are:

Protection

- The integument or skin separates the animal from its external environment and helps to maintain a constant internal environment.
- The inflammatory cells in the skin provide defense against intruding antigens.
- The pigment melanin protects against harmful ultraviolet rays in sunlight.
- The lipid and oil-like secretion of different glands acts as another barrier against chemicals and also prevent heat loss.

Thermoregulation

- The average body temperature is maintained by the action of sweat glands as well as the hair on the skin of mammals.

- Evaporation of watery perspiration from the skin helps to cool and regulate body temperature in hot environments.
- Similarly, the hair also aids in the regulation of body temperature, and facilitation of evaporation of
- For the elimination of heat, integumentary blood vessels dilate so that skin becomes a radiator whereas, for the conservation of heat, the vessels constrict.

Excretion

- The secretion of sweat and sebaceous glands contains some amount of urea and other ions that aid in excretion. Excess vitamin B is also removed in the form of sweat.
- The skin is a minor excretory organ for some substances, especially when kidney function is impaired and aromatic substances, e.g. garlic and other spices.

Formation of Vitamin D

- A lipid-based substance, 7-Dehydrocholesterol, in the skin is converted to vitamin D by sunlight.
- This vitamin is used in the formation and maintenance of bone, along with calcium and phosphate.

Cutaneous Sensation

- There are sensory receptors in the dermis that are sensitive to touch, pressure, temperature, or pain.
- The stimulation generates nerve impulses in sensory nerves that are transmitted to the cerebral cortex.

Absorption

- Skin is capable of absorbing some substances which include some drugs, hormone replacement therapy during the menopause, and nicotine as an aid

to smoking cessation in transdermal patches and some toxic chemicals like mercury.

Integumentary System Diseases

Bacterial infection

Impetigo

- Impetigo is a highly infectious bacterial infection commonly caused by *Staphylococcus aureus*.
- It begins with superficial pustules, usually around the nose and mouth. It is spread by direct contact and is common in children and immunosuppressed individuals.

Cellulitis

- Cellulitis is a spreading infection caused by some anaerobic bacteria, including *Streptococcus pyogenes* and *Clostridium perfringens* that enter through a cut in the skin.
- Their spread is facilitated by the formation of enzymes that break down the connective tissue that generally isolates an area of inflammation.
- If untreated, the bacteria may enter the blood, causing septicemia.

Fungal Infection

Ringworm and tinea pedis

- These are superficial skin infections.
- In ringworm infection, there is an outward spreading ring of inflammation, which mostly affects the scalp, feet, and groin and is easily spread to others.
- Tinea pedis (athlete's foot) affects the skin between the toes.

Viral Infection

Human papillomavirus (HPV)

- HPV causes warts or verrucas that are spread by direct contact. This creates a proliferation of the epidermis and development of a small firm growth, which is nearly always benign.

Herpesviruses

- Rashes seen in chickenpox and shingles are caused by the herpes zoster virus.
- Other herpes viruses like HSP1 and HSP2 cause cold sores and genital herpes, respectively.

Inflammatory diseases

Eczema (Dermatitis)

- Eczema is a common inflammatory skin disease that may be either acute or chronic.
- Acute dermatitis is characterized by redness, swelling, and exudation of serous fluid usually accompanied by *pruritus* (itching) and finally leading to crusting and scaling.
- In the case of chronic conditions, the skin thickens and may become leathery due to longterm scratching, which may cause infection.

Acne vulgaris

- Acne is commonest in adolescent males and is thought to be caused by increased levels of testosterone after puberty.
- This is caused when the sebaceous glands (in hair follicles) become blocked and then infected, leading to inflammation and pustule formation.

Malignant tumors

Basal cell carcinoma

- Basan cell carcinoma is the least malignant and most common type of skin cancer.
- This tumor is associated with long-term exposure to sunlight and is, thus, most likely to occur on sun-exposed sites, usually the head or neck.
- Cancer appears as a shiny nodule, and later this breaks down, becoming an ulcer with irregular edges, commonly called a rodent ulcer.

Malignant melanoma

- Malignant melanoma is a malignant proliferation of melanocytes, usually originating in a mole that enlarges and may have an irregular outline.
- The melanocytes may ulcerate and bleed and are observed most commonly in young and middle-aged adults.
- This tumor develops as a result of recurrent episodes of intensive exposure to sunlight, including repeated episodes of sunburn, especially in childhood.

SKELETAL SYSTEM ANATOMY AND PHYSIOLOGY

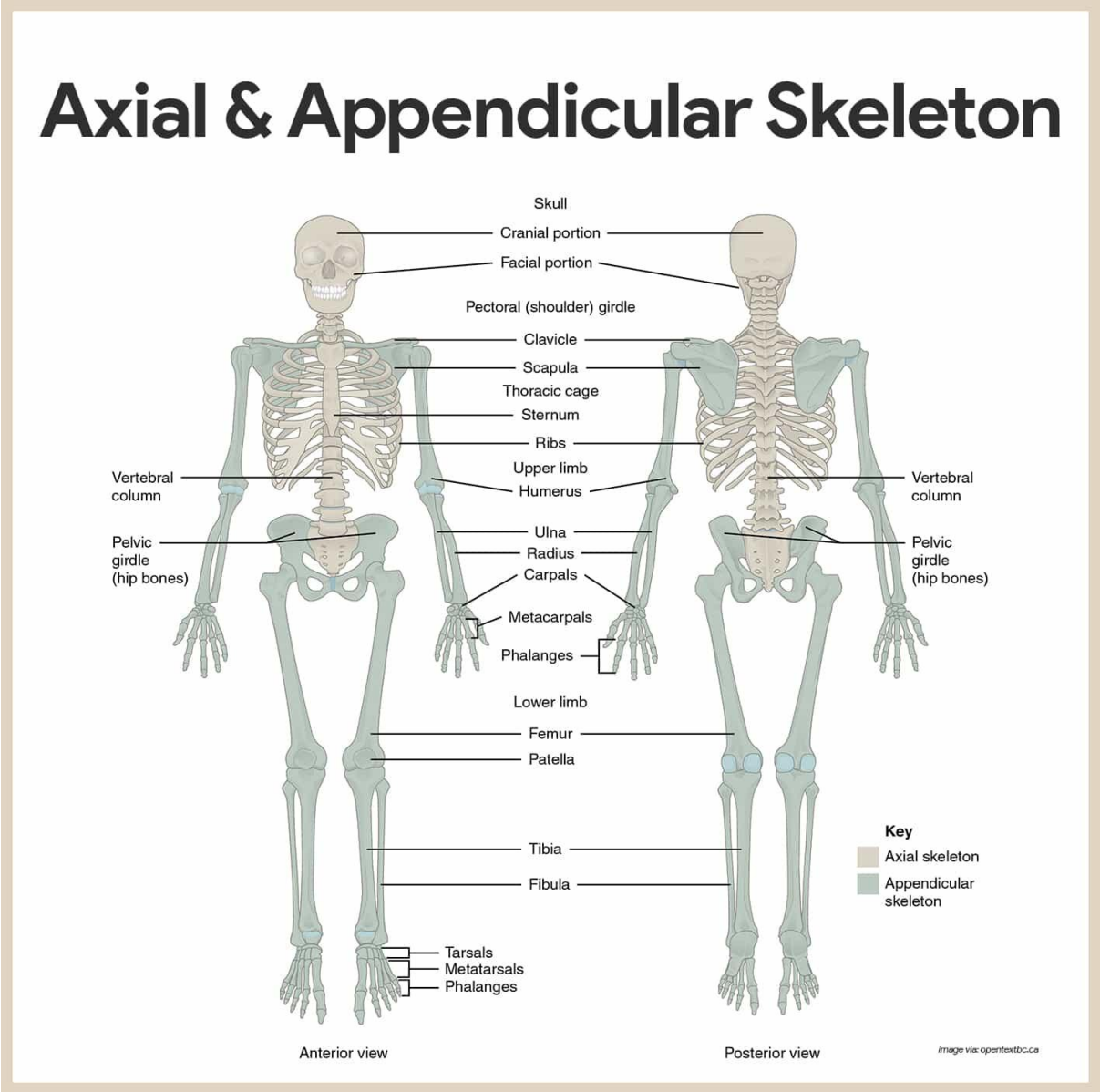
Functions of the Skeletal System

Besides contributing to body shape and form, our bones perform several important body functions.

- **Support.** Bones, the "steel girders" and "reinforced concrete" of the body, form the internal framework that supports the body and cradle its soft organs; the bones of the legs act as pillars to support the body trunk when we stand, and the rib cage supports the thoracic wall.
- **Protection.** Bones protect soft body organs; for example, the fused bones of the skull provide a snug enclosure for the brain, the vertebrae surround the spinal cord, and the rib cage helps protect the vital organs of the thorax.
- **Movement.** Skeletal muscles, attached to bones by tendons, use the bones as levers to move the body and its parts.
- **Storage.** Fat is stored in the internal cavities of bones; bone itself serves as a storehouse for minerals, the most important of which are calcium and phosphorus; because most of the body's calcium is deposited in the bones as calcium salts, the bones are a convenient place to get more calcium ions for the blood as they are used up.
- **Blood cell formation.** Blood cell formation, or hematopoiesis, occurs within the marrow cavities of certain bones.

ANATOMY OF THE SKELETAL SYSTEM

The skeleton is subdivided into two divisions: the axial skeleton, the bones that form the longitudinal axis of the body, and the appendicular skeleton, the bones of the limbs and girdles.



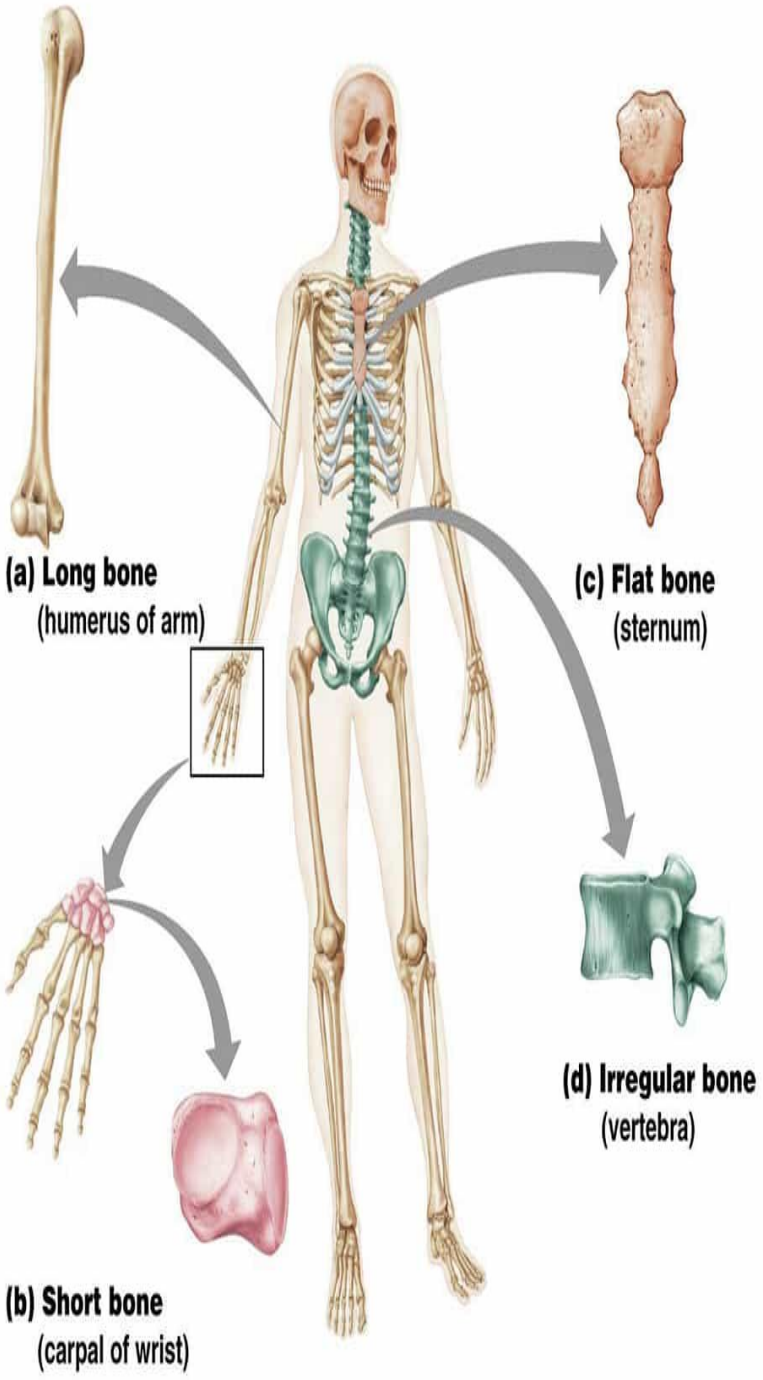
CLASSIFICATION OF BONES

The adult skeleton is composed of 206 bones and there are two basic types of osseous, or bone, tissue: compact bone and spongy bone, and are classified into four groups according to shape: long, short, flat, and irregular.

- **Compact bone.** Compact bone is dense and looks smooth and homogeneous.

- **Spongy bone.** Spongy bone is composed of long, needle-like pieces of bone and lots of open space.
- **Long bones.** Long bones are typically longer than they are wide; as a rule, they have a shaft with heads at both ends, and are mostly compact bone.
- **Short bones.** Short bones are generally cube-shaped and mostly contains spongy bone; **sesamoid bones**, which form within tendons, are a special type of short bone.
- **Flat bones.** Flat bones are thin, flattened, and usually curved; they have two thin layers of compact bone sandwiching a layer of spongy bone between them.
- **Irregular bones.** Bones that do not fit one of the preceding categories are called irregular bones.

Classification of Bones



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Long Bone

The structure of a long bone is shown both through gross anatomy and microscopic anatomy.

Gross Anatomy

The gross structure of a long bone consists of the following:

- **Diaphysis.** The diaphysis, or shaft, makes up most of the bone's length and is composed of compact bone; it is covered and protected by a fibrous connective tissue membrane, the **periosteum**.
- **Sharpey's fibers.** Hundreds of connective tissue fibers called **perforating** or **Sharpey's**, **fibers** secure the periosteum to the underlying bone.
- **Epiphyses.** The epiphyses are the ends of the long bone; each epiphysis consists of a thin layer of compact bone enclosing an area filled with spongy bone.
- **Articular cartilage.** Articular cartilage, instead of a periosteum, covers its external surface; because the articular cartilage is glassy hyaline cartilage, it provides a smooth, slippery surface that decreases friction at joint surfaces.
- **Epiphyseal line.** In adult bones, there is a thin line of bony tissue spanning the epiphysis that looks a bit different from the rest of the bone in the area; this is the epiphyseal line.
- **Epiphyseal plate.** The epiphyseal line is a remnant of the epiphyseal plate (a flat plate of hyaline cartilage) seen in young, growing bone; epiphyseal plates can cause the lengthwise growth of a long bone; by the end of puberty, when hormones inhibit long bone growth, epiphyseal

plates have been completely replaced by bones, leaving only the epiphyseal lines to mark their previous location.

- **Yellow marrow.** In adults, the cavity of the shaft is primarily a storage area for adipose (fat) tissue called the yellow marrow, or **medullary**, cavity.
- **Red marrow.** However, in infants, this area forms blood cells and red marrow is found there; in adult bones, red marrow is confined to cavities in the spongy bone of flat bones and epiphyses of some long bones.
- **Bone markings.** Even when looking casually at bones, one can see that their surfaces are not smooth but scarred with bumps, holes, and ridges; these bone markings reveal where muscles, tendons, and ligaments were attached and where blood vessels and nerves passed.
- **Categories of bone markings.** There are two categories of bone markings: (a) **projections**, or **processes**, which grow out from the bone surface, and (b) **depressions**, or cavities which are indentations in the bone; a little trick for remembering some of the bone markings are all the terms beginning with T are projections, while those beginning with F (except facet) are depressions.

Microscopic Anatomy

To the naked eye, spongy bone has a spiky, open appearance, whereas compact bone appears to be very dense.

- **Osteocytes.** The mature bone cells, osteocytes, are found within the matrix in tiny cavities called **lacunae**.
- **Lamellae.** The lacunae are arranged in concentric circles called lamellae around central (**Haversian**) canals.

- **Osteon.** Each complex consisting of central canals and matrix rings is called an osteon, or **Haversian system**.
- **Canaliculi.** Tiny canals, canaliculi, radiate outward from the central canals to all lacunae; the canaliculi form a transportation system that connects all the bone cells to the nutrient supply through the hard bone matrix.
- **Perforating canals.** The communication pathway from the outside of the bone to its interior (and the central canals) is completed by perforating (**Volkmann's**) canals, which run into the compact bone at right angles to the shaft.

Axial Skeleton

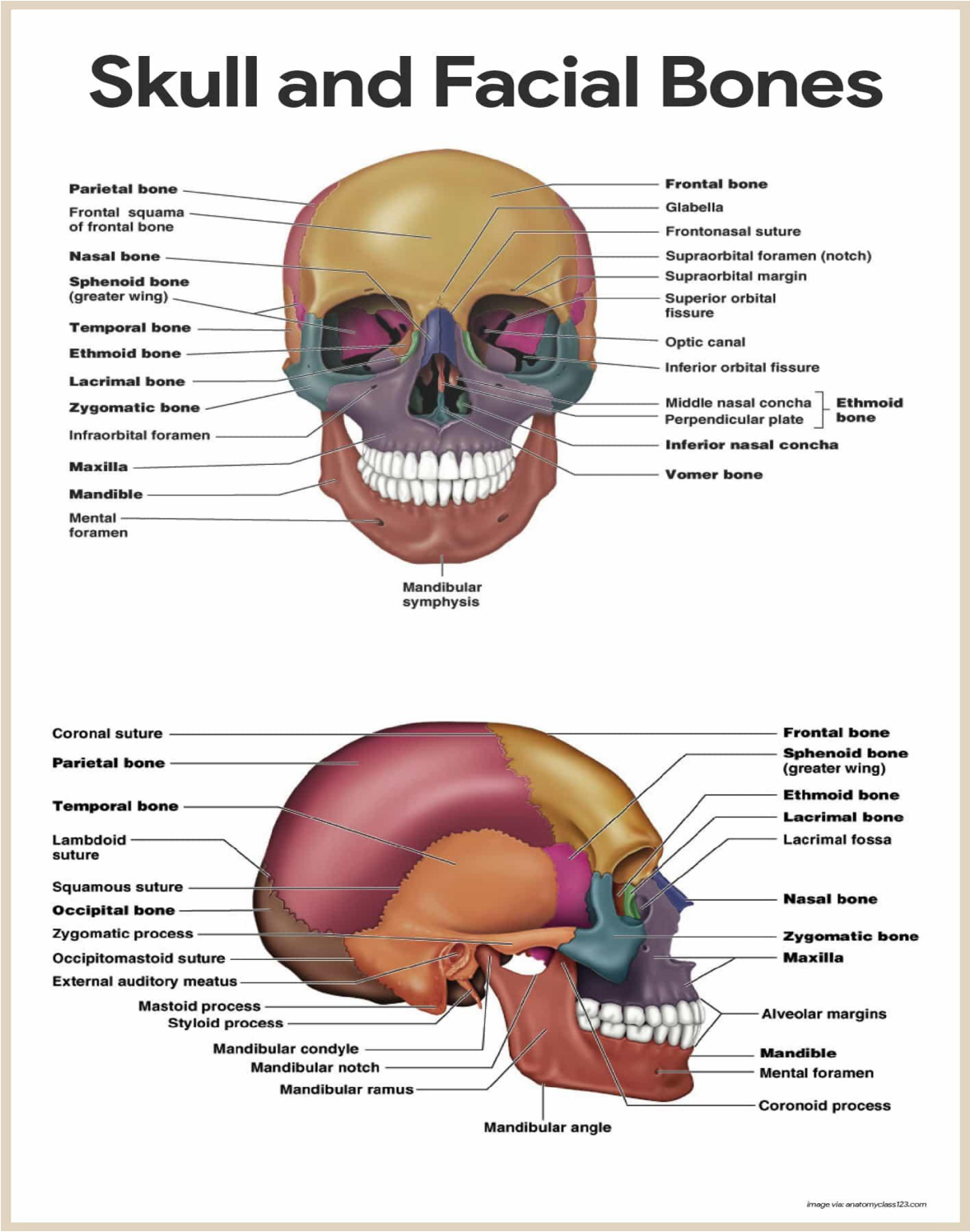
The axial skeleton, which forms the longitudinal axis of the body, is divided into three parts: the skull, the vertebral column, and the bony thorax.

Skull

The skull is formed by two sets of bones: the cranium and the facial bones.

Cranium

The cranium encloses and protects the fragile brain tissue and is composed of eight large flat bones.



- **Frontal bone.** The frontal bone forms the forehead, the bony projections under the eyebrows, and the superior part of each eye's orbits.

- **Parietal bones.** The paired parietal bones form most of the superior and lateral walls of the cranium; they meet in the midline of the skull at the **sagittal suture** and form the **coronal suture**, where they meet the frontal bone.
- **Temporal bones.** The temporal bones lie inferior to the parietal bones; they join them at the **squamous sutures.**

There are several bone markings that appear at the ***temporal bone***:

1. **External acoustic meatus.** The external acoustic meatus is a canal that leads to the eardrum and middle ear; it is the route by which sound enters the ear.
2. **Styloid process.** The styloid process, a sharp, needlelike projection, is just inferior to the external auditory meatus.
3. **Zygomatic process.** The zygomatic process is a thin bridge of bone that joins with the cheekbone (**zygomatic bone**) anteriorly.
4. **Mastoid process.** The mastoid process, which full of air cavities (**mastoid sinuses**), is a rough projection posterior and inferior to the **external acoustic meatus**; it provides an attachment site for some muscles of the neck.
5. **Jugular foramen.** The jugular foramen, at the junction of the occipital and temporal bones, allows passage of the jugular vein, the largest vein of the head, which drains the brain; just anterior to it in the cranial cavity is the **internal acoustic meatus**, which transmits cranial nerves VII and VIII.

- **Occipital bone**. The occipital bone joins the parietal bones anteriorly at the lambdoid suture; in the base of the occipital bone is a large opening, the **foramen magnum**, which surrounds the lower part of the brain allows the spinal cord to connect with the brain.

- **Sphenoid bone.** The butterfly-shaped sphenoid bone spans the width of the skull and forms part of the floor of the cranial cavity; in the midline of the sphenoid is a small depression, the **sella turcica** or **Turk's saddle**, which forms a snug enclosure for the pituitary gland.
- **Foramen ovale.** The foramen ovale, a large oval opening in line with the posterior end of the sella turcica, allows fibers of cranial nerve V to pass to the chewing muscles of the lower jaw.
- **Optic canal.** The optic canal allows the optic nerve to pass to the eye.
- **Superior orbital fissure.** The slitlike superior orbital fissure is where the cranial nerves controlling eye movements pass.
- **Sphenoid sinuses.** The central part of the sphenoid bone is riddled with air cavities, the sphenoid sinuses.
- **Ethmoid bone.** The ethmoid bone is very irregularly shaped and lies anterior to the sphenoid; it forms the roof of the nasal cavity and part of the medial walls of the orbits.
- **Crista galli.** Projecting from its superior surface is the crista galli; the outermost covering of the brain attaches to this projection.
- **Cribriform plates**. These holey areas, the cribriform plates, allow nerve fibers carrying impulses from the olfactory receptors of the nose to reach the brain.
- **Superior and middle nasal conchae.** Extensions of the ethmoid bone, the superior and middle nasal conchae, form part of the lateral walls of the nasal cavity and increase the turbulence of air flowing through the nasal passages.

Facial Bones

Fourteen bones compose the face; twelve are paired, only the mandible and vomer are single.

- **Maxillae.** The two maxillae, or **maxillary bones**, fuse to form the upper jaw; all facial bones except the mandible join the maxillae; thus, they are the main or "keystone", bones of the face; the maxillae carry the upper teeth in the **alveolar margin**.
- **Palatine bones.** The paired palatine bones lie posterior to the palatine processes of the maxillae; they form the posterior part of the hard palate.
- **Zygomatic bones.** The zygomatic bones are commonly referred to as the cheek bones; they also form a good-sized portion of the lateral walls of the orbits, or eye sockets.
- **Lacrimal bones.** The lacrimal bones are finger-sized bones forming part of the medial walls of each orbit; each lacrimal bones has a groove that serves as a passageway for tears.
- **Nasal bones.** The small rectangular bones forming the bridge of the nose are the nasal bones.
- **Vomer bone.** The single bone in the medial line of the nasal cavity is the vomer; the vomer forms most of the bony nasal septum.
- **Inferior nasal conchae.** The interior nasal conchae are thin, curved bones projecting medially from the lateral walls of the nasal cavity.
- **Mandible.** The mandible, or lower jaw, is the largest and strongest bone of the face; it joins the temporal bones on each side of the face, forming the only freely movable joints in the skull; the horizontal part of the mandible (**the body**) forms the chin; two upright bars of bone (**the rami**) extend from the body to connect the mandible to the temporal bone.

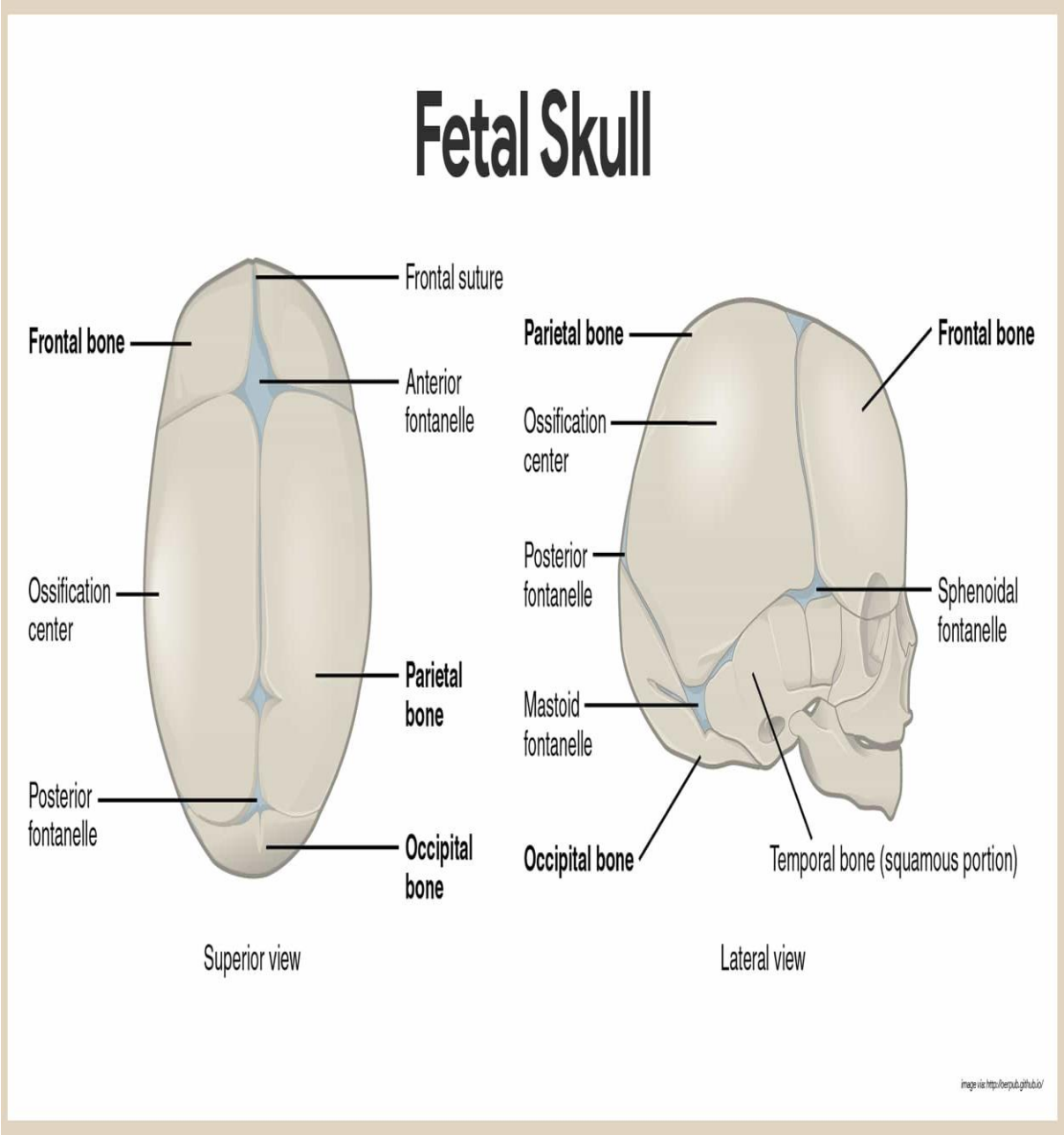
The Hyoid Bone

Though not really part of the skull, the hyoid bone is closely related to the mandible and temporal bones.

- **Location.** It is suspended in the midneck region about 2 cm (1 inch) above the larynx, where it is anchored by ligaments to the styloid processes of the temporal bones.
- **Parts.** Horseshoe-shaped, with a body and two pairs of horns, or cornua, the hyoid bone serves as a movable base for the tongue and as an attachment point for neck muscles that raise and lower the larynx when we swallow and speak.

Fetal Skull

The skull of a fetus or newborn infant is different in many ways from an adult skull.

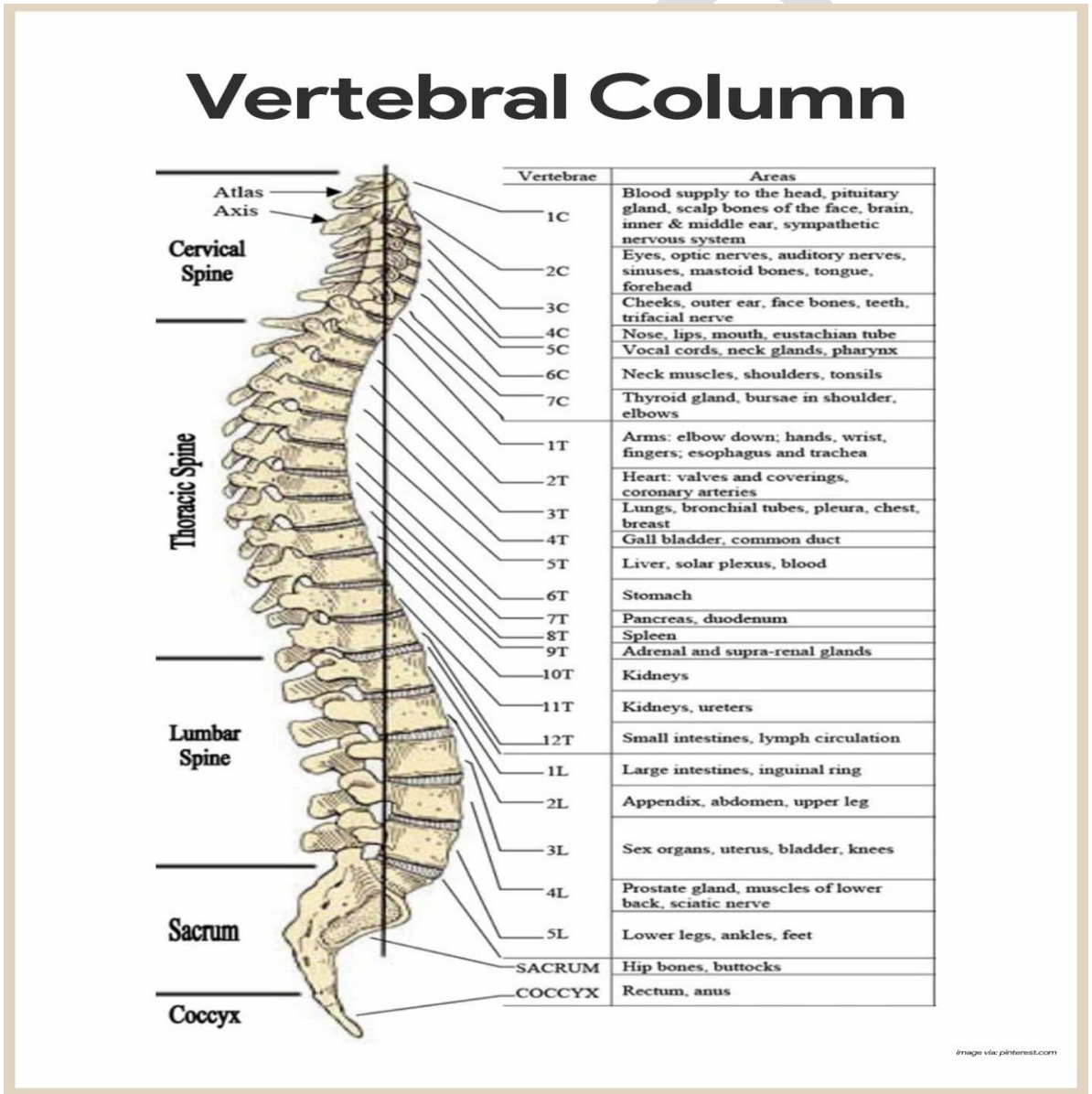


- **Size.** The adult skull represents only one-eighth of the total body length, whereas that of a newborn infant is one-fourth as long as its entire body.
- **Fontanels.** In the newborn, the skull also has a fibrous regions that have yet to be converted to bone; these fibrous membranes connecting the cranial bones are called fontanels.

- **Anterior fontanel.** The largest fontanel is the diamond-shaped anterior fontanel; the fontanel allows the fetal skull to be compressed slightly during birth.

Vertebral Column (Spine)

Serving as the axial support of the body, the vertebral column, or spine, extends from the skull, which it supports, to the pelvis, where it transmits the weight of the body to the lower limbs.



Vertebrae	Areas
1C	Blood supply to the head, pituitary gland, scalp bones of the face, brain, inner & middle ear, sympathetic nervous system
2C	Eyes, optic nerves, auditory nerves, sinuses, mastoid bones, tongue, forehead
3C	Cheeks, outer ear, face bones, teeth, trifacial nerve
4C	Nose, lips, mouth, eustachian tube
5C	Vocal cords, neck glands, pharynx
6C	Neck muscles, shoulders, tonsils
7C	Thyroid gland, bursae in shoulder, elbows
1T	Arms: elbow down; hands, wrist, fingers; esophagus and trachea
2T	Heart: valves and coverings, coronary arteries
3T	Lungs, bronchial tubes, pleura, chest, breast
4T	Gall bladder, common duct
5T	Liver, solar plexus, blood
6T	Stomach
7T	Pancreas, duodenum
8T	Spleen
9T	Adrenal and supra-renal glands
10T	Kidneys
11T	Kidneys, ureters
12T	Small intestines, lymph circulation
1L	Large intestines, inguinal ring
2L	Appendix, abdomen, upper leg
3L	Sex organs, uterus, bladder, knees
4L	Prostate gland, muscles of lower back, sciatic nerve
5L	Lower legs, ankles, feet
SACRUM	Hip bones, buttocks
COCCYX	Rectum, anus

- **Composition.** The spine is formed from **26 irregular bones** connected and reinforced by ligaments in such a way that a flexible, curved structure results.
- **Spinal cord.** Running through the central cavity of the vertebral column is the delicate spinal cord, which the vertebral column surrounds and protects.
- **Vertebrae.** Before birth, the spine consists of 33 separate bones called **vertebrae**, but 9 of these eventually fuse to form the two composite bones, the **sacrum** and the **coccyx**, that construct the inferior portion of the vertebral column.
- **Cervical vertebrae.** Of the 24 single bones, the **7** vertebrae of the neck are cervical vertebrae.
- **Thoracic vertebrae.** The next **12** are the thoracic vertebrae.
- **Lumbar vertebrae.** The remaining **5** supporting the lower back are lumbar vertebrae.
- **Intervertebral discs.** The individual vertebrae are separated by pads of flexible fibrocartilage-intervertebral discs- that cushion the vertebrae and absorb shock while allowing the spine flexibility.
- **Primary curvatures.** The spinal curves in the thoracic and sacral regions are referred to as primary curvatures because they are present when we are born.
- **Secondary curvatures.** The curvatures in the cervical and lumbar regions are referred to as secondary curvatures because they develop some time after birth.
- **Body or centrum.** Disc-like, weight-bearing part of the vertebra facing anteriorly in the vertebral column.

- **Vertebral arch.** Arch formed from the joining of all posterior extensions, the **laminae** and **pedicles**, from the vertebral body.
- **Vertebral foramen.** Canal through which the spinal cord passes.
- **Transverse processes.** Two lateral projections from the vertebral arch.
- **Spinous process.** Single projection arising from the posterior aspect of the vertebral arch (actually the fused laminate).
- **Superior and inferior articular processes.** Paired projections lateral to the vertebral foramen, allowing a vertebra to form joints with adjacent vertebrae.

Cervical Vertebrae

The seven cervical vertebrae (C1 to C7) form the neck region of the spine.

- **Atlas.** The atlas (**C1**) has no body; the superior surfaces of its transverse processes contain large depressions that receive the occipital condyles of the skull.
- **Axis.** The axis (**C2**) acts as a pivot for the rotation of the atlas (and skull) above; it has a large upright process, the **dens**, which acts as the pivot point.
- **Foramina.** The transverse processes of the cervical vertebrae contain foramina (**openings**) through which the vertebral arteries pass on their way to the brain above.

Thoracic Vertebrae

The twelve thoracic vertebrae (T1 to T12) are all typical.

- **Size.** They are larger than the cervical vertebrae and are distinguished by the fact that they are the only vertebrae to articulate with the ribs.
- **Shape**. The body is somewhat heart-shaped and has two costal facets on each side, which receive the heads of the ribs.

- **Transverse processes.** The two transverse processes of each thoracic vertebrae articulate with the nearby knoblike tubercles of the ribs.
- **Spinous process.** The spinous process is long and hooks sharply downward, causing the vertebra to look like a giraffe's head viewed from the side.

Lumbar Vertebrae

The five lumbar vertebrae (L1 to L5) have massive, blocklike bodies.

- **Spinous processes.** Their short, hatchet-shaped spinous processes make them look like a moose head from the lateral aspect.
- **Strength.** Because most of the stress on the vertebral column occurs in the lumbar region, these are the sturdiest of the vertebrae.

Sacrum

The sacrum is formed by the fusion of five vertebrae.

Sacrum

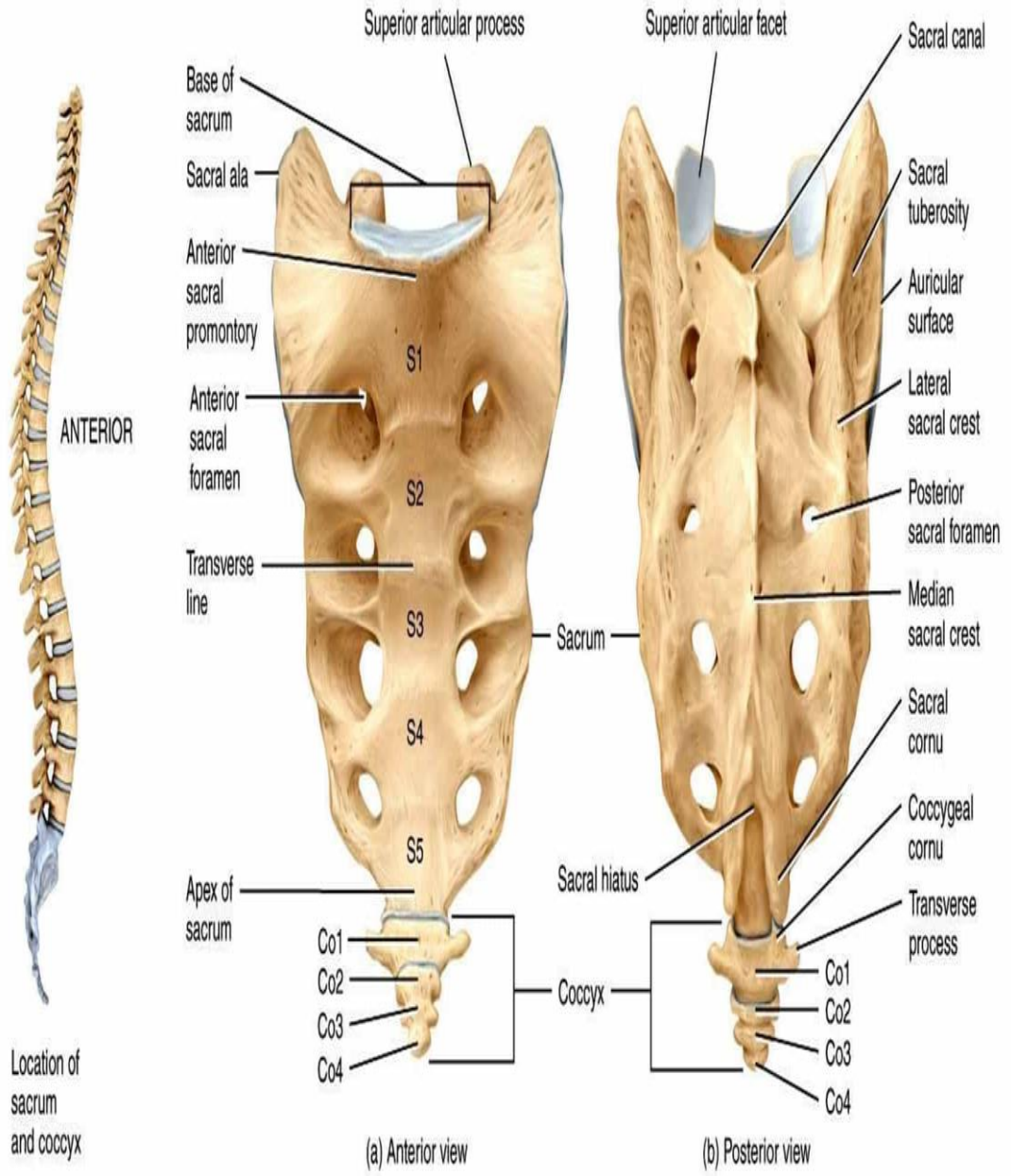


Figure 07.20ab Tortora - PHA 11/e

image via: meducation.net

- **Alae.** The winglike alae articulate laterally with the hip bones, forming the sacroiliac joints.
- **Median sacral crest.** Its posterior midline surface is roughened by the median sacral crest, the fused spinous processes of the sacral vertebrae.
- **Posterior sacral foramina.** This is flanked laterally by the posterior sacral foramina.
- **Sacral canal.** The vertebral canal continues inside the sacrum as the sacral canal and terminates in a large inferior opening called the **sacral hiatus**.

Coccyx

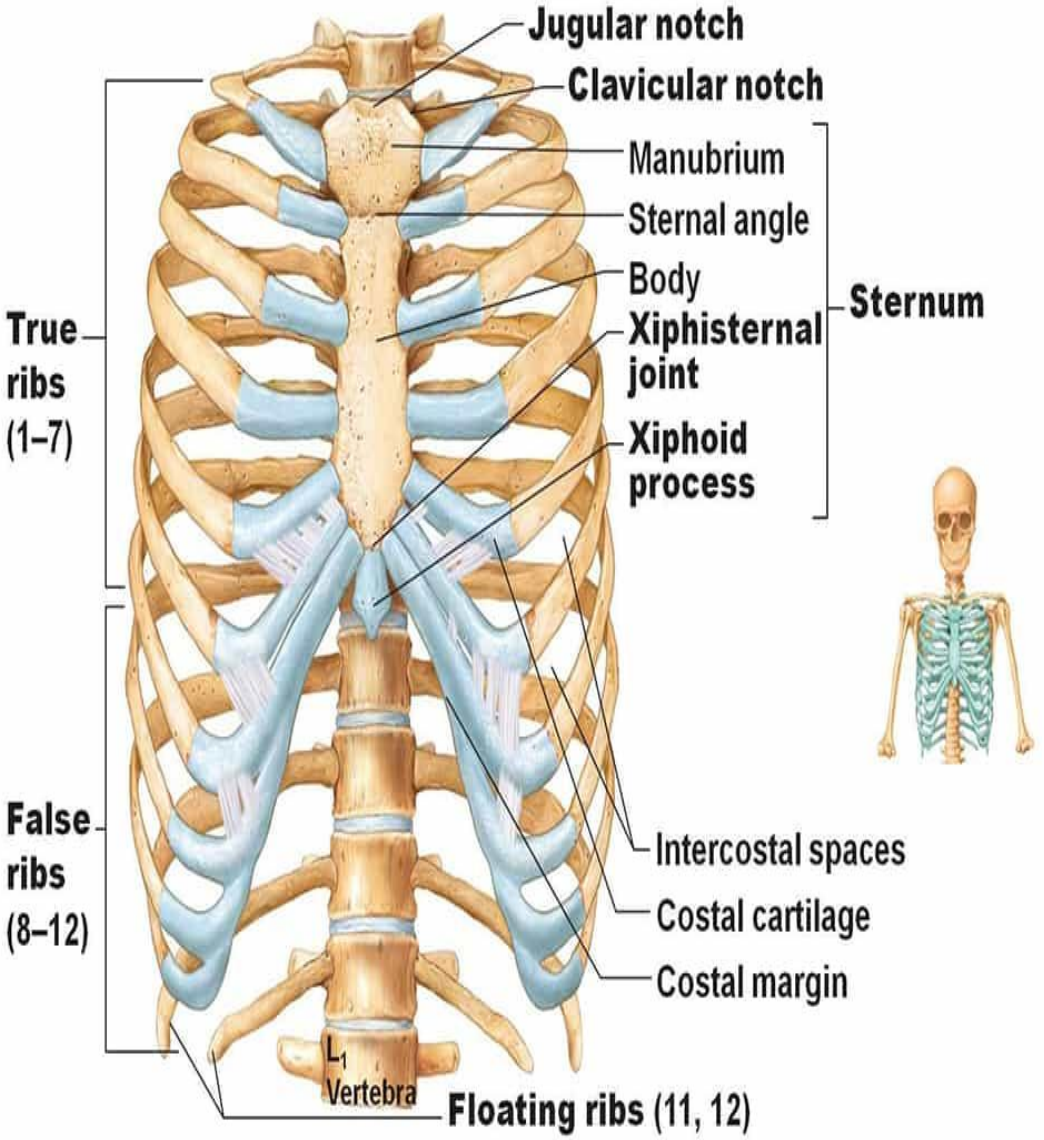
The coccyx is formed from the fusion of three to five tiny, irregular shaped vertebrae.

- **Tailbone.** It is the human "tailbone", a remnant of the tail that other vertebrate animals have.

Thoracic Cage

The sternum, ribs, and thoracic vertebrae make up the bony thorax; The bony thorax is routinely called the thoracic cage because it forms a protective, cone-shaped cage of slender bones around the organs of the thoracic cavity.

Thoracic Cage



(a) Skeleton of the thoracic cage, anterior view

image via: studyblue.com

Sternum

The sternum (breastbone) is a typical flat bone and the result of the fusion of three bones- the **manubrium**, **body**, and **xiphoid process**.

- **Landmarks.** The sternum has three important bony landmarks- the **jugular notch**, the **sternal angle**, and the **xiphisternal joint**.
- **Jugular notch.** The jugular notch (concave upper border of the manubrium) can be palpated easily, generally it is at the level of the third thoracic vertebra.
- **Sternal angle.** The sternal angle results where the manubrium and the body meet at a slight angle to each other, so that a transverse ridge is formed at the level of the second ribs.
- **Xiphisternal joint.** The xiphisternal joint, the point where the sternal body and xiphoid process fuse, lies at the level of the ninth thoracic vertebra.

Ribs

Twelve pairs of ribs form the walls of the bony thorax.

- **True ribs.** The true ribs, the first seven pairs, attach directly to the sternum by costal cartilages.
- **False ribs.** False ribs, the next five pairs, either attach indirectly to the sternum or are not attached to the sternum at all.
- **Floating ribs.** The last two pairs of false ribs lack the sternal attachments, so they are called the floating ribs.

Appendicular Skeleton

The appendicular skeleton is composed of 126 bones of the limbs and the pectoral and pelvic girdles, which attach the limbs to the axial skeleton.

Bones of the Shoulder Girdle

Each shoulder girdle, or **pectoral girdle**, consists of two bones – a clavicle and a scapula.

Humerus and Scapula

(Posterior View)

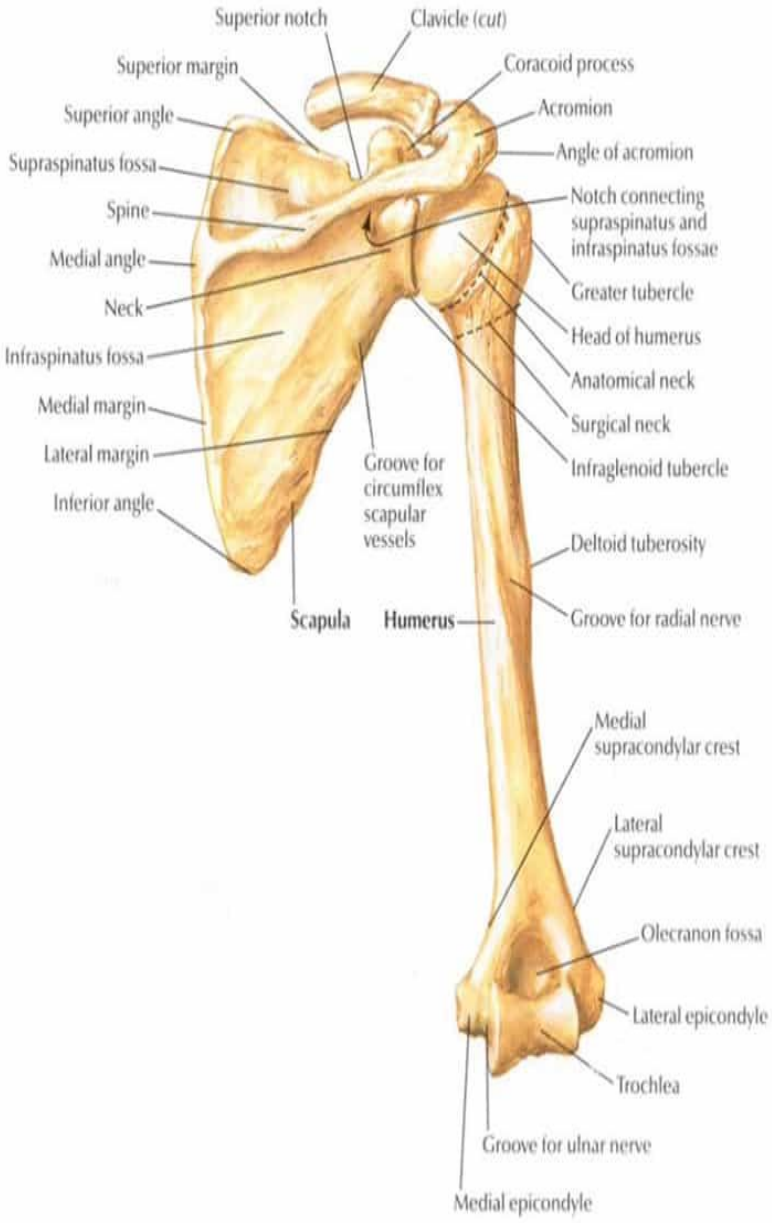


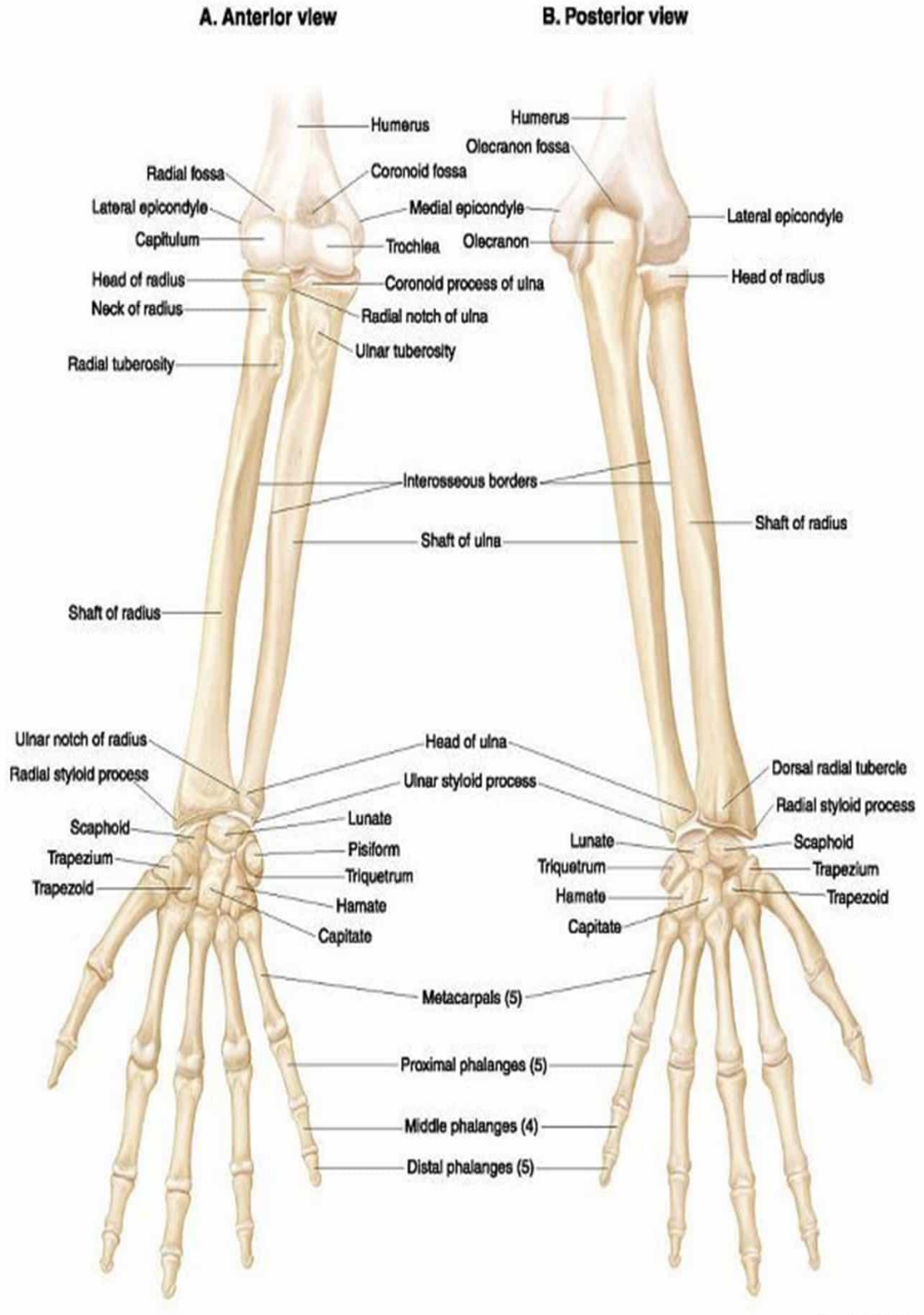
image via: pinterest.com

- **Clavicle.** The clavicle, or **collarbone**, is a slender, doubly curved bone; it attaches to the manubrium of the sternum medially and to the scapula laterally, where it helps to form the shoulder joint; it acts as a brace to hold the arm away from the top of the thorax and helps prevent shoulder dislocation.
- **Scapulae.** The scapulae, or **shoulder blades**, are triangular and commonly called "wings" because they flare when we move our arms posteriorly.
- **Parts of the scapula.** Each scapula has a flattened body and two important processes- the **acromion** and the **coracoid**.
- **Acromion.** The acromion is the enlarged end of the spine of the scapula and connects with the clavicle laterally at the **acromioclavicular joint**.
- **Coracoid.** The beaklike coracoid process points over the top of the shoulder and anchors some of the muscles of the arm; just medial to the coracoid process is the large **suprascapular notch,** which serves as a nerve passageway.
- **Borders of the scapula.** The scapula has three borders- superior, medial (vertebral), and lateral (axillary).
- **Angles of the scapula.** It also has three angles- superior, inferior, and lateral; the **glenoid cavity**, a shallow socket that receives the head of the arm bone, is in the lateral angle.
- **Factors to free movement of the shoulder girdle.** Each shoulder girdle attaches to the axial skeleton at only one point- the **sternoclavicular joint**; the loose attachment of the scapula allows it to slide back and forth against the thorax as muscles act; and, the glenoid cavity is shallow, and the shoulder joint is poorly reinforced by ligaments.

Bones of the Upper Limb

Thirty separate bones form the skeletal framework of each upper limb; they form the foundations of the arm, forearm, and hand.

Forearm


A. Anterior view
B. Posterior view
Humerus
Radial fossa
Coronoid fossa
Lateral epicondyle
Medial epicondyle
Capitulum
Trochlea
Head of radius
Coronoid process of ulna
Neck of radius
Radial notch of ulna
Ulnar tuberosity
Radial tuberosity
Interosseous borders
Shaft of ulna
Shaft of radius
Ulnar notch of radius
Radial styloid process
Head of ulna
Ulnar styloid process
Scaphoid
Lunate
Trapezium
Pisiform
Trapezoid
Triquetrum
Hamate
Capitate
Metacarpals (5)
Proximal phalanges (5)
Middle phalanges (4)
Distal phalanges (5)
Humerus
Olecranon fossa
Lateral epicondyle
Olecranon
Head of radius
Shaft of radius
Dorsal radial tubercle
Radial styloid process
Lunate
Scaphoid
Triquetrum
Trapezium
Hamate
Trapezoid
Capitate
image via: opentextbc.ca

Arm

The arm is formed by a single bone, the humerus, which is a typical long bone.

- **Anatomical neck.** Immediately inferior to the head is a slight constriction called anatomical neck.
- **Tubercles.** Anterolateral to the head are two bony projections separated by the **intertubercular sulcus**– the **greater** and **lesser tubercles**, which are sites of muscle attachment.
- **Surgical neck.** Just distal to the tubercles is the surgical neck, so named because it is the most frequently fractured part of the humerus.
- **Deltoid tuberosity.** In the midpoint of the shaft is a roughened area called the deltoid tuberosity, where the large, fleshy deltoid muscle of the shoulder attaches.
- **Radial groove.** Nearby, the radial groove runs obliquely down the posterior aspect of the shaft; this groove marks the course of the radial nerve, an important nerve of the upper limb.
- **Trochlea and capitulum.** At the distal end of the humerus is the medial trochlea, which looks somewhat like a spool, and the lateral ball-like capitulum; both of these processes articulate with the bones of the forearm.
- **Fossa.** Above the trochlea anteriorly is a depression, the **coronoid fossa**; on the posterior surface is the **olecranon fossa**; these two depressions, which are flanked by **medial** and **lateral epicondyles**, allow the corresponding processes of the ulna to move freely when the elbow is bent and extended.

Forearm

Two bones, the radius, and the ulna, form the skeleton of the forearm.

- **Radius.** When the body is in the anatomical position, the radius is the lateral bone; that is, it is on the thumb side of the forearm; when the hand is rotated so that the palm faces backward, the distal end of the radius crosses over and ends up medial to the ulna.
- **Radioulnar Joints.** Both proximally and distally the radius and ulna articulate at small radioulnar joints and the two bones are connected along their entire length by the flexible **interosseous membrane**.
- **Styloid process.** Both the ulna and the radius have as styloid process at their distal end.
- **Radial tuberosity.** The disc-shaped head of the radius also forms a joint with the capitulum of the humerus; just below the head is the radial tuberosity, where the tendon of the biceps muscle attaches.
- **Ulna.** When the upper limb is in the anatomical position, the ulna is the medial bone (on the little-finger side) of the forearm.
- **Trochlear notch.** On its proximal end are the coronoid process and the posterior olecranon process, which are separated by the trochlear notch; together, these two processes grip the trochlea of the humerus in a pliers-like joint.

Hand

The skeleton of the hand consists of carpals, the metacarpals, and the phalanges.

- **Carpal bones.** The eight carpal bones, arranged in two irregular rows of four bones each, form the part of the hand called **carpus**, or, more commonly, the **wrist**; the carpals are bound together by ligaments that restrict movements between them.

- **Metacarpals.** The metacarpals are numbered 1 to 5 from the thumb side of the hand to the little finger; when the fist is clenched, the heads of the metacarpals become obvious as the "**knuckles**".
- **Phalanges.** The phalanges are the bones of the fingers; each hand contains 14 phalanges; there are three in each finger (proximal, middle, and distal), except in the thumb, which has only two)proximal and distal.

Bones of the Pelvic Girdle

The pelvic girdle is formed by two coxal bones, or ossa coxae, commonly called hip bones.

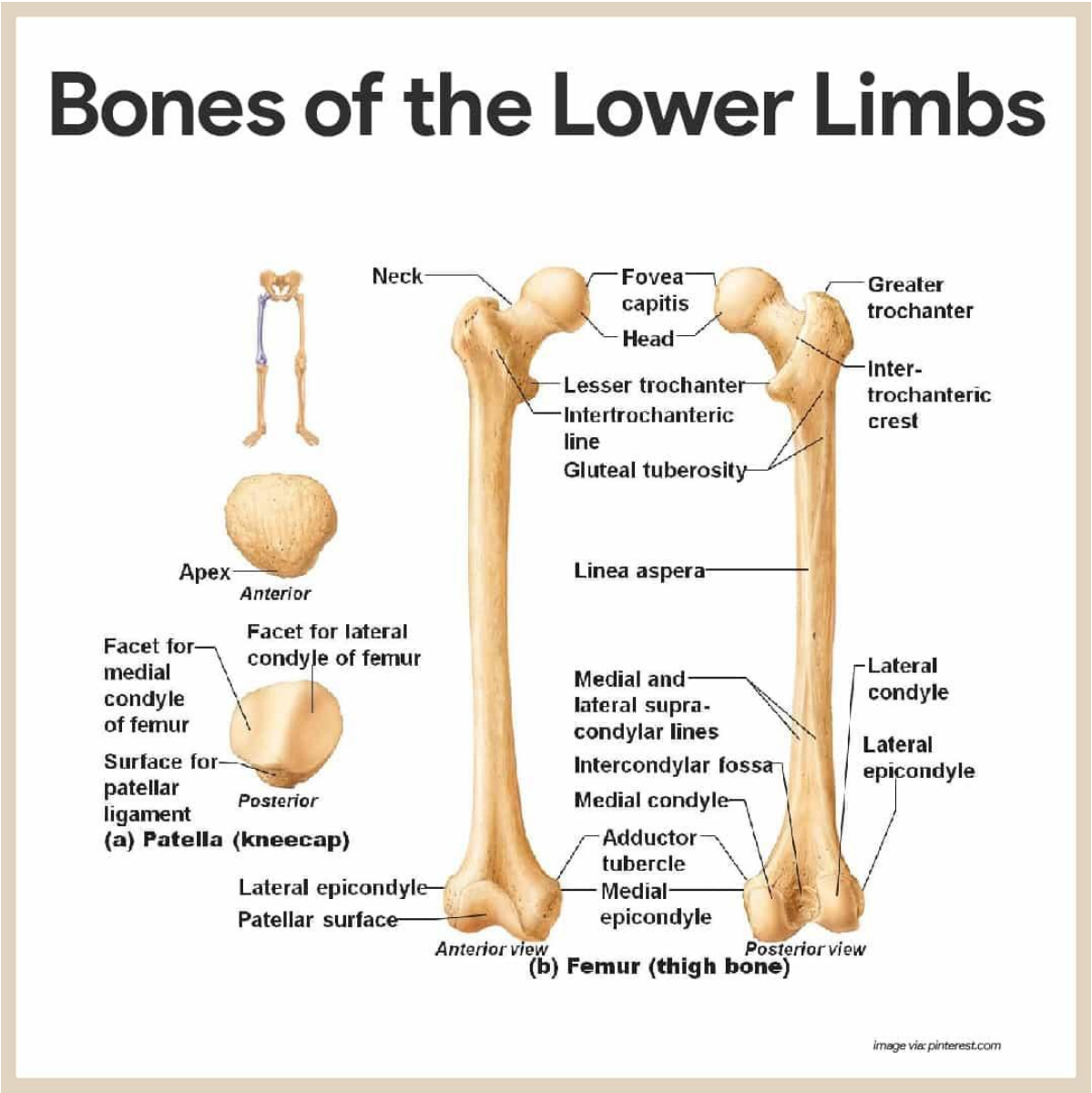
- **Pelvic girdle.** The bones of the pelvic girdle are large and heavy, and they are attached securely to the axial skeleton; bearing weight is the most important function of this girdle because the total weight of the upper body rests on the bony pelvis.
- **Sockets.** The sockets, which receives the thigh bones, are deep and heavily reinforced by ligaments that attach the limbs firmly to the girdle.
- **Bony pelvis.** The reproductive organs, urinary bladder, and part of the large intestine lie within and are protected by the bony pelvis.
- **Ilium.** The ilium, which connects posteriorly with the sacrum at the **sacroiliac joint**, is a large, flaring bone that forms most of the hip bone; when you put your hands on your hips, they are resting over the **alae**, or winglike portions, of the ilia.
- **Iliac crest.** The upper edge of an ala, the iliac crest, is an important anatomical landmark that is always kept in mind by those who give intramuscular injections; the iliac crest ends anteriorly in the **anterior superior iliac spine** and posteriorly in the **posterior superior iliac spine**.

- **Ischium.** The ischium is the "sit-down" bone, so called because it forms the most inferior part of the coxal bone.
- **Ischial tuberosity.** The ischial tuberosity is a roughened area that receives weight when you are sitting.
- **Ischial spine.** The ischial spine, superior to the tuberosity, is another important anatomical landmark, particularly in pregnant women, because it narrows the outlet of the pelvis through which the baby must pass during the birth process.
- **Greater sciatic notch.** Another important structural feature of the ischium is the greater sciatic notch, which allows blood vessels and the large sciatic nerve to pass from the pelvis posteriorly into the thigh.
- **Pubis.** The pubis, or **pubic bone**, is the most anterior part of the coxal bone.
- **Obturator foramen.** An opening that allows blood vessels and nerves to pass into the anterior part of the thigh.
- **Pubic symphysis.** The pubic bones of each hip bones fuse anteriorly to form a cartilaginous joint, the pubic symphysis.
- **Acetabulum.** The ilium, ischium, and pubis fuse at a deep socket called the acetabulum, which means "vinegar cup"; the acetabulum receives the head of the thigh bone.
- **False pelvis.** The false pelvis is superior to the true pelvis; it is the area medial to the flaring portions of the ilia.
- **True pelvis.** The true pelvis is surrounded by bone and lies inferior to the flaring parts of the ilia and the pelvic brim; the dimensions of the true pelvis of the woman are very important because they must be large enough to allow the infant's head to pass during childbirth.

- **Outlet and inlet.** The dimensions of the cavity, particularly the outlet (the inferior opening of the pelvis measured between the ischial spines, and the inlet (superior opening between the right and left sides of the pelvic brim) are critical, and thus they are carefully measured by the obstetrician.

Bones of the Lower Limbs

The lower limbs carry the total body weight when we are erect; hence, it is not surprising that the bones forming the three segments of the lower limbs (thigh, leg, and foot) are much thicker and stronger than the comparable bones of the upper limb.



Thigh

The **femur**, or thigh bone, is the only bone in the thigh; it is the heaviest, strongest bone in the body.

- **Parts.** Its proximal end has a ball-like head, a neck, and **greater** and **lesser trochanters** (separated anteriorly by the **intertrochanteric line** and posteriorly by the **intertrochanteric crest**).

- **Gluteal tuberosity.** These markings and the gluteal tuberosity, located on the shaft, all serve as sites for muscle attachment.
- **Head.** The head of the femur articulates with the acetabulum of the hip bone in a deep, secure socket.
- **Neck.** However, the neck of the femur is a common fracture site, especially in old age.
- **Lateral and medial condyles.** Distally on the femur are the lateral and medial condyles, which articulate with the tibia below; posteriorly these condyles are separated by the deep **intercondylar fossa**.
- **Patellar surface.** Anteriorly on the distal femur is the smooth patellar surface, which forms a joint with the patella, or kneecap.

Leg

Connected along their length by an **interosseous membrane**, two bones, the tibia and fibula, form the skeleton of the leg.

- **Tibia.** The tibia, or **shinbone**, is larger and more medial; at the proximal end, the medial and lateral condyles articulate with the distal end of the femur to form the knee joint.
- **Tibial tuberosity.** The patellar (kneecap) ligament attaches to the tibial tuberosity, a roughened area on the anterior tibial surface.
- **Medial malleolus.** Distally, a process called medial malleolus forms the inner bulge of the ankle.
- **Anterior border.** The anterior surface of the tibia is a sharp ridge, the anterior border, that is unprotected by the muscles; thus, it is easily felt beneath the skin.
- **Fibula.** The fibula, which lies along the tibia and forms joints with it both proximally and distally, is thin and sticklike; the fibula has no part in forming the knee joint.

- **Lateral malleolus.** Its distal end, the lateral malleolus, forms the outer part of the ankle.

Foot

The foot, composed of the tarsals, metatarsals, and phalanges, has two important functions. It supports our body weight and serves as a lever that allows us to propel our bodies forward when we walk and run.

- **Tarsus.** the tarsus, forming the posterior half of the foot, is composed of **seven tarsal bones**.
- **Calcaneus and Talus.** Body weight is carried mostly by the two largest tarsals, the calcaneus, or **heel bone**, and the talus (ankle), which lies between the tibia and the calcaneus.
- **Metatarsals. Five** metatarsals form the sole.
- **Phalanges. 14 phalanges** form the toes; each toe has three phalanges, except the great toe, which has two.
- **Arches.** The bones in the foot are arranged to form three strong arches: two longitudinal (medial and lateral) and one transverse.

Joints

Joints, also called **articulations**, have two functions: they hold the bones together securely, but also give the rigid skeleton mobility.

- **Classification.** Joints are classified in two ways- functionally and structurally.
- **Functional classification.** The functional classification focuses on the amount of movement the joint allows.

- **Types of functional joints.** There are **synarthroses** or immovable joints; **amphiarthroses**, or slightly movable joints, and **diarthrosis**, or freely movable joints.
- **Diarthroses.** Freely movable joints predominate in the limbs, where mobility is important.
- **Synarthroses and amphiarthroses.** Immovable and slightly movable joints are restricted mainly to the axial skeleton, where firm attachments and protection of internal organs are priorities.
- **Structural classification.** Structurally, there are **fibrous**, **cartilaginous**, and **synovial** joints; these classifications are based on whether fibrous tissue, cartilage, or a joint cavity separates the bony regions at the joint.

Fibrous Joints

In fibrous joints, the bones are united by fibrous tissue.

- **Examples.** The best examples of this type of joint are the **sutures** of the skull; in sutures, the irregular edges of the bones interlock and are bound tightly together by connective tissue fibers, allowing essentially no movement.
- **Syndesmoses.** In syndesmoses, the connecting fibers are longer than those of sutures; thus the joint has more "give"; the joint connecting the distal ends of the tibia and fibula is a syndesmosis.

Cartilaginous Joints

In cartilaginous joints, the bone ends are connected by cartilage.

- **Examples.** Examples of this joint type that are slightly movable are the **pubic symphysis** of the pelvis and the **intervertebral joints** of the spinal column, where the articulating bone surfaces are connected by pads (discs) of fibrocartilage.

- **Synarthrotic cartilaginous joints.** The hyaline cartilage epiphyseal plates of growing long bones and the cartilaginous joints between the first ribs and the sternum are immovable cartilaginous joints.

Synovial Joints

Synovial joints are joints in which the articulating bone ends are separated by a joint cavity containing a **synovial fluid**; they account for all joints of the limbs.

Types of Synovial Joints

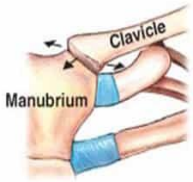
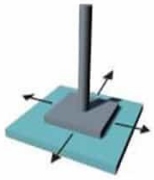
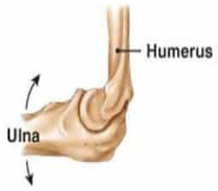
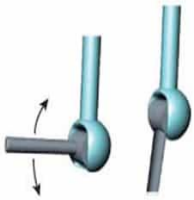
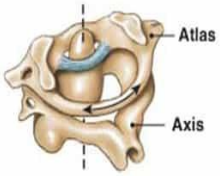
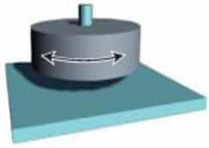
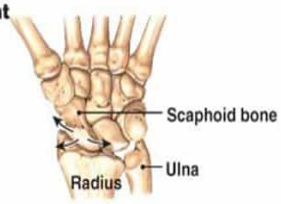
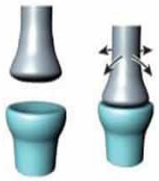
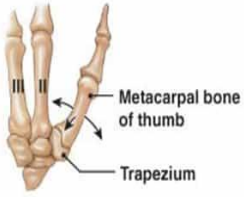
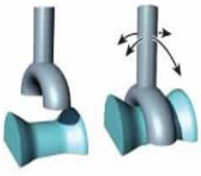
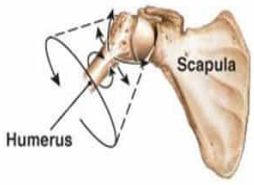
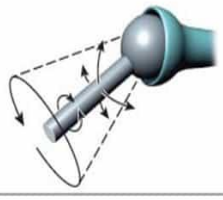
Types of Synovial Joints	Models of Joint Motion	Examples
Gliding joint 		• Acromioclavicular and sternoclavicular joints • Intercarpal and intertarsal joints • Vertebrocostal joints • Sacro-iliac joints
Hinge joint 		• Elbow joints • Knee joints • Ankle joints • Interphalangeal joints
Pivot joint 		• Atlas/axis • Proximal radio-ulnar joints
Ellipsoid joint 		• Radiocarpal joints • Metacarpophalangeal joints 2–5 • Metatarsophalangeal joints
Saddle joint 		• First carpometacarpal joints
Ball-and-socket joint 		• Shoulder joints • Hip joints

image via: highlands.edu

- **Articular cartilage.** Articular cartilage covers the ends of the bones forming the joints.
- **Fibrous articular capsule**. The joint surfaces are enclosed by a sleeve or a capsule of fibrous connective tissue, and their capsule is lined with a smooth **synovial membrane** (the reason these joints are called synovial joints).
- **Joint cavity.** The articular capsule encloses a cavity, called the joint cavity, which contains lubricating synovial fluid.
- **Reinforcing ligaments.** The fibrous capsule is usually reinforced with ligaments.
- **Bursae.** Bursae are flattened fibrous sacs lined with synovial membrane and containing a thin film of synovial fluid; they are common where ligaments, muscles, skin, tendons, or bones rub together.
- **Tendon sheath.** A tendon sheath is essentially an elongated bursa that wraps completely around a tendon subjected to friction, like a bun around a hotdog.

Types of Synovial Joints Based on Shape

The shapes of the articulating bone surfaces determine what movements are allowed at a joint; based on such shapes, our synovial joints can be classified as plane, hinge, pivot, condyloid, saddle, and ball-and-socket joints.

- **Plane joint.** In a plane joint, the articular surfaces are essentially flat, and only short slipping or gliding movements are allowed; the movements of plane joints are **nonaxial**, that is, gliding does not involve rotation around any axis; the intercarpal joints of the wrist are best examples of plane joints.
- **Hinge joint.** In a hinge joint, the cylindrical end of one bone fits into a trough-shaped surface on another bone; angular movement is allowed

in just one plane, like a mechanical hinge; hinge joints are classified as **uniaxial**; they allow movement in only one axis, and examples are the elbow joint, ankle joint, and the joints between the phalanges of the fingers.

- **Pivot joint.** In a pivot joint, the rounded end of one bone fits into a sleeve or ring of bone; because the rotating bone can turn only around its long axis, pivot joints are also **uniaxial joints**; the proximal radioulnar joint and the joint between the atlas and the dens of the axis are examples.
- **Condyloid joint.** In a condyloid joint, the egg-shaped articular surface fits into an oval concavity in another; condyloid joints allow the moving bone to travel (1) from side to side and (2) back and forth but the bone cannot rotate around its long axis; movement occurs around two axes, hence these are **biaxial joints**.
- **Saddle joints.** In saddle joints, each articular surface has both convex and concave areas, like a saddle; these **biaxial joints** allow essentially the same movements as condyloid joints; the best examples of saddle joints are the carpometacarpal joints in the thumb.
- **Ball-and-socket joint.** In a ball-and-socket joint, the spherical head of one bone fits into a round socket in another; these **multiaxial joints** allow movement in all axes, including rotation, and are the most freely moving synovial joints; the shoulder and hip are examples.

UNIT III

Blood

Blood is one of the most important components of life. Almost any animal that possesses a circulatory system has blood. From an evolutionary perspective,

blood was speculated to have risen from a type of cell that was responsible for phagocytosis and nutrition. Billions of years later, blood and the circulatory system have drastically helped the evolution of more complex lifeforms.

What is Blood?

Blood is a fluid connective tissue that consists of plasma, blood cells and platelets. It circulates throughout our body delivering oxygen and nutrients to various cells and tissues. It makes up 8% of our body weight. An average adult possesses around 5-6 litres of blood.

Types of Blood Cells

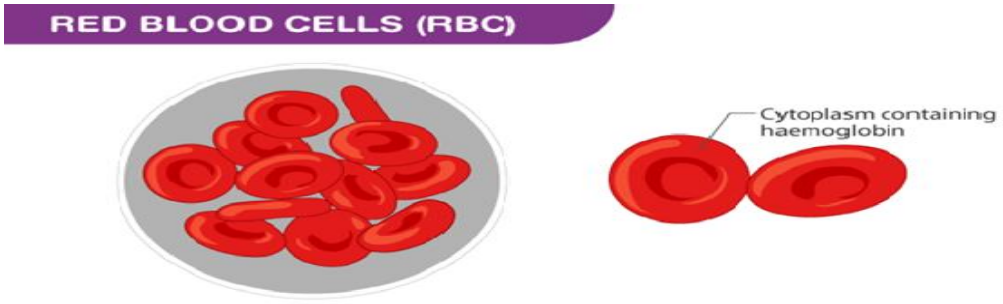
We have seen blood consist of cells known as formed elements of blood. These cells have their own functions and roles to play in the body. The blood cells which circulate all around the body are as follows:

Red blood cells (Erythrocytes)

RBCs are biconcave cells and without nucleus in humans; also known as erythrocytes. RBCs contain the iron-rich protein called haemoglobin; give blood its red colour. RBCs are the most copious blood cells produced in bone marrows. Their main function is to transport oxygen from and to various tissues and organs.

White blood cells (Leucocytes)

Leucocytes are colourless blood cells. They are colourless because it is devoid of haemoglobin. They are further classified as granulocytes and agranulocytes. WBCs mainly contribute to immunity and defence mechanism.

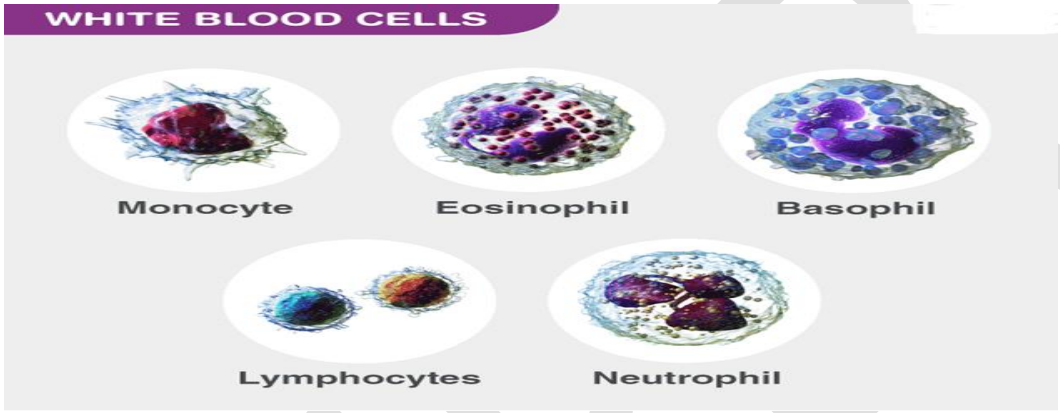


Red Blood Cells are red due to **Hemoglobin**, which is a **transport molecule** and also a **pigment.** As a result, blood is red.

Types of White Blood Cells

There are five different types of White blood cells and are classified mainly based on the presence and absence of granules.

- Granulocytes
- Agranulocytes



There are **five types of white blood cells** present in the blood

Granulocytes

They are leukocytes, with the presence of granules in their cytoplasm. The granulated cells include- eosinophil, basophil, and neutrophil.

Eosinophils:

- They are the cells of leukocytes, which are present in the immune system.
- These cells are responsible for combating infections in parasites of vertebrates and for controlling mechanisms associated with allergy and asthma.
- Eosinophil cells are small granulocyte, which are produced in the bone marrow and makes 2 to 3 per cent of whole WBCs. These cells are present in high concentrations in the digestive tract.

Basophils

- They are the least common of the granulocytes, ranging from 0.5 to 1 per cent of WBCs.
- They contain large cytoplasmic granules, which plays a vital role in mounting a non-specific immune response to pathogens, allergic reactions by releasing histamine and dilates the blood vessels.
- These white blood cells have the ability to be stained when exposed to basic dyes, hence referred to as basophil.
- These cells are best known for their role in asthma and their result in inflammation and bronchoconstriction in the airways.
- They secrete serotonin, histamine and heparin.

Neutrophils

- They are normally found in the bloodstream.
- They are predominant cells, which are present in pus.
- Around 60 to 65 per cent of WBCs are neutrophils with a diameter of 10 to 12 micrometres.
- The nucleus is 2 to 5 lobed and cytoplasm has very fine granules.
- Neutrophil helps in the destruction of bacteria with lysosomes, and it acts as a strong oxidant.
- Neutrophils are stained only using neutral dyes. Hence, they are called so.
- Neutrophils are also the first cells of the immune system to respond to an invader such as a bacteria or a virus.
- The lifespan of these WBCs extend for up to eight hours and are produced every day in the bone marrow.

Agranulocytes

They are leukocytes, with the absence of granules in their cytoplasm. Agranulocytes are further classified into monocytes and lymphocytes.

Monocytes

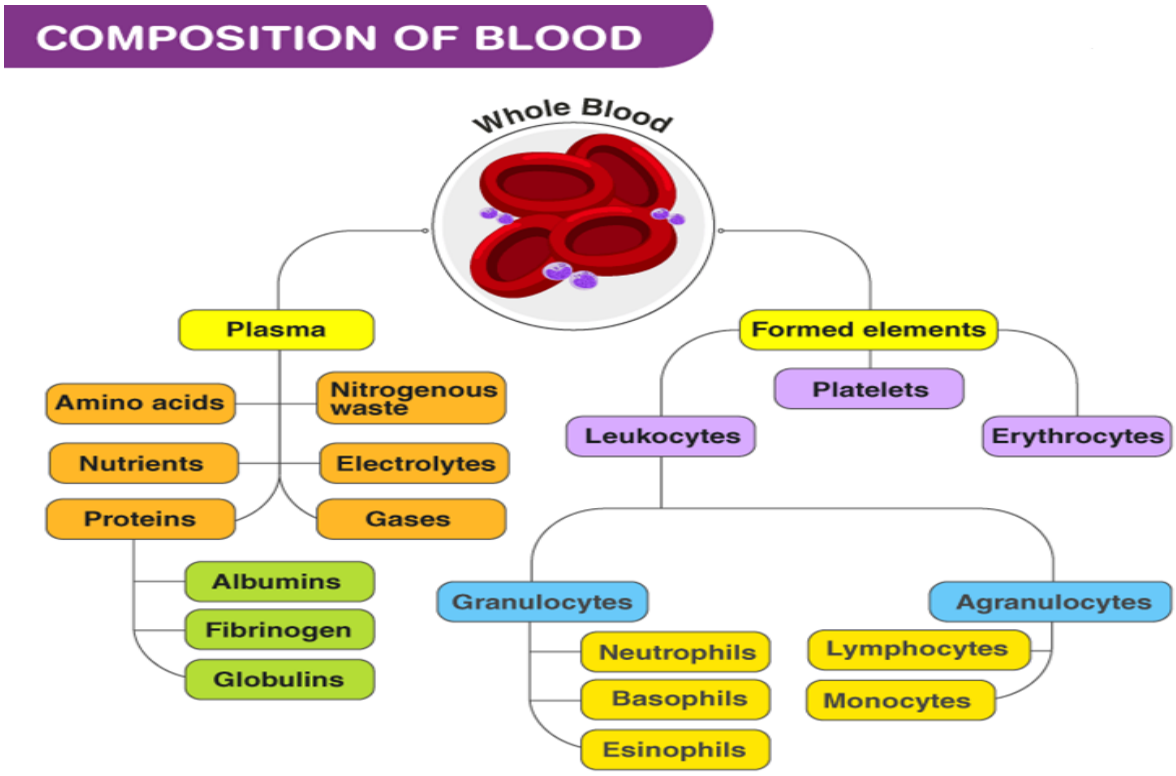
- These cells usually have a large bilobed nucleus, with a diameter of 12 to 20 micrometres.
- The nucleus is generally of half-moon shaped or kidney-shaped and it occupies 6 to 8 per cent of WBCs.
- They are the garbage trucks of the immune system.
- The most important functions of monocytes are to migrate into tissues and clean up dead cells, protect against the blood-borne pathogens and they move very quickly to the sites of infections in the tissues.
- These white blood cells have a single bean-shaped nucleus, hence referred to as Monocytes.

Lymphocytes

- They play a vital role in producing antibodies.
- Their size ranges from 8 to 10 micrometres.
- They are commonly known as natural killer cells.
- They play an important role in body defence.
- These white blood cells are colourless cells formed in lymphoid tissue, hence referred to as lymphocytes.
- There are two main types of lymphocytes – B lymphocytes and T lymphocytes.
- These cells are very important in the immune systems and are responsible for humoral and cell-mediated immunity.

Platelets (Thrombocytes)

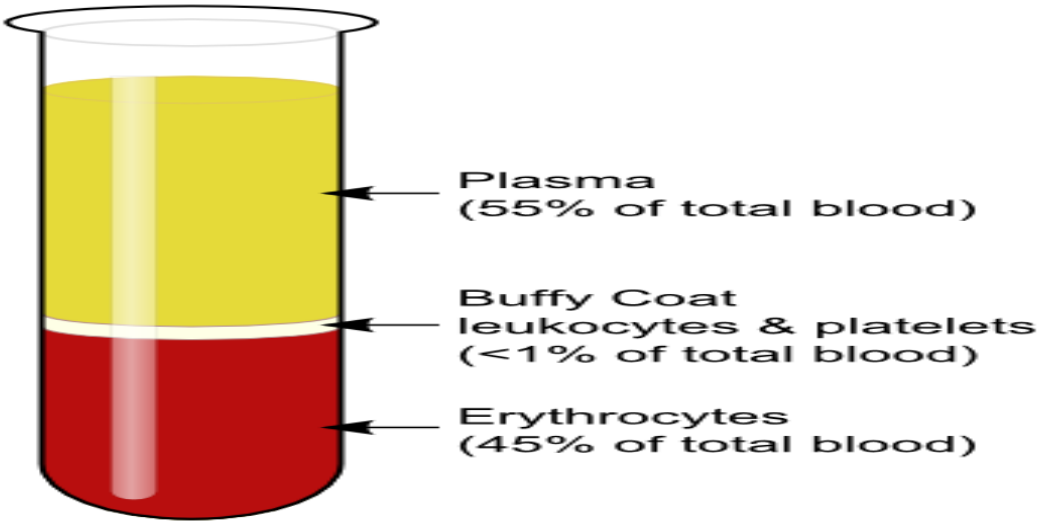
- Thrombocytes are specialized blood cells produced from bone marrow.
- Platelets come into play when there is bleeding or haemorrhage.
- They help in clotting and coagulation of blood. Platelets help in coagulation during a cut or wound.



Composition of Blood: Plasma, RBCs, WBCs and platelets

Components of Blood

There are many cellular structures in the composition of blood. When a sample of blood is spun in a centrifuge machine, they separate into the following constituents: **Plasma, buffy coat and erythrocytes.**



Plasma

The liquid state of blood can be contributed to plasma as it makes up ~55% of blood. It is pale yellow in colour and when separated, it consists of salts, nutrients, water and enzymes. Blood plasma also contains important proteins and other components necessary for overall health. Hence, blood plasma transfusions are given to patients with liver failure and life-threatening injuries.

Red Blood Cells (RBC)

Red blood cells consist of Haemoglobin, a protein. They are produced by the bone marrow to primarily carry oxygen to the body and carbon dioxide away from it.

White Blood Cells (WBC)

White blood cells are responsible for fighting foreign pathogens (such as bacteria, viruses, fungi) that enter our body. They circulate throughout our body and originate from the bone marrow.

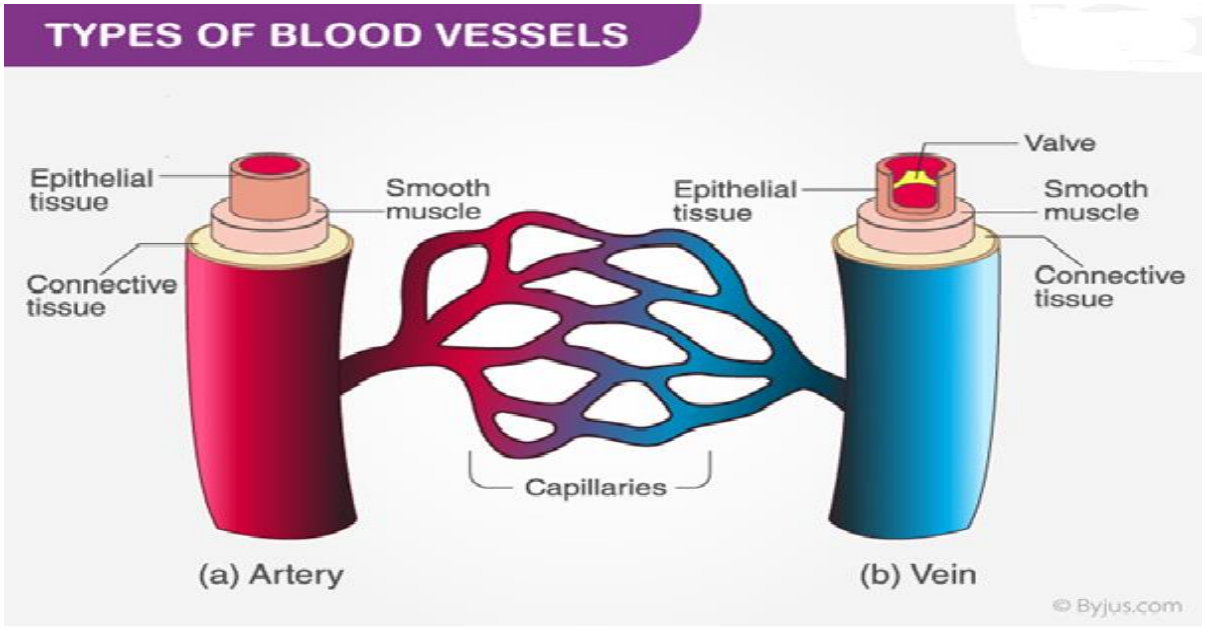
Platelets

Tiny disc-shaped cells that help regulate blood flow when any part of the body is damaged, thereby aiding in fast recovery through clotting of blood.

The above-stated elements form the composition of blood in humans. The only vertebrate without haemoglobin is the crocodile icefish. It derives its oxygen requirement directly from the cold, oxygen-rich water where it lives.

Blood Vessels

There are different types of blood vessels in our body each carrying out specialized functions.



Blood vessels are categorized into arteries, veins and capillaries

Types of Blood Vessels

Three types of blood vessels are:

- Arteries
- Veins
- Capillaries

Arteries

Arteries are strong tubes and muscular in nature. These blood vessels carry oxygen-rich blood from the heart to all the tissues of the body. Aorta is one of the main arteries that arise from the heart and branches further.

Veins

Veins are elastic blood vessels which carry deoxygenated blood from all parts of the body to the heart. An exception is the umbilical and pulmonary veins. The Pulmonary vein carries oxygenated blood to the heart from the lungs and umbilical vein carries oxygenated blood from the placenta to the foetus.

Capillaries

On reaching tissues, arteries branch further into extremely thin tubes called capillaries. Capillaries bring about the exchange of substances between blood and tissues.

Sinusoids

Sinusoids are a special type of wider capillaries present in bone marrow, liver, lymph nodes, spleen and some endocrine glands. They may be continuous, discontinuous or fenestrated.

Layers of Blood Vessels

Both arteries and veins consist of three layers.

- **Tunica Intima**: It is one of the innermost and thinnest layers of arteries and veins. It comprises endothelial cells. They are in direct contact with the flow of blood.
- **Tunica Media**: It is the middle layer of an artery or vein. Tunica media is made up of smooth muscle cells.
- **Tunica Externa:** It surrounds tunica media. It is made up of collagen and also supported by the elastic lamina in arteries.

Functions of Blood

Blood is responsible for the following body functions:

1. **Fluid Connective Tissue**

   Blood is a fluid connective tissue composed of 55% plasma and 45% formed elements including WBCs, RBCs, and platelets. Since these living cells are suspended in plasma, blood is known as a fluid connective tissue and not just fluid.

2. **Provides oxygen to the cells**

   Blood absorbs oxygen from the lungs and transports it to different cells of the body. The waste carbon dioxide moves from the blood to the lungs and exhaled.

3. **Transports Hormone and Nutrients**

   The digested nutrients such as glucose, vitamins, minerals, and proteins are absorbed into the blood through the capillaries in the villi lining the small intestine.

   The hormones secreted by the endocrine glands are also transported by the blood to different organs and tissues.

4. **Homeostasis**

   Blood helps to maintain the internal body temperature by absorbing or releasing heat.

5. **Blood Clotting at Site of Injury**

   The platelets help in the clotting of blood at the site of injury. Platelets along with the fibrin form clot at the wound site

6. **Transport of waste to the Kidney and Liver**

   Blood enters the kidney where it is filtered to remove nitrogenous waste out of the blood plasma. The toxins from the blood are also removed by the liver.

7. **Protection of body against pathogens**

   The White Blood Cells fight against infections. They multiply rapidly during the infections.

Frequently Asked Questions

1. What is blood?

Blood is a fluid connective tissue which comprises plasma, various types of blood cells and platelets. The main function of blood is to deliver oxygen and nutrients to various cells and tissues of the body.

2. State the types of blood cells found in human blood.

Blood cells are classified into the following types:

- Erythrocytes or red blood cells
- Leucocytes or white blood cells

3. State the different types of white blood cells found in the blood.

White blood cells can be classified as follows:

- lymphocytes
- monocytes
- neutrophils
- eosinophils
- basophils

4. What are granulocytes?

Granulocytes are leukocytes with the granule-like structures, that contain enzymes capable of digesting microorganisms. Granulocytes are further classified into eosinophil, basophil, and neutrophil.

5. What are agranulocytes?

Agranulocytes are a type of white blood cell that has no distinct granules in their cytoplasm. However, they form an important part of the body's immune system. They are further classified into monocytes and lymphocytes.

6. Name the various components of blood.

Blood is primarily broken down into the following components:

- Plasma
- RBC
- WBC
- Platelets

7. What are the various types of blood vessels present in our body?

Blood vessels are classified as follows:

- Veins
- Arteries

- Capillaries

8. What are sinusoids?

Sinusoids are very small vessels predominantly located inside the bone marrow, liver and spleen. Sinusoids are usually a little larger than capillaries.

9. Name the various layers of blood vessels.

- Tunica Intima
- Tunica Media
- Tunica Adventitia or Externa

10. Name the major functions of blood.

- Helps in homeostasis
- Provides oxygen to the cells
- Transports hormone and nutrients
- Helps to in the clotting process

11. What gives blood its red colour?

Blood contains haemoglobin, which contains heme (iron). It is responsible for giving blood a characteristic red appearance.

Blood Groups-ABO Blood Group and Rh Group System

- Blood is a fluid connective tissue and the most crucial component of the circulatory system.
- In a healthy person, approximately 5 liters (12 pints) of blood circulates throughout their body.
- In this article, blood groups and their types are explained in detail.

Composition of blood is rather interesting. It consists of **erythrocytes, leukocytes and platelets** suspended in plasma along with the millions of different molecules with its own specific roles and functions.

Even though components of blood are the same for all humans, there are various blood types.

In fact, there are more than **40 blood groups**, but all of them are not clinically significant. The discovery of the ***ABO blood group*** created great excitement as until then, all blood had been assumed to be the same.

Blood Group System

Karl Landsteiner, an Austrian scientist discovered the ABO blood group system in the year 1900.

In his experiments, he mixed different blood types and noted that the plasma from certain blood type produced **agglutinates** or **formed clusters** which were caused by the absence of molecules on red blood cells and resulting in antibodies to defeat that molecule.

He then made a note of the agglutination and divided the blood types into 4 different groups. For the discovery of ABO blood group, he was awarded the Nobel Prize.

The blood grouping system is pivotal in blood transfusion. Our immune system recognizes another blood type as foreign and attacks it if introduced in the body causing a ***transfusion reaction***. Any inappropriate match with the Rh and ABO blood types, causes the most serious and life-threatening transfusion reactions. Therefore, before blood transfusion, it is suggested to have a blood group checked.

What are ABO and Rh blood groups?

During the blood transfusion, the two most important group systems examined are the ***ABO-system*** and the ***Rhesus system***.

The ABO blood group system consists of 4 types of blood group – **A, B, AB,** and **O** and is mainly based on the antigens and antibodies on red blood cells and in the plasma.

Both antigens and antibodies are protein molecules in which antigens are present on the surface of Red Blood Cells and antibodies are present in the plasma which is involved in defending mechanisms.

On the other hand, the Rh blood group system consists of **50 defined blood group antigens**. In the Rh system, the most important antigens are **D, C, c, E, and e**. The ABO and Rh blood systems are discussed in detail below.

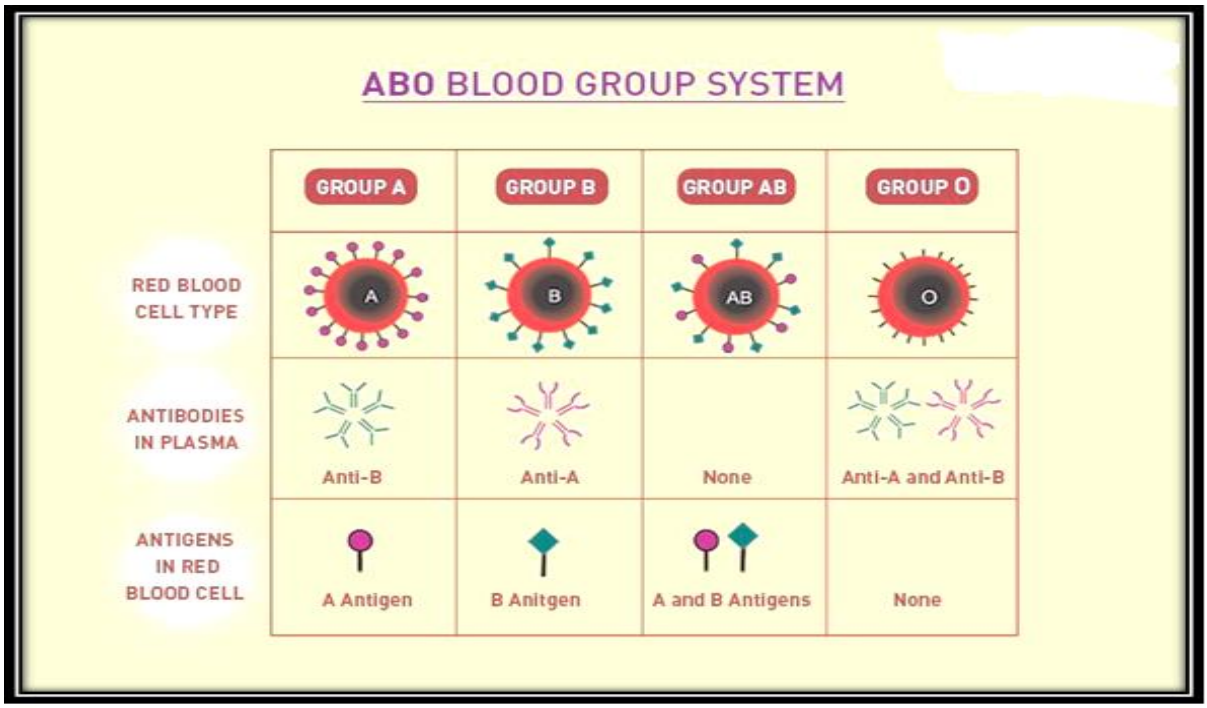
1. ABO blood Group system

The basis of ABO grouping is of two antigens- **Antigen A and Antigen B**. The ABO grouping system is classified into four types based on the presence or absence of antigens on the red blood cells surface and plasma antibodies.

- **Group A** – contains antigen A and antibody B.
- **Group B** –contains antigen B and antibody A.
- **Group AB** –contains both A and B antigen and no antibodies (neither A nor B).
- **Group O** – contains neither A nor B antigen and both antibodies A and B.

The ABO group system is important during blood donation or blood transfusion as mismatching of blood group can lead to clumping of red blood cells with various disorders. It is important for the blood cells to match while transfusing i.e. donor-recipient compatibility is necessary.

For example, a person of **blood group A can receive blood either from group A or O** as there are no antibodies for A and O in blood group A.



As shown in the above table, individuals of blood group O are called as ***universal donors***, whereas individuals of blood group AB are ***universal recipients***.

2. Rh Blood Group System

In addition to the ABO blood grouping system, the other prominent one is the Rh blood group system.

About two-thirds of the population contains the third antigen on the surface of their red blood cells known as ***Rh factor*** or ***Rh antigen***; this decides whether the blood group is positive or negative.

If the Rh factor is present, an individual is ***rhesus positive*** (Rh+ve); if an Rh factor is absent individual is ***rhesus negative*** (Rh-ve) as they produce Rh antibodies. Therefore, compatibility between donor and individual is crucial in this case as well.

LYMPHATIC SYSTEM

- Lymphatic system is a closed system of lymph channels or lymph vessels,

through which lymph flows. It is a **one-way system** and allows the lymph flow from tissue spaces toward the blood.

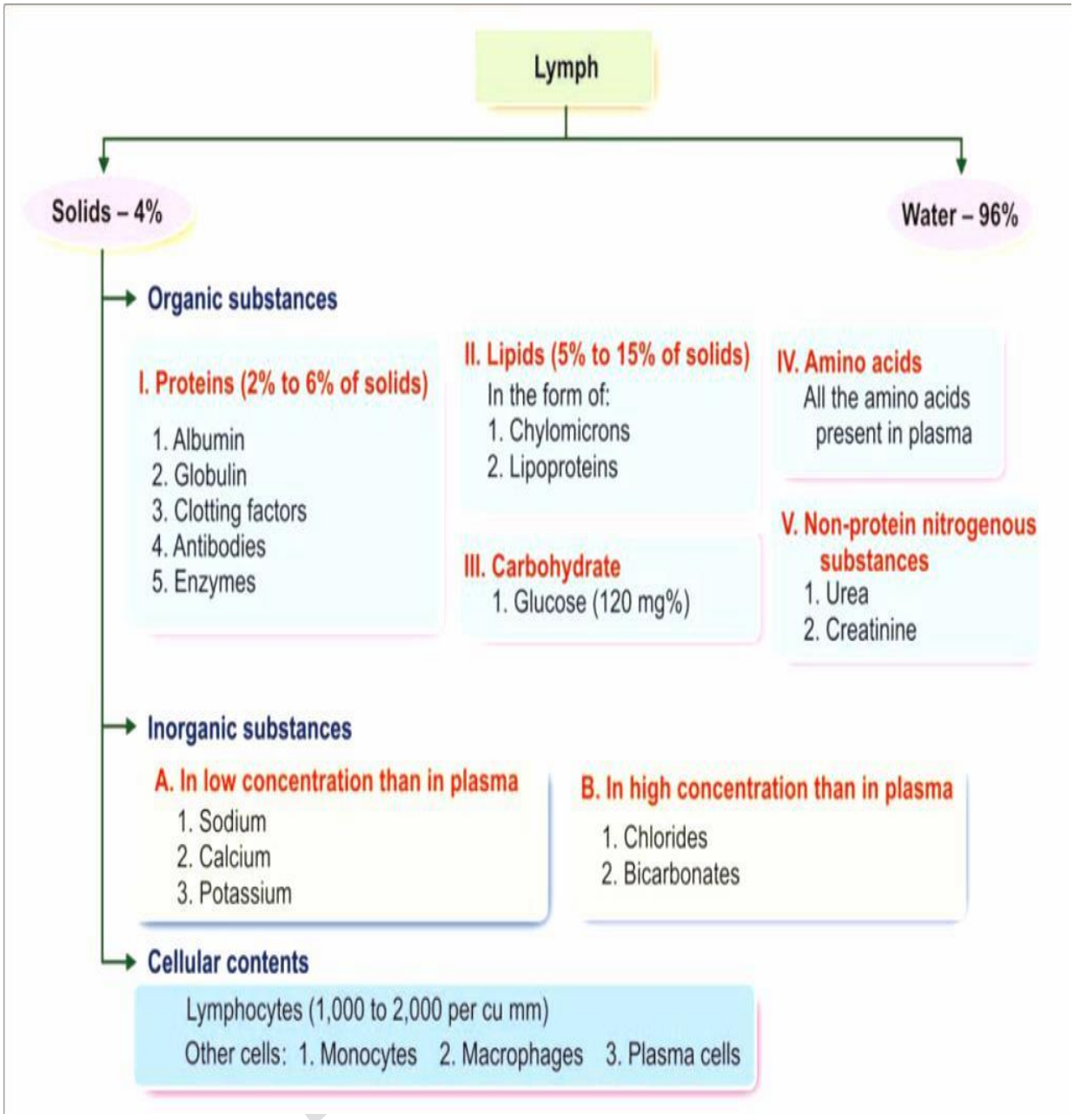
- **Organization of Lymphatic System**

- Lymphatic system arises from tissue spaces as a meshwork of delicate vessels. These vessels are called **lymph capillaries.**
- Lymph capillaries start from tissue spaces as enlarged blind-ended terminals called **capillary bulbs.** These bulbs contain valves, which allow flow of lymph in only one direction.
- There are some muscle fibers around these bulbs. These muscle fibers cause contraction of bulbs so that, lymph is pushed through the vessels.
- Lymph capillaries are lined by endothelial cells. Capillaries unite to form large lymphatic vessels.
- The structure of lymph capillaries is slightly different from that of the blood capillaries. Lymph capillaries are more porous and the cells lie overlapping on one another. This allows the fluid to move into the lymph capillaries and not in the opposite direction.
- The lymphatic system consists of:
- Lymph
- Lymph vessels
- Lymph nodes
- Lymph organs, e.g. Spleen and Thymus
- Diffuse lymphoid tissue, e.g. Tonsils
- Bone marrow

- **LYMPH**

- Lymph is a clear watery fluid, similar in composition to plasma, with the important exception of plasma proteins and identical in composition to interstitial fluid.
- The major difference between interstitial fluid and lymph is location: Interstitial fluid is found between cells, and lymph is located within lymphatic vessels and lymphatic tissue.
- About 120 mL of lymph flows into blood per hour. Out of this, about 100 mL/hour flows through thoracic duct and 20 mL/ hour flows through the right lymphatic duct.
- **Lymphatic tissue** is a specialized form of reticular connective tissue that contains large numbers of lymphocytes.
- Lymph transports the plasma proteins that seep out of the capillary beds back to the bloodstream. It also carries away larger particles, e.g. bacteria and cell debris from damaged tissues, which can then be filtered out and destroyed by the lymph nodes.

- **COMPOSITION OF LYMPH**



- **FUNCTIONS OF LYMPH**
- To return the proteins from tissue spaces into blood.
- It is responsible for redistribution of fluid in the body.
- Bacteria, toxins and other foreign bodies are removed from tissues via lymph.
- Lymph flow is responsible for the maintenance of structural and functional integrity of tissue.
- Lymph flow serves as an important route for intestinal fat absorption.
- It plays an important role in immunity by transport of lymphocytes.

- **LYMPH NODES**
- Lymph nodes are small glandular structures located in the course of lymph vessels. The lymph nodes are also called lymph glands or lymphatic nodes.
- They are scattered throughout the body, both superficially and deep, and usually occur in groups.
- Lymph nodes function as a type of filter. As lymph enters one end of a lymph node, foreign substances are trapped by the reticular fibers within the sinuses of the node. Then macrophages destroy some foreign substances by phagocytosis, while lymphocytes destroy others by immune responses.
- The filtered lymph then leaves the other end of the lymph node. Since there are many afferent lymphatic vessels that bring lymph into a lymph node and only one or two efferent lymphatic vessels that transport lymph

out of a lymph node, the slow flow of lymph within the lymph nodes allows additional time for lymph to be filtered.

- Additionally, all lymph flows through multiple lymph nodes on its path through the lymph vessels.
- **Functions of Lymph Nodes**
- Lymph nodes serve as filters which filter bacteria and toxic substances from the lymph.
- When lymph passes through the lymph nodes, it is filtered, i.e. the water and electrolytes are removed. But, the proteins and lipids are retained in the lymph.
- Bacteria and other toxic substances are destroyed by macrophages of lymph nodes. Because of this, lymph nodes are called defense barriers.

UNIT IV

PERIPHERAL NERVOUS SYSTEM

The peripheral nervous system consists of nerves and scattered groups of neuronal cell bodies (ganglia) found outside the CNS.

Structure of a Nerve

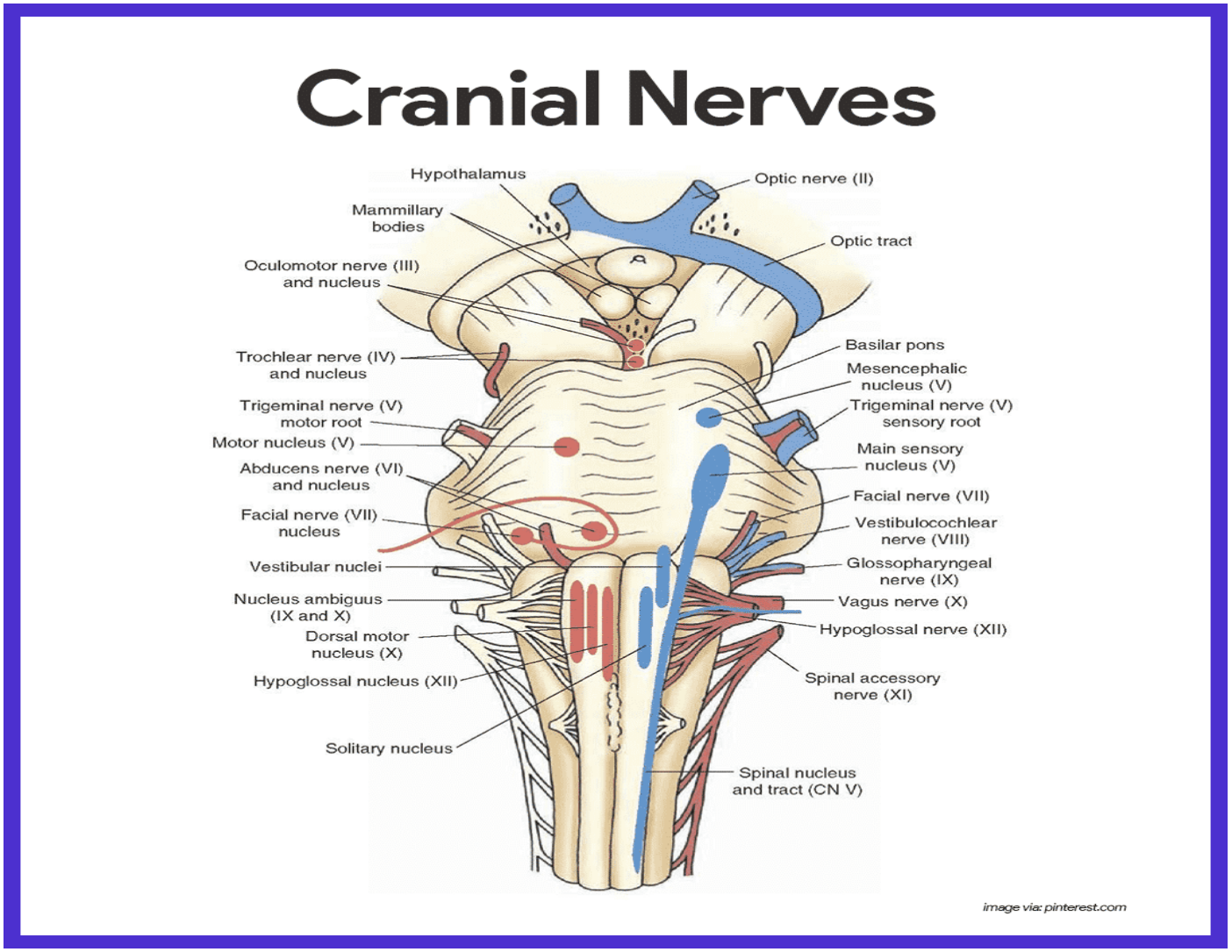
A nerve is a bundle of neuron fibers found outside the CNS.

- **Endoneurium.** Each fiber is surrounded by a delicate connective tissue sheath, an endoneurium.
- **Perimeurium.** Groups of fibers are bound by a coarser connective tissue wrapping, the perineurium, to form fiber bundles, or **fascicles**.
- **Epineurium.** Finally, all the fascicles are bound together by a tough fibrous sheath, the epineurium, to form the cordlike nerve.

- **Mixed nerves.** Nerves carrying both sensory and motor fibers are called mixed nerves.
- **Sensory nerves.** Nerves that carry impulses toward the CNS only are called sensory, or afferent, nerves.
- **Motor nerves.** Those that carry only motor fibers are motor, or efferent, nerves.

Cranial Nerves

The 12 pairs of cranial nerves primarily serve the head and the neck.



- **Olfactory.** Fibers arise from the olfactory receptors in the nasal mucosa and synapse with the olfactory bulbs; its function is purely sensory, and it carries impulses for the sense of smell.
- **Optic.** Fibers arise from the retina of the eye and form the optic nerve; its function is purely sensory, and carries impulses for vision.
- **Oculomotor.** Fibers run from the midbrain to the eye; it supplies motor fibers to four of the six muscles (superior, inferior, and medial rectus, and inferior oblique) that direct the eyeball; to the eyelid; and to the internal eye muscles controlling lens shape and pupil size.
- **Trochlear.** Fibers run from the midbrain to the eye; it supplies motor fibers for one external eye muscle (superior oblique).
- **Trigeminal.** Fibers emerge from the pons and form three divisions that run to the face; it conducts sensory impulses from the skin of the face and mucosa of the nose and mouth; also contains motor fibers that activate the chewing muscles.
- **Abducens.** Fibers leave the pons and run to the eye; it supplies motor fibers to the lateral rectus muscle, which rolls the eye laterally.
- **Facial.** Fibers leave the pons and run to the face; it activates the muscles of facial expression and the lacrimal and salivary glands; carries sensory impulses from the taste buds of the anterior tongue.
- **Vestibulocochlear.** fibers run from the equilibrium and hearing receptors of the inner ear to the brain stem; its function is purely sensory; vestibular branch transmits impulses for the sense of balance, and cochlear branch transmits impulses for the sense of hearing.
- **Glossopharyngeal.** Fibers emerge from the medulla and run to the throat; it supplies motor fibers to the pharynx (throat) that promote swallowing and saliva production; it carries sensory impulses from the

taste buds of the posterior tongue and from pressure receptors of the carotid artery.

- **Vagus.** Fibers emerge from the medulla and descend into the thorax and abdominal cavity; the fibers carry sensory impulses from and motor impulses to the pharynx, larynx, and the abdominal and thoracic viscera; most motor fibers are parasympathetic fibers that promote digestive activity and help regulate heart activity.
- **Accessory.** Fiber arise from the medulla and superior spinal cord and travel to muscles of the neck and back; mostly motor fiber that activate the sternocleidomastoid and trapezius muscles.
- **Hypoglossal.** Fibers run from the medulla to the tongue; motor fibers control tongue movements;; sensory fibers carry impulses from the tongue.

Spinal Nerves and Nerve Plexuses

The 31 pairs of human spinal nerves are formed by the combination of the ventral and dorsal roots of the spinal cord.

- **Rami.** Almost immediately after being formed, each spinal nerve divides into dorsal and ventral rami, making each spinal nerve only about 1/2 inch long; the rami contains both sensory and motor fibers.
- **Dorsal rami.** The smaller dorsal rami serve the skin and muscles of the posterior body trunk.
- **Ventral rami.** The ventral rami of spinal nerves T1 through T12 form the intercostal nerves, which supply the muscles between the ribs and the skin and muscles of the anterior and lateral trunk.
- **Cervical plexus.** The cervical plexus originates from the C1-C5, and **phrenic nerve** is an important nerve; it serves the diaphragm, and skin and muscles of the shoulder and neck.

- **Brachial plexus.** The **axillary nerve** serve the deltoid muscles and skin of the shoulder, muscles, and skin of superior thorax; the r**adial nerve** serves the triceps and extensor muscles of the forearm, and the skin of the posterior upper limb; the **median nerve** serves the flexor muscles and skin of the forearm and some muscles of the hand; the **musculocutaneous nerve** serves the flexor muscles of arm and the skin of the lateral forearm; and the **ulnar nerve** serves some flexor muscles of forearm; wrist and many hand muscles, and the skin of the hand.
- **Lumbar plexus.** The **femoral nerve** serves the lower abdomen, anterior and medial thigh muscles, and the skin of the anteromedial leg and thigh; the **obturator nerve** serves the adductor muscles of the medial thigh and small hip muscles, and the skin of the medial thigh and hip joint.
- **Sacral plexus.** The **sciatic nerve** (largest nerve in the body) serves the lower trunk and posterior surface of the thigh, and it splits into the common fibular and tibial nerves; the **common fibular nerve** serves the lateral aspect of the leg and foot, while the **tibial nerve** serves the posterior aspect of leg and foot; the **superior and inferior gluteal nerves** serve the gluteal muscles of the hip.

INTRODUCTION TO AUTONOMIC NERVOUS SYSTEM

1. What is nervous system? Classify nervous system and write its functions.

- The nervous system is a highly complex part of body that coordinates its actions and sensory information by transmitting signals to and from different parts of its body.

- The nervous system detects environmental changes that impact the body, then works in tandem with the endocrine system to respond to such events.
- The nervous system is the major controlling, regulatory, and communicating system in the body.
- It is the center of all mental activity including thought, learning, and memory.
- Together with the endocrine system, the nervous system is responsible for regulating and maintaining homeostasis.
- Through its receptors, the nervous system keeps us in touch with our environment, both external and internal.
- Like other systems in the body, the nervous system is composed of organs, principally the brain, spinal cord, nerves, and ganglia.
- These, in turn, consist of various tissues, including nerve, blood, and connective tissue. Together these carry out the complex activities of the nervous system.
- The various activities of the nervous system can be grouped together as three general, overlapping functions:
    - Sensory
    - Integrative
    - Motor
- Millions of sensory receptors detect changes, called stimuli, which occur inside and outside the body. They monitor such things as temperature, light, and sound from the external environment.
- Inside the body, the internal environment, receptors detect variations in pressure, pH, carbon dioxide concentration, and the levels of

various electrolytes. All of this gathered information is called sensory input.

- Sensory input is converted into electrical signals called nerve impulses that are transmitted to the brain. There the signals are brought together to create sensations, to produce thoughts, or to add to memory; Decisions are made each moment based on the sensory input. This is integration.
- Based on the sensory input and integration, the nervous system responds by sending signals to muscles, causing them to contract, or to glands, causing them to produce secretions. Muscles and glands are called effectors because they cause an effect in response to directions from the nervous system. This is the motor output or motor function.

CLASSIFICATION OF HUMAN NERVOUS SYSTEM

The nervous system as a whole is divided into two subdivisions: the **central nervous system** (CNS) and the **peripheral nervous system (PNS).**

The Central Nervous System

- The brain and spinal cord are the organs of the central nervous system.

The Peripheral Nervous System

- The organs of the peripheral nervous system are the nerves and ganglia.
- Nerves are bundles of nerve fibers, much like muscles are bundles of muscle fibers.
- Cranial nerves and spinal nerves extend from the CNS to peripheral organs such as muscles and glands.
- Ganglia are collections, or small knots, of nerve cell bodies outside the CNS.
- The peripheral nervous system is further subdivided into an **afferent (sensory) division** and an **efferent (motor) division**.

- The afferent or sensory division transmits impulses from peripheral organs to the CNS.
- The efferent or motor division transmits impulses from the CNS out to the peripheral organs to cause an effect or action.
- Finally, the efferent or motor division is again subdivided into the **somatic nervous system** and **the autonomic nervous system.**
- The somatic nervous system, also called the somatomotor or somatic efferent nervous system, supplies motor impulses to the skeletal muscles.
- Because these nerves permit conscious control of the skeletal muscles, it is sometimes called the voluntary nervous system.
- The autonomic nervous system, also called the visceral efferent nervous system, supplies motor impulses to cardiac muscle, to smooth muscle, and to glandular epithelium. It is further subdivided into sympathetic and parasympathetic divisions. Because the autonomic nervous system regulates involuntary or automatic functions, it is called the involuntary nervous system.

2. Write the functions and divisions of autonomic nervous system.

The autonomic nervous system is part of peripheral nervous system that acts unconsciously in body.

It regulates various body functions such as:

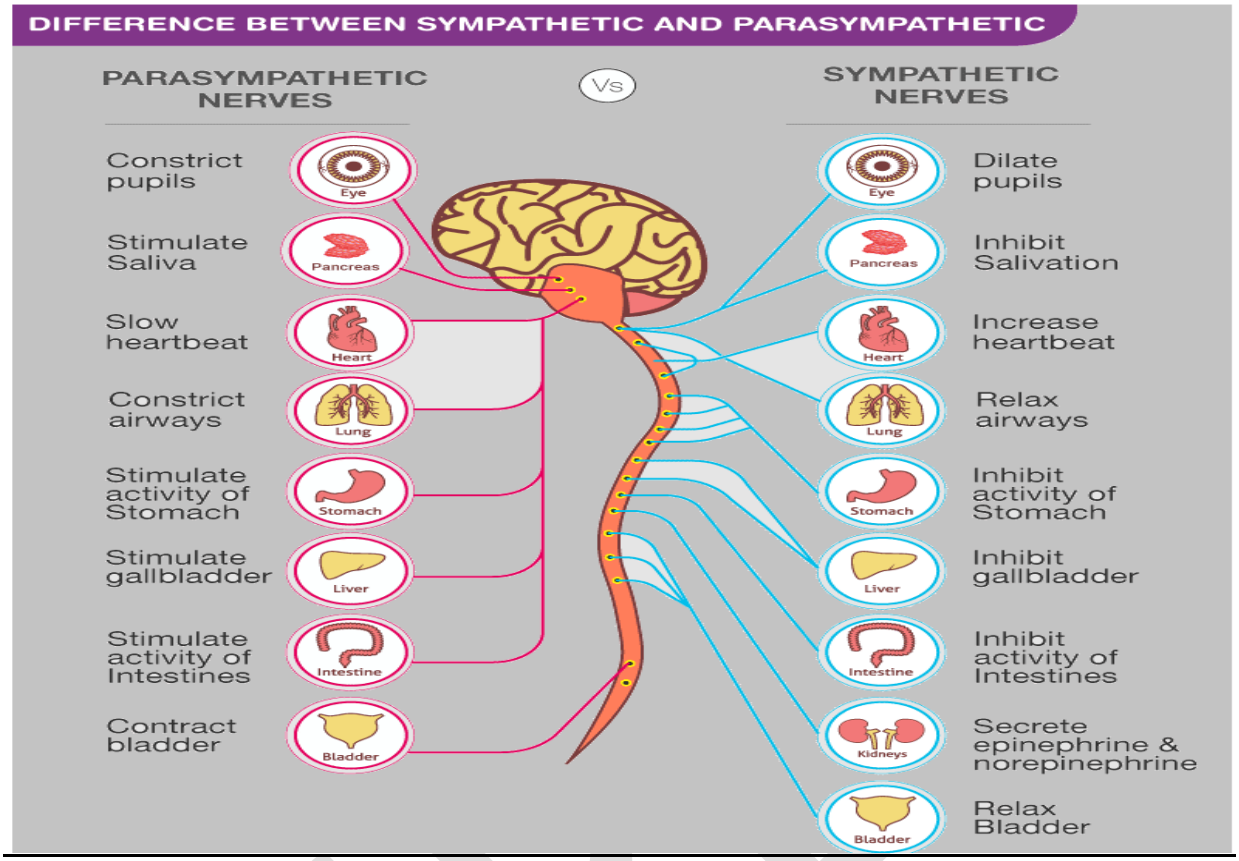
- Heart rate
- Digestion
- Regulation of bp
- Regulation of respiration

- Metabolism
- Exocrine and endocrine secretions
- Sexual arousal
- Urination
- Contractions and relaxations of smooth muscles

The autonomic nervous system is divided into three parts:

- Parasympathetic nervous system [Major NT is Ach]
- Sympathetic nervous system [Major neurotransmitter is NE]
- Enteric nervous system

Sympathetic and Parasympathetic Effects		
Structure	**Sympathetic**	**Parasympathetic**
Eye (pupil)	Dilation	Constriction
Nasal Mucosa	Mucus reduction	Mucus increased
Salivary Gland	Saliva reduction	Saliva increased
Heart	Rate increased	Rate decreased
Arteries	Constriction	Dilation
Lung	Bronchial muscle relaxation	Bronchial muscle contraction
Gastrointestinal Tract	Decreased motility	Increased motility
Liver	Conversion of glycogen to glucose increased	Glycogen synthesis
Kidney	Decreased urine	Increased urine
Bladder	Contraction of sphincter	Relaxation of sphincter
Sweat Glands	↑Sweating	No change



PARASYMPATHETIC NERVOUS SYSTEM

3. Write in brief on parasympathetic nervous system.

- The parasympathetic nervous system originates in the sacral spinal cord and medulla, physically surrounding the sympathetic origin, and works in concert with the sympathetic nervous system.
- Its main function is to activate the "rest and digest" response and return the body to homeostasis after the fight or flight response.
- This system utilises and activates the release of the neurotransmitter acetylcholine.
- Acetylcholine receptors are muscarinic and nictotinic receptors

- **Nicotinic acetylcholine receptors:** These are responsive to nicotine. These are present in skeletal muscles and autonomic ganglia.
- **Muscarinic acetylcholine receptors:** These are particularly responsive to muscarine. These are present in heart, smooth muscles, blood vessels, different glands and eyes.

4. Write Physiology Of Parasympathetic Nervous System

Superior control by anterior and middle part of hypothalamus

↓

Centre of III, VII, IX and X cranial nerve and sacral part of spinal cord

↓

Activate preganglionic neuron/fiber (Long)

↓

Release neurotransmitter-I (Ach) in Autonomic Ganglion/Junction (Junction I)

↓

Stimulate (NN) or (M1) receptor

↓

Activate postganglionic neuron/fiber (Short) after that Ach is destruct by Acetylcholine Esterase

↓

Stimulate (M1), (M2), (M3) or (NN) receptor

↓

Release of neurotransmitter-II (Ach) in Neuron Effector Junction (Junction II)

↓

Produce various action after that Ach is destruct by Acetylcholine esterase

5. Classify cholinergic receptors.

Cholinergic receptors are classified into two types

- Muscarinic receptors
- Nicotinic receptors

A. Muscarinic Receptors

Five types of muscarinic receptors are found. They are M1, M2, M3, M4, and M5.

- **M1 (neuronal):**

These are G-protein coupled receptors, it activate phospholipase C and stimulate Inositol Triphosphate (IP3) and Diacylglycerol (DAG) and increase intracellular calcium level.

These receptors are present in CNS, gastric glands and salivary glands.

(**Function:** Gastric secretion)

Location	**Function**
Autonomic ganglion/junction (Junction– I)	Activation of post ganglionic neuron/fiber

- **M2 (cardiac):**

These are G-protein coupled receptors, it act by opening K+ channels which reduce cyclic AMP (cAMP) level. These are present in Heart.

(**Function:** decrease heart rate, decrese force of contraction, decrease conduction velocity)

Location	**Function**
Heart	• Decrease force of contraction (Negative Inotropic)

	• Decrease heart rate (Negative Chronotropic) • Decrease conduction (Negative dromotropic)

- **M3 (glands, smooth muscles):**

These are G-protein coupled receptors, it activate phospholipase C and stimulate Inositol Triphosphate (IP3) and Diacylglycerol (DAG) and increase intracellular calcium level. These are present in exocrine glands, GI smooth muscles, eye, and blood vessel.

(**Function:** Increase Glandular secretions (sweat, saliva, ocular), Increase motility, vasodilatation)

Location	**Function**
GI smooth muscle	Contraction of GI smooth muscle
Salivary glands	Increase saliva secretion
Lacrimal glands	Increase Lacrimal secretion
Gastric glands	Increase gatric acid secretion
Urinary tract	Contract urinary bladder, produce micturition
Bronchial smooth muscle	Contraction
Eye	Miosis (contraction of pupil), contraction of sphincter pupil.

- **M4 (CNS):** Present in CNS (**Function:** Enhanced locomotion)
- **M5 (CNS):** Present in CNS (**Function:** Not Known)

B. Nicotinic Receptors

Two types of nicotinic receptors are present: N_M and N_N.

- **N_M:**

These are the intrinsic ion channel receptors, it act by opening various ion channels like Na+, K+ and Ca+. It is the part of somatic systems. These are present in the neuromuscular junction and skeletal muscle. **Function:** Skeletal Muscle contraction.

Location	Function
Neuromuscular junction	Skeletal muscle contraction

- **N_N:**

These are intrinsic ion channel receptors. They act by opening various ion channels like sodium ion, calcium ion, potassium ion. They are present in the autonomic ganglion. **Function:** Stimulation of Autonomic ganglia

Location	Function
Autonomic ganglion/junction (Junction – I)	Activation of post ganglionic nerve fibre
Adrenal medulla	Release of adrenaline, noradrenaline
CNS	Inhibitory action

SYMPATHETIC NERVOUS SYSTEM

6. WRITE IN BRIEF ABOUT SYMPATHETIC NERVOUS SYSTEM.

- The sympathetic nervous system originates in the spinal cord and its main function is to activate the physiological changes that occur during the fight-or-flight response.
- Catecholamines are synthesized in neurons and in the chromaffin cells of the adrenal medulla. Examples: **dopamine, noradrenaline and adrenaline**.
- This nervous system utilises and activates the release of norepinephrine in the reaction.
- Noradrenaline is the major neurotransmitter in the peripheral sympathetic nervous system.
- Adrenaline is the primary hormone secreted by adrenal medulla.
- Dopamine is the metabolic precursor of Noradrenaline & Adrenaline in sympathetic system.
- The neurotransmitter at the sympathetic ganglia is Acetylcholine.
- All postganglionic sympathetic fibers release Noradrenaline at the Neuroeffector junction.

7. CLASSIFY ADRENERGIC RECEPTORS/ ADRENOCEPTORS

The adrenergic receptors are G protein-coupled receptors. Two types of adrenergic receptors are:

- **α receptors:** α_1 and α_2. **β receptors**: β_1, β_2 and β_3.

Type	Tissue : Actions

Alpha1	Most vascular smooth muscles: Contraction Pupillary dilator muscle: Mydriasis Heart: Increased force of contraction
Alpha2	Adrenergic nerve terminals: Inhibition of transmitter release Platelets: Aggregation
Beta1	Heart: Increased rate and force of contraction
Beta2	Respiratory, uterine, and vascular smooth muscle: Relaxation Human liver: Glycogenolysis
Beta3	Fat cells: Lipolysis

8. WRITE IN DETAIL ON α – ADRENERGIC RECEPTORS

α_1 adrenergic receptors

- They are present post-synaptically
- The excitatory responses of α_1 receptor activation are mediated through inositol phosphate pathway.
- The inhibitory effects of α_1 receptor activation in the gut results when G-protein coupled receptors acts through an increase in the ionic permeability of K^+ ions leading to hyper-polarization
- When stimulated by agonist these produce excitatory effects in vascular smooth muscle, salivary glands, bronchi, uterus, radial muscle of iris, urinary bladder neck, liver cells
- When stimulated by agonist these produce inhibitory effects in Intestines (relaxation)

- **α_{1A} Receptors:** mainly located in heart, liver, cerebellum, urinary bladder neck & vas deferens
- **α_{1B} Receptors:** mainly located in kidneys & splenic capsule
- **α_{1D} Receptors:** mainly located on hippocampus & prostate

Location	**Function**
Blood vessels	Produce vasoconstriction
Iris	It contract radial muscles and dilate the pupil known as mydriasis
GI tract	Contract the GI sphincter and relax the the GI muscle
Urinary bladder	Contract the trigon and relax the urinary bladder
Glands	Increase the secretion of glands
Uterus	It produce contraction in nonpregnant uterus
Heart	Weak action on heart
Male sex organ	Penile erection and ejaculation
Skin	Contraction of pilomotor muscles.

α_2 Adrenergic Receptors

- They are present pre-synaptically on the sympathetic postganglionic neuron.

- Stimulation of these receptors by NA decreases further release of NA.
- Blocked of these receptors produces more NA.
- Presynaptic α_2 receptors are also located on the cholinergic nerve terminals of the gut.
- When these receptors are activated, the release of ACh is decreased from the cholinergic neuron leading to relaxation.
- α_2 receptors post-synaptically are located in brain, in platelets (causing aggregation) & on β-pancreatic cells (inhibiting insulin release).
- α_{2A} receptors are located in platelets, α_{2B} receptors are located in liver & kidney, α_{2C} receptors are found post-synaptically in the cerebral cortex.
- In brain, the α_2 receptors whether present post-synaptically or pre-synaptically decrease the sympathetic outflow upon their activation

Basis

- α_2 receptor agonists inhibit adenylate cyclase through an inhibitory G-protein (G_i) & reduce the intracellular cAMP concentration which results in a decreased activation of cAMP dependent protein kinase and produces diminished response.

Location	**Function**
Presynaptic nerve ending	It reduce release of noradrenaline
Blood vessels	constriction
CNS	Reduction in central sympathetic flow
Pancreas	Reduce insulin, increase in blood sugar
Platelets	Aggregation of platelets
GI muscle	Relaxation

9. WRITE IN DETAIL ON β – ADRENERGIC RECEPTORS

β_1 – adrenoceptors

- These are mainly found in heart.
- They produce positive inotropic & positive chrontropic effects (i.e. excitatory effects).
- They are also found in kidney.
- They promotes rennin release.

Location	Function
Heart	Increase force of contraction (Positive Inotropic) Increase heart rate (Positive Chronotropic) Increase conduction (Positive dromotropic)
Kidney	Release of renin, so renin activate angiotensinogen I which convert in angiotensinogen II by the help of angiotensinogen converting enzyme (ACE) and activate the aldosterone. Which retain the Na+ and water and increase the blood volume as well as angiotensinogen act on AT-I and AT-II receptor and contract the blood vessels.

β_2 – adrenoceptors

- They are found in bronchi, coronary arteries, uterus & smooth muscles (including gut).
- Their activation causes smooth muscle relaxation (inhibitory effects).

Location	Function
Blood vessels	Produce vasodilation
Lungs	dilate the bronchial smooth muscle
GI tract	relax the the GI muscle
Urinary bladder	relax the urinary bladder
Glands	Increase the secretion of glands
Liver	Glucogenolysis, increase blood sugar
Pancreas	Increase glucagon secretion, increase blood sugar
Adipose tissue	Lipolysis
Uterus	Relaxation of pregnant uterus.

β_3 – adrenoceptors

- These are mainly found on adipocytes
- Activation of these receptors promotes lipolysis (rise in free fatty acids in the blood) & thermogenesis.

Presynaptic β receptors

- These are identified on adrenergic nerve terminals
- Activation of these receptors facilitates the neurotransmitter release (opposite to that usually observed after pre-synaptic α_2 adrenergic receptor activation

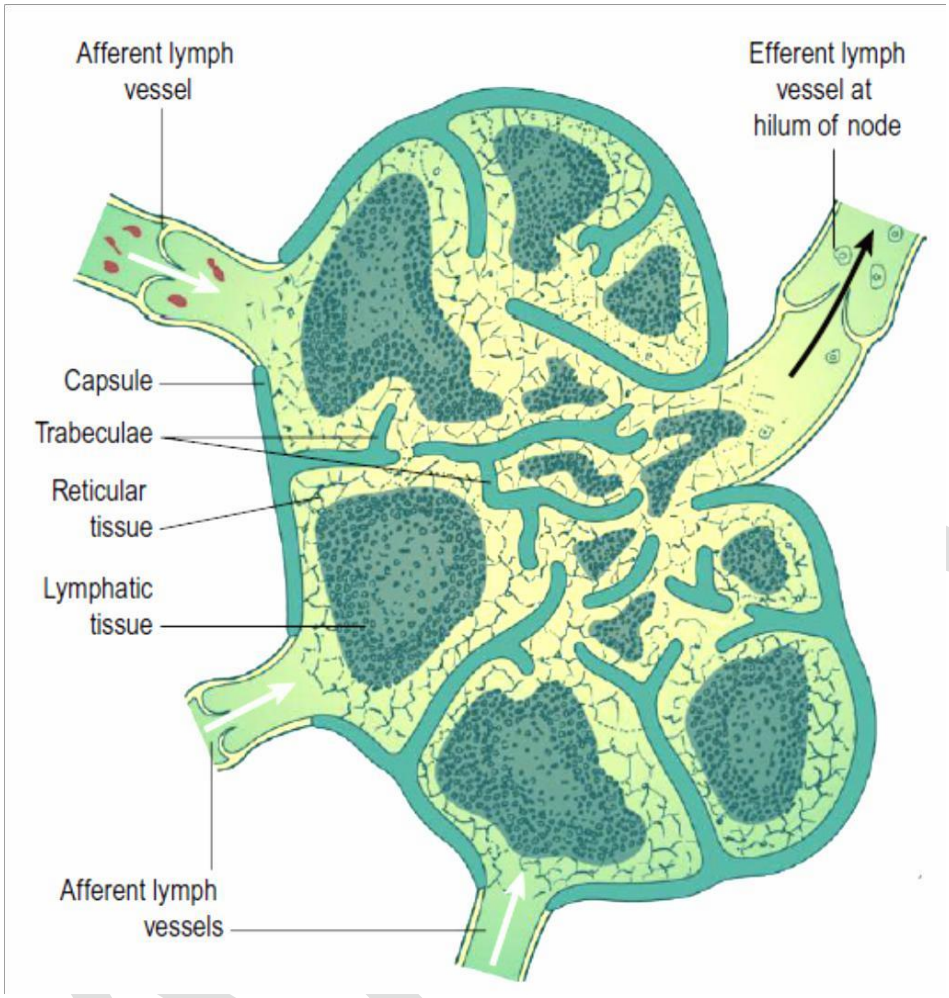
10. WRITE IN DETAIL ON DOPAMINE RECEPTORS

- Dopamine is an endogenous catecholamine neurotransmitter.

- Its actions are mediated through specific dopamine receptors D1, D2, D3, D4 & D5.
- At higher doses it activates β_1 receptors and still higher activates α_1 receptors.
- D1 appears to be more important in the periphery (renal, mesenteric & coronary vascular beds).
- D2 subtype has effect more in CNS.

Basis

- D1 & D5 cause stimulation of adenylate cyclase as a result increase in cAMP takes place. Increase cAMP causes vasodilatation in the renal & mesenteric arteries. As a result increased glomerular filtration, renal blood flow & excretion of sodium also occur.
- D2, D3 & D4 inhibit adenylate cyclase, so decrease in cAMP takes place. It can open K+ channels & blocks Ca+2 channels.
- Dopamine receptors cause peripheral vasodilatation in the renal system and also increases myocardial contractility by direct stimulation of β_1 receptors
- So increase in cardiac output occurs but total peripheral resistance & mean BP is unchanged due to simultaneous renal & splanchnic vasodilatation through D1 receptor.



- **Fig. Lymph Node**

- **Applied Physiology – Swelling of Lymph Nodes**
- During infection or any other processes in a particular region of the body, activities of the lymph nodes in that region increase. This causes swelling of the lymph nodes.
- Sometimes, the swollen lymph nodes cause pain. Most common cause of swollen lymph nodes is infection. Lymph nodes situated

near an infected area swell immediately.

- When the body recovers from infection, the lymph nodes restore their original size gradually, in one or two weeks.

- **Causes for Lymph Node Swelling**
- Skin infection of arm causes swelling of lymph nodes in armpit.
- **Tonsillitis** or throat infection causes swelling of lymph nodes in neck.
- Infection of genital organs or leg results in swelling of lymph nodes in groin.
- Cancer in a particular region may spread into the nearby lymph nodes causing the swelling.
- Examples: **Throat cancer** may spread into lymph nodes in neck. **Lung cancer** may spread into lymph nodes in chest. **Breast cancer** may spread into lymph nodes in armpit.
- **Intestinal cancer** may spread into lymph nodes in abdomen.

- Spleen
- The spleen contains reticular and lymphatic tissue and is the largest lymph organ. The spleen lies in the left hypochondriac region of the abdominal cavity between the fundus of the stomach and the diaphragm.
- It is purplish in colour and varies in size in different individuals, but is usually about 12 cm long, 7 cm wide and 2.5 cm thick. It weighs about 200 g.

- **Structure**
- The spleen is slightly oval in shape with the hilum on the lower medial border. The anterior surface is covered with peritoneum. It is enclosed in a fibroblastic capsule that dips into the organ, forming trabeculae.
- The cellular material, consisting of lymphocytes and macrophages, is called splenic pulp, and lies between the trabeculae. Red pulp is the part suffused with blood and white pulp consists of areas of lymphatic tissue where there are sleeves of lymphocytes and macrophages around blood vessels.
- The structures entering and leaving the spleen at the hilum are:
- Splenic artery, a branch of the coeliac artery
- Splenic vein, a branch of the portal vein
- Lymph vessels (efferent only)
- Nerves

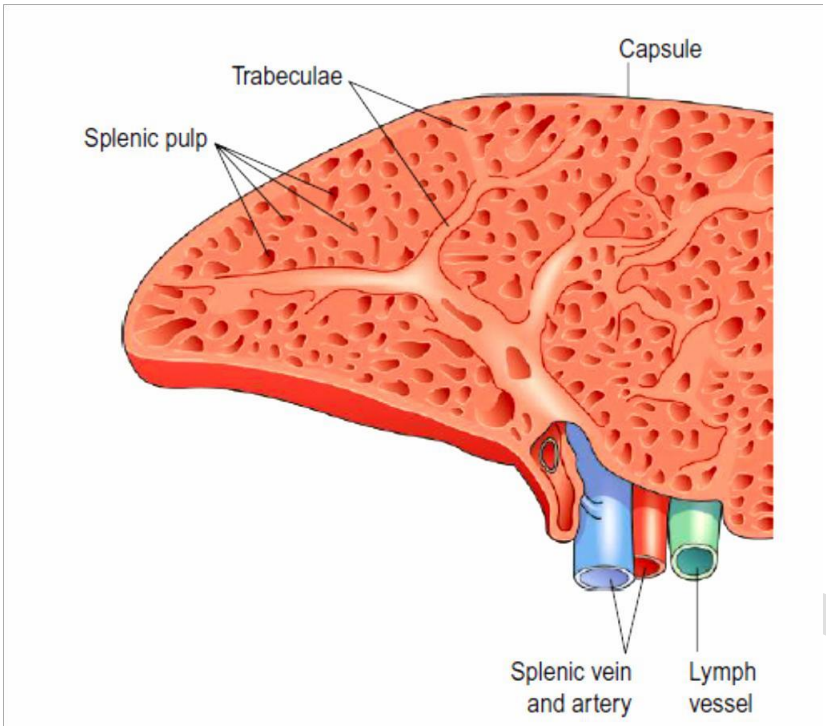


Figure 6.8 A section through the spleen.

- Functions
- **Phagocytosis:** Old and abnormal erythrocytes are mainly destroyed in the spleen, and the breakdown products, bilirubin and iron, are transported to the liver via the splenic and portal veins. Other cellular material, e.g. leukocytes, platelets and bacteria, is phagocytosed in the spleen.
- **Storage of blood:** The spleen contains up to 350 mL of blood, and in response to sympathetic stimulation can rapidly return most of this volume to the circulation, e.g. in haemorrhage.
- **Immune response:** The spleen contains T- and B-lymphocytes, which are activated by the presence of antigens, e.g. in infection. Lymphocyte proliferation during serious infection can cause enlargement of the spleen.

- **Erythropoiesis:** The spleen and liver are important sites of fetal blood cell production, and the spleen can also fulfil this function in adults in times of great need.

SPECIAL SENSES

Functions of Special Senses

The functions of the five special senses include:

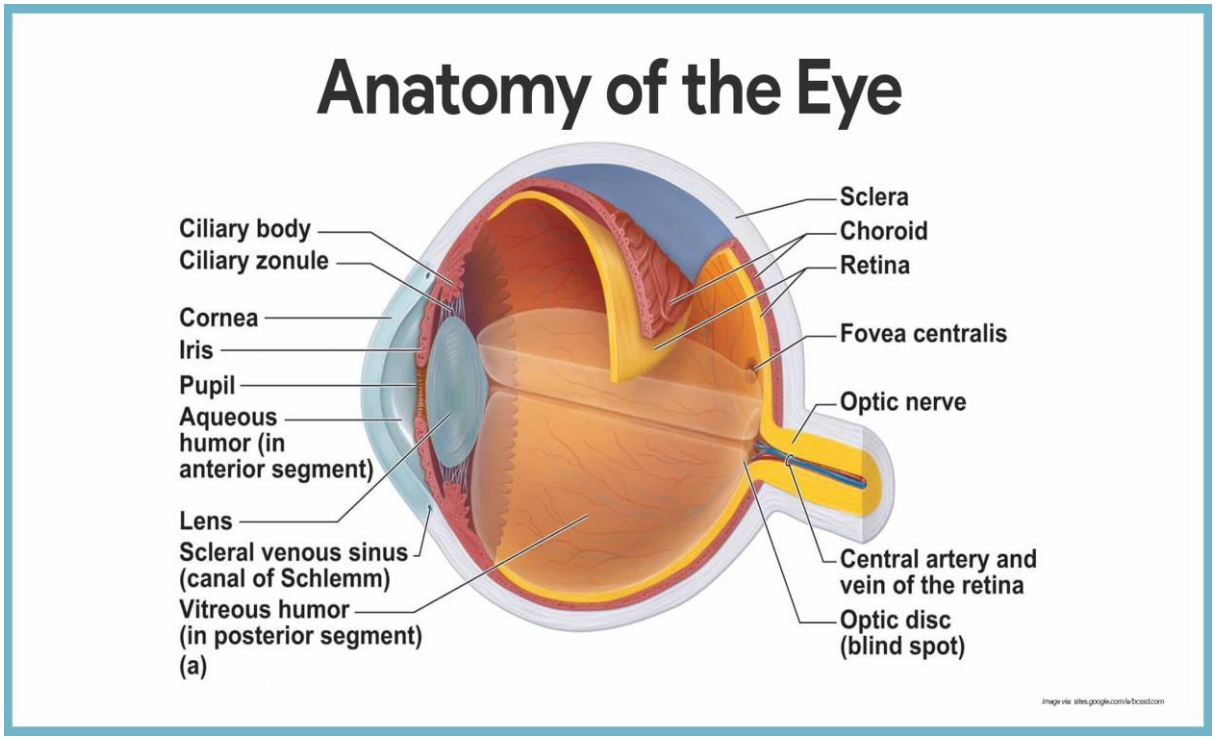
1. **Vision.** Sight or vision is the capability of the eye(s) to focus and detect images of visible light on photoreceptors in the retina of each eye that generates electrical nerve impulses for varying colors, hues, and brightness.
2. **Hearing.** Hearing or audition is the sense of sound perception.
3. **Taste.** Taste refers to the capability to detect the taste of substances such as food, certain minerals, and poisons, etc.
4. **Smell.** Smell or olfaction is the other "chemical" sense; odor molecules possess a variety of features and, thus, excite specific receptors more or less strongly; this combination of excitatory signals from different receptors makes up what we perceive as the molecule's smell.
5. **Touch.** Touch or somatosensory, also called tactition or mechanoreception, is a perception resulting from activation of neural receptors, generally in the skin including hair follicles, but also in the tongue, throat, and mucosa.

THE EYE AND VISION

Vision is the sense that has been studied most; of all the sensory receptors in the body 70% are in the eyes.

Anatomy of the Eye

Vision is the sense that requires the most "learning", and the eye appears to delight in being fooled; the old expression "You see what you expect to see" is often very true.

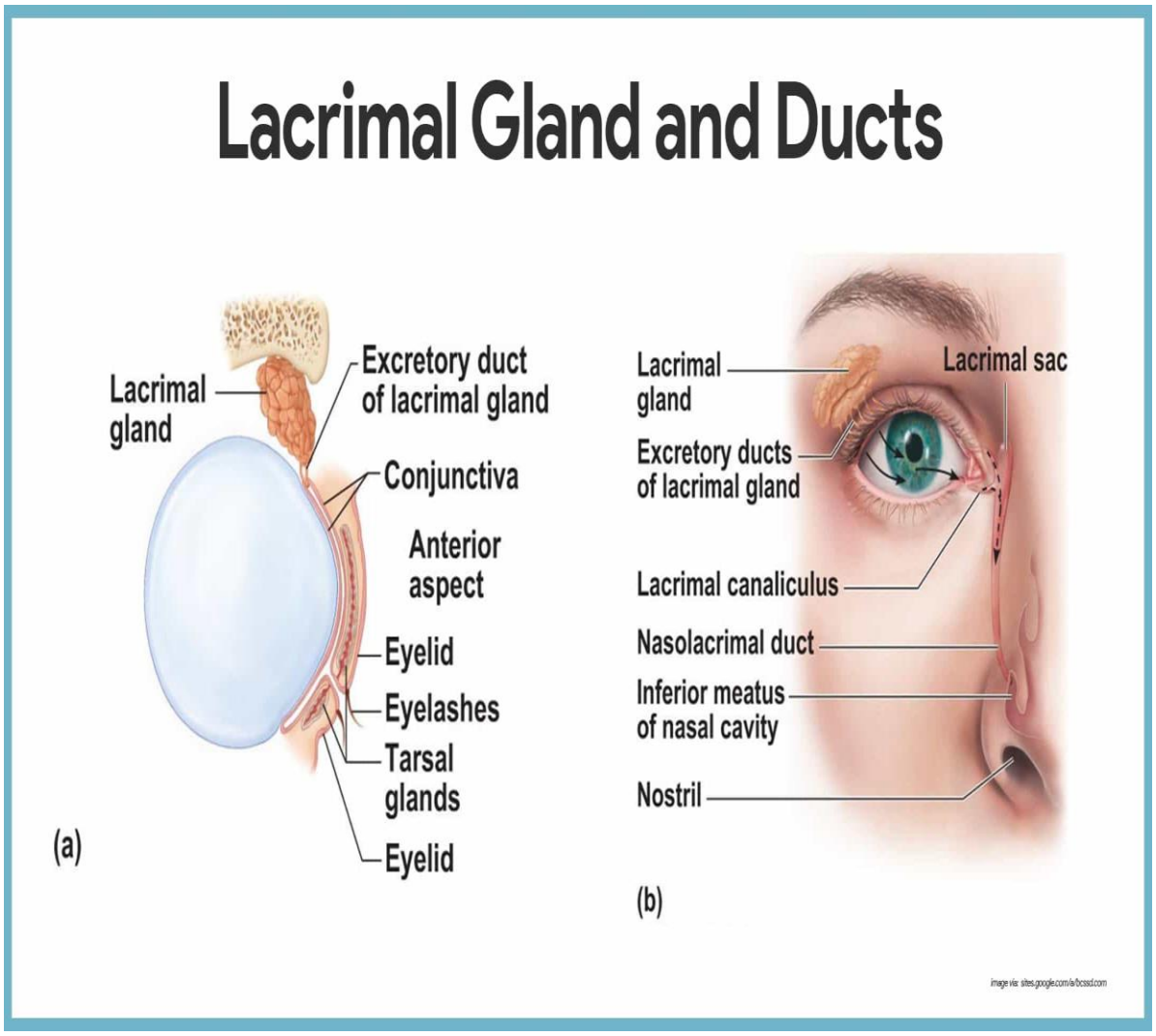


External and Accessory Structures

The accessory structures of the eye include the extrinsic eye muscles, eyelids, conjunctiva, and lacrimal apparatus.

- **Eyelids.** Anteriorly, the eyes are protected by the eyelids, which meet at the medial and lateral corners of the eye, the **medial** and **lateral commissure (canthus)**, respectively.
- **Eyelashes.** Projecting from the border of each eyelid are the eyelashes.
- **Tarsal glands.** Modified sebaceous glands associated with the eyelid edges are the tarsal glands; these glands produce an oily secretion that lubricates the eye; **ciliary glands**, modified sweat glands, lie between the eyelashes.
- **Conjunctiva.** A delicate membrane, the conjunctiva, lines the eyelids and covers part of the outer surface of the eyeball; it ends at the edge of the cornea by fusing with the corneal epithelium.
- **Lacrimal apparatus.** The lacrimal apparatus consists of the lacrimal gland and a number of ducts that drain the lacrimal secretions into the nasal cavity.
- **Lacrimal glands**. The lacrimal glands are located above the lateral end of each eye; they continually release a salt solution (**tears**) onto the anterior surface of the eyeball through several small ducts.
- **Lacrimal canaliculi.** The tears flush across the eyeball into the **lacrimal canaliculi** medially, then into the **lacrimal sac**, and finally into the **nasolacrimal duct**, which empties into the nasal cavity.
- **Lysozyme.** Lacrimal secretion also contains antibodies and lysozyme, an enzyme that destroys bacteria; thus, it cleanses and protects the eye surface as it moistens and lubricates it.

- **Extrinsic eye muscle.** Six **extrinsic**, or **external**, **eye muscles** are attached to the outer surface of the eye; these muscles produce gross eye movements and make it possible for the eyes to follow a moving object; these are the **lateral rectus**, m**edial rectus**, **superior rectus**, **inferior rectus**, **inferior oblique**, and **superior oblique**.



Internal Structures: The Eyeball

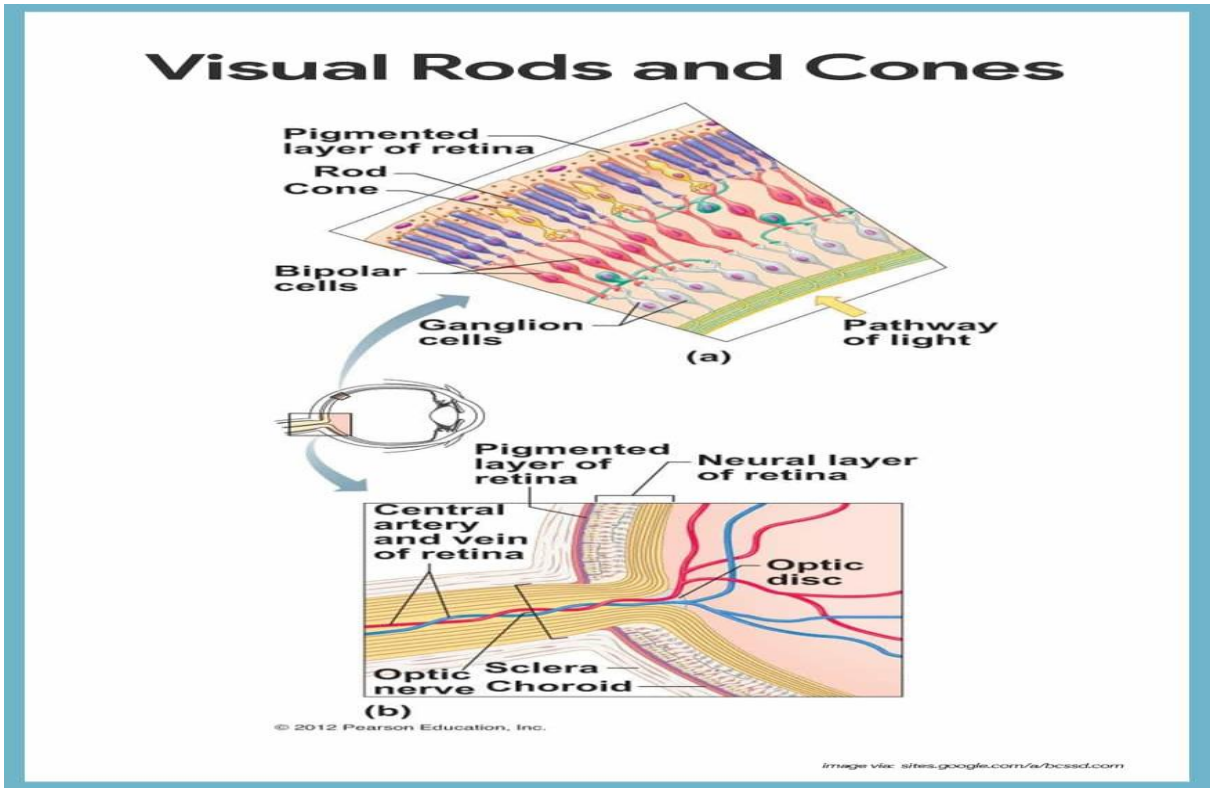
The eye itself, commonly called the eyeball, is a hollow sphere; its wall is composed of three layers, and its interior is filled with fluids called humors that help to maintain its shape.

Layers Forming the Wall of the Eyeball

Now that we have covered the general anatomy of the eyeball, we are ready to get specific.

- **Fibrous layer.** The outermost layer, called the fibrous layer, consists of the protective sclera and the transparent cornea.
- **Sclera.** The sclera, thick, glistening, white connective tissue, is seen anteriorly as the "white of the eye".
- **Cornea.** The central anterior portion of the fibrous layer is crystal clear; this "window" is the cornea through which light enters the eye.
- **Vascular layer.** The middle eyeball of the layer, the vascular layer, has three distinguishable regions: the **choroid**, the **ciliary body**, and the **iris**.
- **Choroid.** Most posterior is the choroid, a blood-rich nutritive tunic that contains a dark pigment; the pigment prevents light from scattering inside the eye.
- **Ciliary body.** Moving anteriorly, the choroid is modified to form two smooth muscle structures, the **ciliary body**, to which the lens is attached by a suspensory ligament called **ciliary zonule**, and then the **iris**.
- **Pupil.** The pigmented iris has a rounded opening, the pupil, through which light passes.
- **Sensory layer.** The innermost sensory layer of the eye is the delicate two-layered **retina**, which extends anteriorly only to the ciliary body.

- **Pigmented layer.** The outer pigmented layer of the retina is composed pigmented cells that, like those of the choroid, absorb light and prevent light from scattering inside the eye.
- **Neural layer.** The transparent inner neural layer of the retina contains millions of receptor cells, the **rods** and **cones**, which are called **photoreceptors** because they respond to light.
- **Two-neuron chain.** Electrical signals pass from the photoreceptors via a two-neuron chain-**bipolar cells** and then **ganglion cells**– before leaving the retina via **optic nerve** as nerve impulses that are transmitted to the optic cortex; the result is vision.
- **Optic disc.** The photoreceptor cells are distributed over the entire retina, except where the optic nerve leaves the eyeball; this site is called the **optic disc**, or **blind spot**.
- **Fovea centralis.** Lateral to each blind spot is the fovea centralis, a tiny pit that contains only cones.



Lens

Light entering the eye is focused on the retina by the lens, a flexible biconvex, crystal-like structure.

- **Chambers.** The lens divides the eye into two segments or chambers; the **anterior (aqueous) segment**, anterior to the lens, contains a clear, watery fluid called **aqueous humor**; the **posterior (vitreous) segment** posterior to the lens, is filled with a gel-like substance called either **vitreous humor**, or the vitreous body.
- **Vitreous humor.** Vitreous humor helps prevent the eyeball from collapsing inward by reinforcing it internally.
- **Aqueous humor.** Aqueous humor is similar to blood plasma and is continually secreted by a special of the choroid; it helps maintain intraocular pressure, or the pressure inside the eye.

- **Canal of Schlemm.** Aqueous humor is reabsorbed into the venous blood through the scleral venous sinus, or canal of Schlemm, which is located at the junction of the sclera and cornea.

Eye Reflexes

Both the external and internal eye muscles are necessary for proper eye function.

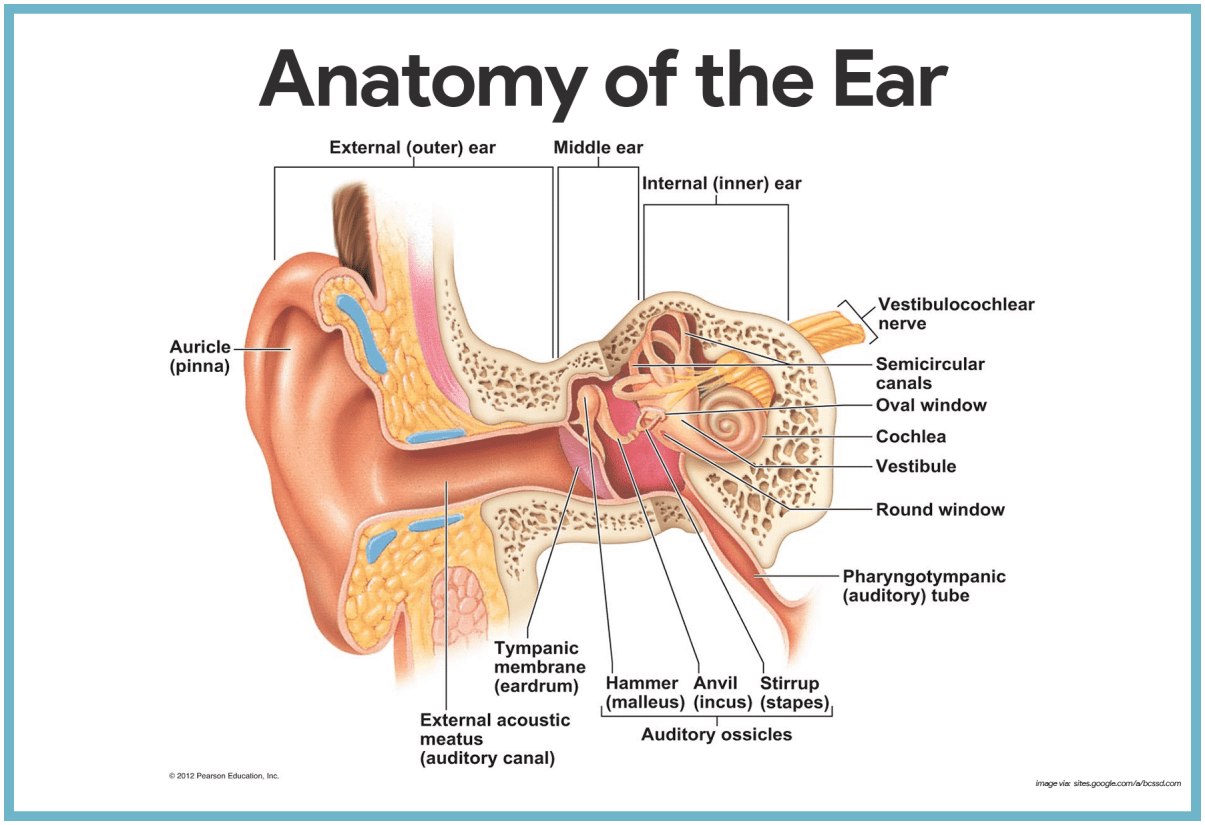
- **Photopupillary reflex.** When the eyes are suddenly exposed to bright light, the pupils immediately constrict; this is the photopupillary reflex; this protective reflex prevents excessively bright light from damaging the delicate photoreceptors.
- **Accommodation pupillary reflex.** The pupils also constrict reflexively when we view close objects; this accommodation pupillary reflex provides for more acute vision.

THE EAR: HEARING AND BALANCE

At first glance, the machinery for hearing and balance appears very crude.

Anatomy of the Ear

Anatomically, the ear is divided into three major areas: the external, or outer, ear; the middle ear, and the internal, or inner, ear.



External (Outer) Ear

The external, or outer, ear is composed of the auricle and the external acoustic meatus.

- **Auricle.** The auricle, or **pinna**, is what most people call the "ear"- the shell-shaped structure surrounding the auditory canal opening.
- **External acoustic meatus.** The external acoustic meatus is a short, narrow chamber carved into the temporal bone of the skull; in its skin-lined walls are the **ceruminous glands**, which secrete waxy, **yellow cerumen** or **earwax**, which provides a sticky trap for foreign bodies and repels insects.

- **Tympanic membrane.** Sound waves entering the auditory canal eventually hit the tympanic membrane, or **eardrum**, and cause it to vibrate; the canal ends at the ear drum, which separates the external from the middle ear.

Middle Ear

The middle ear, or tympanic cavity, is a small, air-filled, mucosa-lined cavity within the temporal bone.

- **Openings.** The tympanic cavity is flanked laterally by the eardrum and medially by a bony wall with two openings, the **oval window** and the inferior, membrane-covered **round window**.
- **Pharyngotympanic tube.** The pharyngotympanic tube runs obliquely downward to link the middle ear cavity with the throat, and the mucosae lining the two regions are continuous.
- **Ossicles.** The tympanic cavity is spanned by the three smallest bones in the body, the ossicles, which transmit the vibratory motion of the eardrum to the fluids of the inner ear; these bones, named for their shape, are the **hammer**, or **malleus**, the **anvil**, or **incus**, and the **stirrup**, or **stapes**.

Internal (Inner) Ear

The internal ear is a maze of bony chambers, called the **bony**, or **osseous**, **labyrinth**, located deep within the temporal bone behind the eye socket.

- **Subdivisions.** The three subdivisions of the bony labyrinth are the spiraling, pea-sized cochlea, the vestibule, and the semicircular canals.
- **Perilymph.** The bony labyrinth is filled with a plasma-like fluid called perilymph.
- **Membranous labyrinth.** Suspended in the perilymph is a membranous labyrinth, a system of membrane sacs that more or less follows the shape of the bony labyrinth.
- **Endolymph.** The membranous labyrinth itself contains a thicker fluid called endolymph.

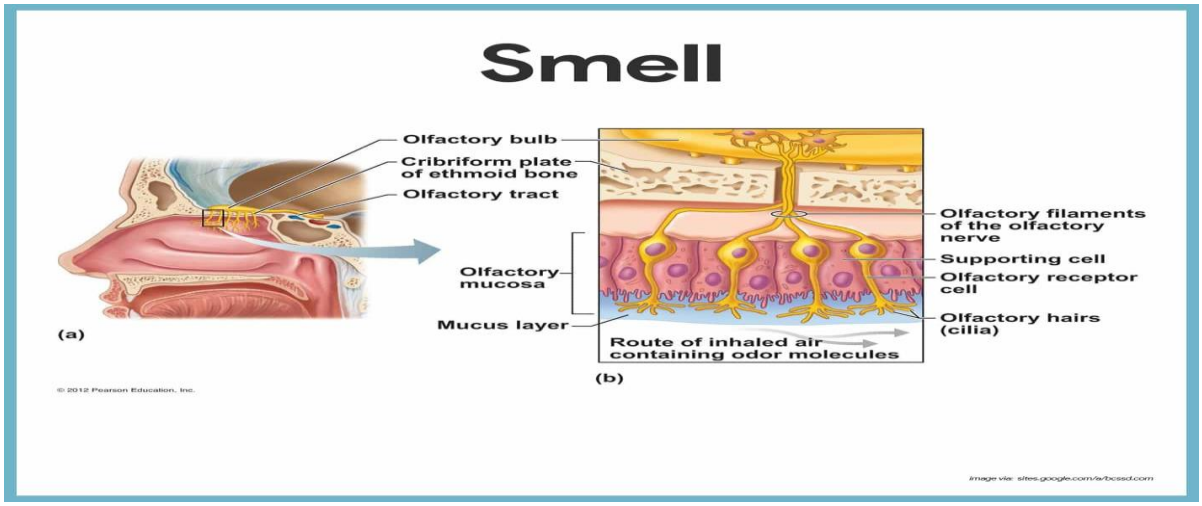
Chemical Senses: Taste and Smell

The receptors for taste and olfaction are classified as chemoreceptors because they respond to chemicals in solution.

Olfactory Receptors and the Sense of Smell

Even though our sense of smell is far less acute than that of many other animals, the human nose is still no slouch in picking up small differences in

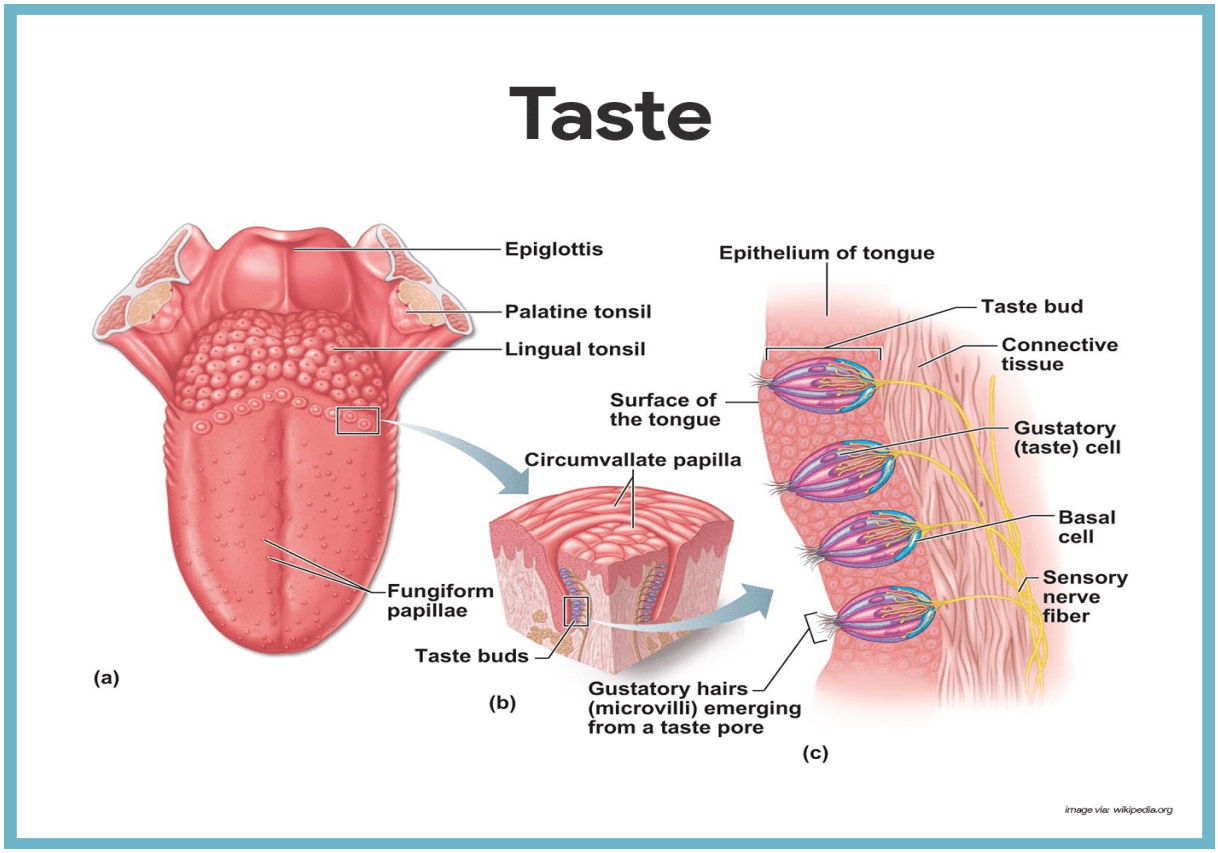
odors.



- **Olfactory receptors.** The thousands of olfactory receptors, receptors for the sense of smell, occupy a postage stamp-sized area in the roof of each nasal cavity.
- **Olfactory receptor cells.** The olfactory receptor cells are neurons equipped with **olfactory hairs**, long cilia that protrude from the nasal epithelium and are continuously bathed by a layer of mucus secreted by underlying glands.
- **Olfactory filaments.** When the olfactory receptors located on the cilia are stimulated by chemicals dissolved in the mucus, they transmit impulses along the olfactory filaments, which are bundled axons of olfactory neurons that collectively make up the olfactory nerve.
- **Olfactory nerve.** The olfactory nerve conducts the impulses to the olfactory cortex of the brain.

Taste Buds and the Sense of Taste

The word taste comes from the Latin word **taxare**, which means "to touch, estimate, or judge".



- **Taste buds.** The taste buds, or specific receptors for the sense of taste, are widely scattered in the oral cavity; of the 10, 000 or so taste buds we have, most are on the tongue.
- **Papillae.** The dorsal tongue surface is covered with small peg-like projections, or papillae.
- **Circumvallate and fungiform papillae.** The taste buds are found on the sides of the large round circumvallate papillae and on the tops of the more numerous fungiform papillae.

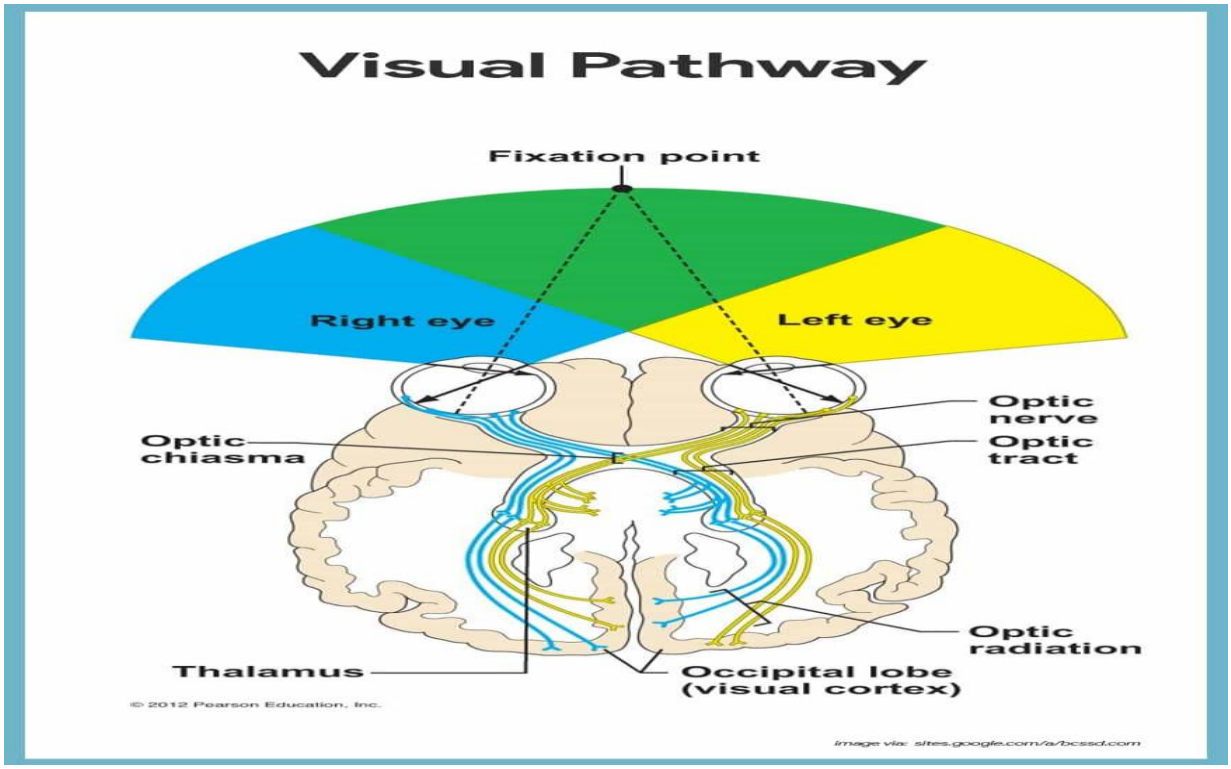
- **Gustatory cells.** The specific cells that respond to chemicals dissolved in the saliva are epithelial cells called gustatory cells.
- **Gustatory hairs.** Their long microvilli- the gustatory hairs- protrude through the taste pore, and when they are stimulated, they depolarize and impulses are transmitted to the brain.
- **Facial nerve.** The facial nerve (VII) serves the anterior part of the tongue.
- **Glossopharyngeal and vagus nerves.** The other two cranial nerves- the glossopharyngeal and vagus- serve the other taste bud-containing areas.
- **Basal cells.** Taste bud cells are among the most dynamic cells in the body, and they are replaced every seven to ten days by basal cells found in the deeper regions of the taste buds.

Physiology of the Special Senses

The processes that makes our special senses work include the following:

Pathway of Light through the Eye and Light Refraction

When light passes from one substance to another substance that has a different density, its speed changes and its rays are bent, or refracted.



- **Refraction.** The refractive, or bending, power of the cornea and humors is constant; however, that of the lens can be changed by changing its shape- that is, by making it more or less convex, so that light can be properly focused on the retina.
- **Lens.** The greater the lens convexity, or bulge, the more it bends the light; the flatter the lens, the less it bends the light.
- **Resting eye.** The resting eye is "set" for distant vision; in general, light from a distance source approaches the eye as parallel rays and the lens does not need to change shape to focus properly on the retina.
- **Light divergence.** Light from a close object tends to scatter and to diverge, or spread out, and the lens must bulge more to make close vision possible; to achieve this, the ciliary body contracts allowing the lens to become more convex.

- **Accommodation.** The ability of the eye to focus specifically for close objects (those less than 20 feet away) is called accommodation.
- **Real image.** The image formed on the retina as a result of the light-bending activity of the lens is a real image- that is, it is reversed from left to right, upside down, and smaller than the object.

Visual Fields and Visual Pathways to the Brain

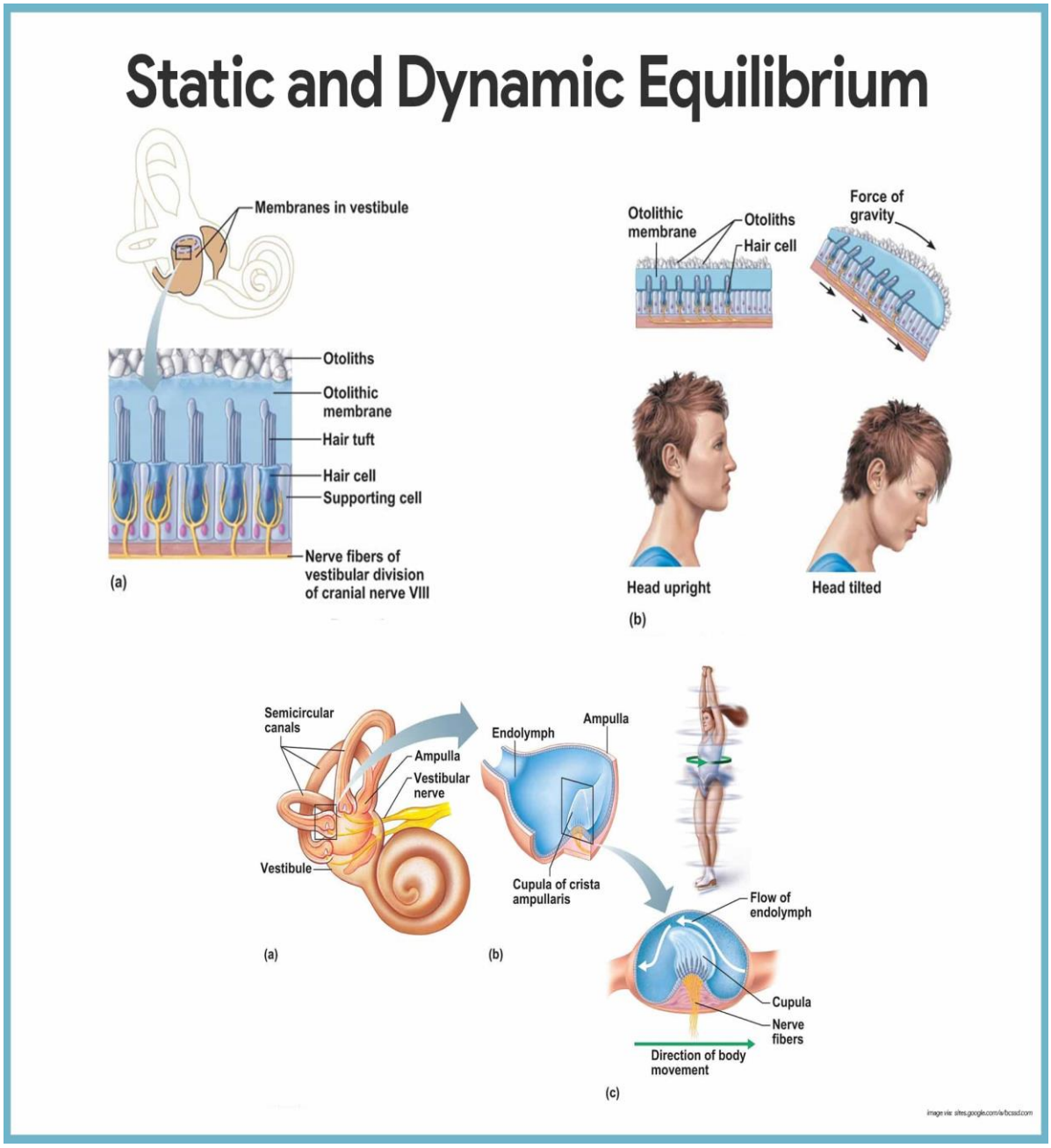
Axons carrying impulses from the retina are bundled together at the posterior aspect of the eyeball and issue from the back of the eye as the optic nerve.

- **Optic chiasma.** At the optic chiasma, the fibers from the medial side of each eye cross over to the opposite side of the brain.
- **Optic tracts.** The fiber tracts that result are the optic tracts; each optic tract contains fibers from the lateral side of the eye on the same side and the medial side of the opposite eye.
- **Optic radiation.** The optic tract fibers synapse with neurons in the thalamus, whose axons form the optic radiation, which runs to the occipital lobe of the brain; there they synapse with the cortical cells, and visual interpretation, or seeing, occurs.
- **Visual input.** Each side of the brain receives visual input from both eyes-from the lateral field of vision of the eye on its own side and from the medial field of the other eye.
- **Visual fields.** Each eye "sees" a slightly different view, but their visual fields overlap quite a bit; as a result of these two facts,

humans have binocular vision, literally "**two-eyed vision**" provides for depth perception, also called "**three-dimensional vision**" as our visual cortex fuses the two slightly different images delivered by the two eyes.

Mechanisms of Equilibrium

The equilibrium receptors of the inner ear, collectively called the vestibular apparatus, can be divided into two functional arms- one arm responsible for monitoring static equilibrium and the other involved with dynamic equilibrium.



Static Equilibrium

Within the membrane sacs of the vestibule are receptors called maculae that are essential to our sense of static equilibrium.

- **Maculae.** The maculae report on changes in the position of the head in space with respect to the pull of gravity when the body is not moving.

- **Otolithic hair membrane.** Each macula is a patch of receptor (hair) cells with their "hairs" embedded in the otolithic hair membrane, a jelly-like mass studded with **otoliths**, tiny stones made of calcium salts.
- **Otoliths.** As the head moves, the otoliths roll in response to changes in the pull of gravity; this movement creates a pull on the gel, which in turn slides like a greased plate over the hair cells, bending their hairs.
- **Vestibular nerve.** This event activates the hair cells, which send impulses along the vestibular nerve (a division of cranial nerve VIII) to the cerebellum of the brain, informing it of the position of the head in space.

Dynamic Equilibrium

The dynamic equilibrium receptors, found in the semicircular canals, respond to angular or rotatory movements of the head rather than to straight-line movements.

- **Semicircular canals.** The semicircular canals are oriented in the three planes of space; thus regardless of which plane one moves in, there will be receptors to detect the movement.
- **Crista ampullaris.** Within the ampulla, a swollen region at the base of each membranous semicircular canal is a receptor region called crista ampullaris, or simply crista, which consists of a tuft of hair cells covered with a gelatinous cap called the **cupula**.
- **Head movements.** When the head moves in an arclike or angular direction, the endolymph in the canal lags behind.

- **Bending of the cupula.** Then, as the cupula drags against the stationary endolymph, the cupula bends- like a swinging door- with the body's motion.
- **Vestibular nerve.** This stimulates the hair cells, and impulses are transmitted up the vestibular nerve to the cerebellum.

Mechanism of Hearing

The following is the route of sound waves through the ear and activation of the cochlear hair cells.

- **Vibrations.** To excite the hair cells in the **organ of Corti** in the inner ear, sound wave vibrations must pass through air, membranes, bone and fluid.
- **Sound transmission.** The cochlea is drawn as though it were uncoiled to make the events of sound transmission occurring there easier to follow.
- **Low frequency sound waves.** Sound waves of low frequency that are below the level of hearing travel entirely around the cochlear duct without exciting hair cells.
- **High frequency sound waves.** But sounds of higher frequency result in pressure waves that penetrate through the cochlear duct and basilar membrane to reach the scala tympani; this causes the basilar membrane to vibrate maximally in certain areas in response to certain frequencies of sound, stimulating particular hair cells and sensory neurons.
- **Length of fibers.** The length of the fibers spanning the basilar membrane tune specific regions to vibrate at specific frequencies; the higher notes- 20, 000 Hertz (Hz)- are detected by shorter hair cells along the base of the basilar membrane.

CARDIOVASCULAR SYSTEM

SYLLABUS

Heart-anatomy of heart, blood circulation, blood vessels, structure and functions of artery, vein and capillaries, elements of conduction system of heart and heart beat, its regulation by autonomic nervous system, cardiac output, cardiac cycle. Regulation of blood pressure, pulse, electrocardiogram and disorders of heart.

12.1 INTRODUCTION:

- The cardiovascular system (CVS) consists of the blood, the heart and blood vessels.
- For blood to reach body cells and exchange materials with them, it must be pumped continuously by the heart through the body's blood vessels.
- The heart beats about 100,000 times every day, which adds up to about 35 million beats in a year and approximately 2.5 billion times in an average lifetime. The left side of the heart pumps blood through blood vessels. The right side of the heart pumps blood through the lungs, enabling blood to pick up oxygen and unload carbon dioxide.
- This chapter contains the detail of structure of the heart and the unique properties that permit it to pump blood and disorders related to CVS.

12.2 ANATOMY OF HEART:

- The heart is a muscular organ about the size of a closed fist that functions as the body's circulatory pump.
- It takes in deoxygenated blood through the veins and delivers it to the lungs for oxygenation before pumping it into the various arteries.

- The heart is located in the thoracic cavity medial to the lungs and posterior to the sternum.
- On its superior end, the base of the heart is attached to the aorta, pulmonary arteries and veins and the vena cava. The inferior tip of the heart, known as the apex, rests just superior to the diaphragm.
- The base of the heart is located along the body's midline with the apex pointing toward the left side.
- Because the heart points to the left, about 2/3 of the heart's mass is found on the left side of the body and the other 1/3 is on the right.

12.2.1 LOCATION:

- The heart is relatively small, roughly about 12 cm (5 in.) long, 9 cm (3.5 in.) wide and 6 cm (2.5 in.) thick, with an average mass of 250 g (8 oz) in adult females and 300 g (10 oz) in adult males.
- The heart rests on the diaphragm, near the midline of the thoracic cavity.
- The heart lies in the mediastinum, an anatomical region that extends from the sternum to the vertebral column, from the first rib to the diaphragm and between the lungs.
- The pointed apex is formed by the tip of the left ventricle (a lower chamber of the heart) and rests on the diaphragm and it is directed anteriorly, inferiorly and to the left.
- The base of the heart is its posterior surface, is formed by the atria (upper chambers) of the heart, mostly the left atrium.
- In addition to the apex and base, the heart has several distinct surfaces and borders (margins).
- The anterior surface is deep to the sternum and ribs. The inferior surface is the part of the heart between the apex and right border and rests mostly on the diaphragm.

- The right border faces the right lung and extends from the inferior surface to the base.
- The left border, also called the pulmonary border, faces the left lung and extends from the base to the apex.

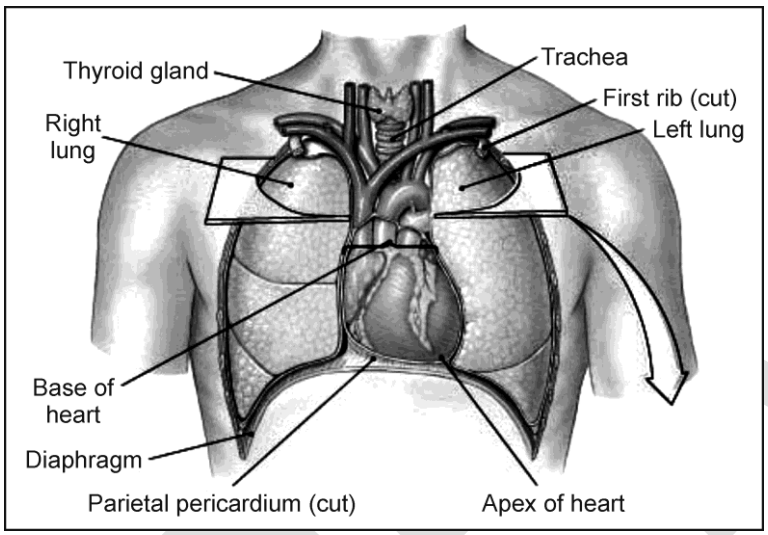


Fig. 12.2.1. Location of heart in thoracic cavity.

- Anterior view of chest cavity showing heart showing position of heart relative to lungs.

12.2.2 PERICARDIUM:

- The membrane that surrounds and protects the heart is the pericardium.
- It confines the heart to its position in the mediastinum, while allowing sufficient freedom of movement for vigorous and rapid contraction.
- The pericardium consists of two main parts:

(1) The Fibrous Pericardium:

- The superficial fibrous pericardium is composed of tough, inelastic, dense irregular connective tissues; its open end is fused to the connective tissues of the blood vessels entering and leaving the heart.

- The fibrous pericardium near the apex of the heart is partially fused to the central tendon of the diaphragm.
- It prevents overstretching of the heart, provides protection and anchors the heart in the mediastinum.

(2) The Serous Pericardium:

- The deeper serous pericardium is a thinner, more delicate membrane that forms a double layer around the heart.
- The outer parietal layer of the serous pericardium is fused to the fibrous pericardium.
- The inner visceral layer of the serous pericardium, also called the epicardium (one of the layers of the heart wall).
- Space between the parietal and visceral layers of the serous pericardium is called as pericardial cavity which contains a thin film of lubricating serous fluid, known as pericardial fluid which reduces friction between the layers of the serous pericardium as the heart moves.

12.2.3 LAYERS OF THE HEART WALL:

- The wall of the heart consists of three layers:

(1) Epicardium (external layer):

- It is composed of two tissue layers. The outermost is called the visceral layer of the serous pericardium, which is thin, transparent and composed of mesothelium.
- Beneath the mesothelium is a variable layer of delicate fibroelastic tissue and adipose tissue.
- The epicardium imparts a smooth, slippery texture to the outermost surface of the heart.
- The epicardium contains blood vessels, lymphatics and vessels that supply the myocardium.

(2) Myocardium (middle layer) :

- The middle myocardium is responsible for the pumping action of the heart and is composed of cardiac muscle tissue, makes up approximately 95% of the heart wall.
- The muscle fibers (cells), like those of striated skeletal muscle tissue, are wrapped and bundled with connective tissue sheaths composed of endomysium and perimysium.
- The cardiac muscle fibers are organized in bundles that swirl diagonally around the heart and generate the strong pumping actions of the heart.
- Although it is striated like skeletal muscle, but it is involuntary like smooth muscle.

(3) Endocardium (inner layer):

- It is thin innermost layer of the heart made up of endothelium overlying a thin layer of connective tissue.
- It provides a smooth lining for the chambers of the heart and covers the valves of the heart.
- The smooth endothelial lining minimizes the surface friction as blood passes through the heart.

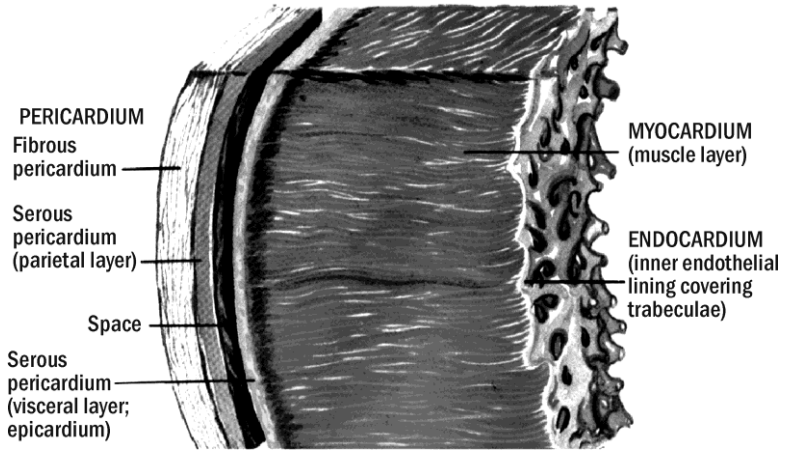


Fig.12.2.3 (2) Layers of heart wall.

- It consist of three layers :

(i) Epicardium : Outer wall joined with pericardium,

(ii) Myocardium : Middle contractile muscle,

(iii) Endocardium : innermost lining of heart wall and vessels.

12.2.4 CHAMBERS OF THE HEART:

- The heart has four chambers, two superior receiving chambers are the atria and the two inferior pumping chambers are the ventricles.
- On the anterior surface of each atrium is a wrinkled pouch like structure called an auricle which slightly increases the capacity of an atrium so that it can hold a greater volume of blood.
- Also on the surface of the heart are a series of grooves, called sulci, which contain coronary blood vessels and a variable amount of fat. Each sulcus marks the external boundary between two chambers of the heart.

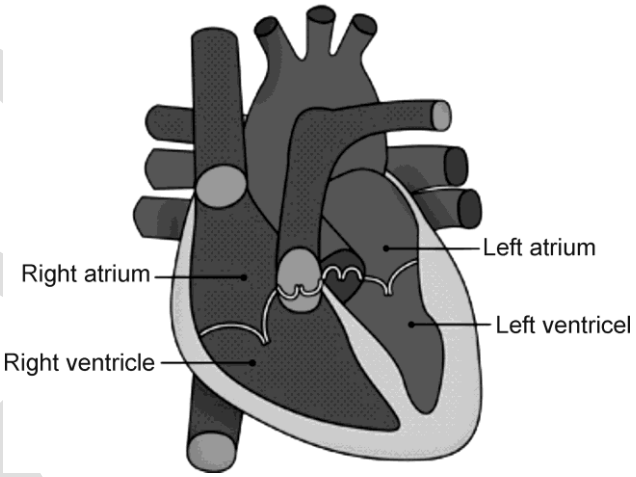


Fig. 12.2.4 (1) Chamber of the heart

Right Atrium :

- The right atrium forms the right border of the heart and receives blood from three veins: the superior vena cava, inferior vena cava and coronary sinus.
- The right atrium is about 2-3 mm (0.08-0.12 in.) in average thickness.
- The anterior and posterior walls of the right atrium are very different,

the inside of the posterior wall is smooth; the inside of the anterior wall is rough due to the presence of muscular ridges called pectinate muscles, which also extend into the auricle.

- Blood passes from the right atrium into the right ventricle through a valve that is called the tricuspid valve because it consists of three leaflets or cusps, also called the right atrioventricular valve.
- Between the right atrium and left atrium is a thin partition called the interatrial septum.
- A prominent feature of this septum is an oval depression called the fossa ovalis (the remnant of the foramen ovale), an opening in the interatrial septum of the fetal heart that normally closes soon after birth.

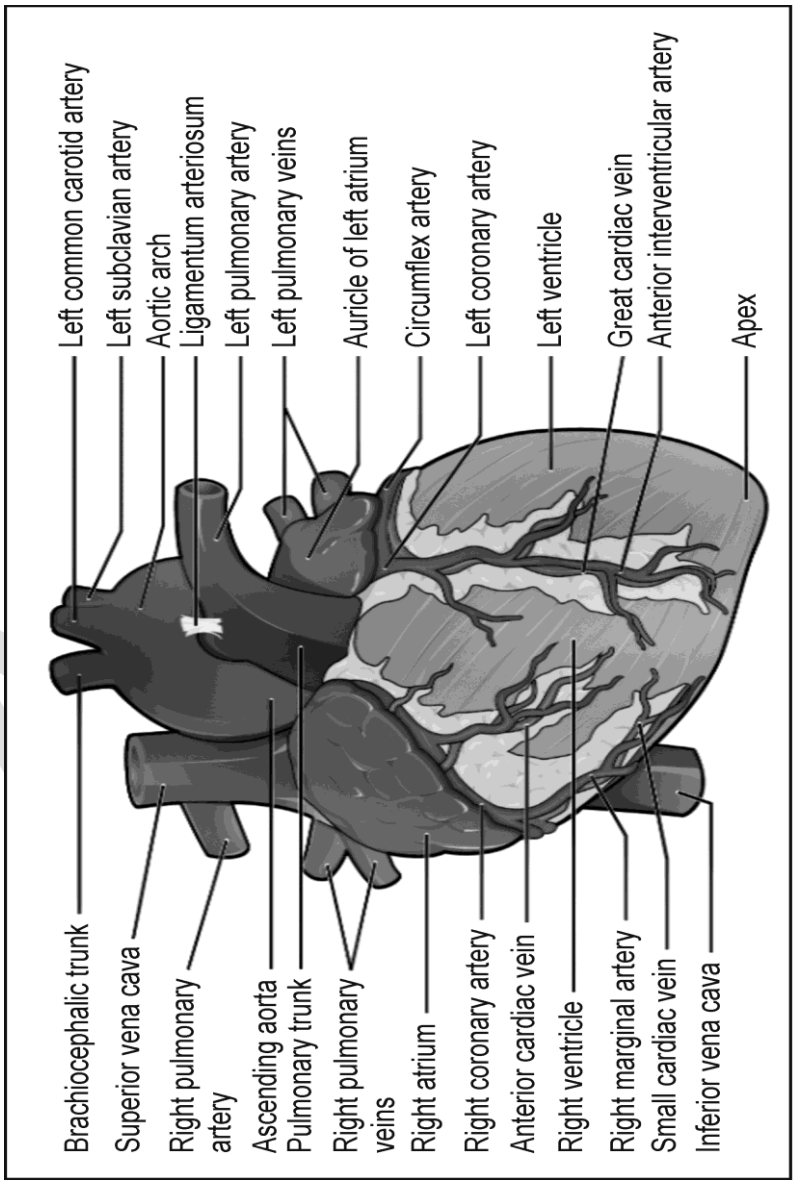
Right Ventricle :

- The right ventricle is about 4-5 mm (0.16-0.2 in.) in average thickness and forms most of the anterior surface of the heart.
- The inside of the right ventricle contains a series of ridges formed by raised bundles of cardiac muscle fibers called trabeculae carneae.
- Blood passes from the right ventricle through the pulmonary valve (pulmonary semilunar valve) into a large artery called the pulmonary trunk, which divides into right and left pulmonary arteries and carries blood to the lungs.
- The right ventricle is separated from the left ventricle by a partition called the interventricular septum.

Left Atrium :

- The left atrium is about the same thickness as the right atrium and forms most of the base of the heart.
- It receives blood from the lungs through four pulmonary veins.

- Like the right atrium, the inside of the left atrium has a smooth posterior wall and anterior wall.
- Blood passes from the left atrium into the left ventricle through the bicuspid (mitral) valve, which, as its name implies, has two cusps, also called as left atrioventricular valve.



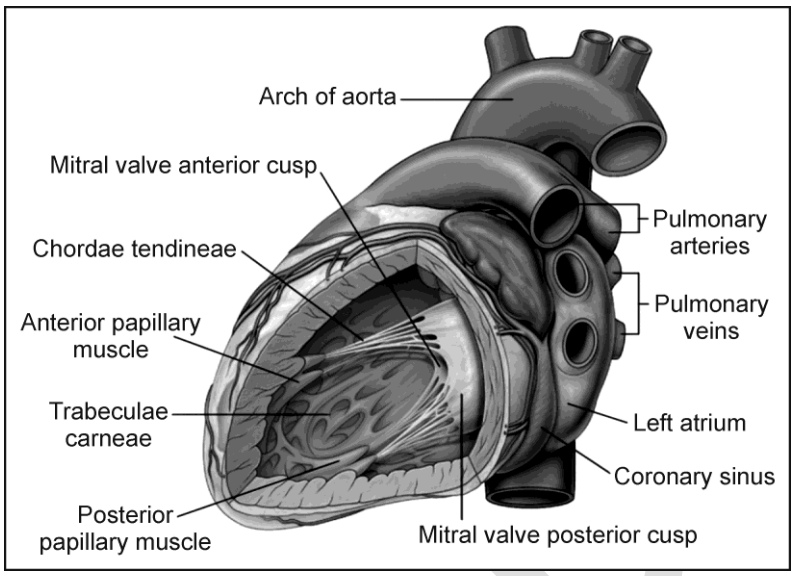


Fig. 12.2.4 (3) Interior view of the heart.

Left Ventricle :

- The left ventricle is the thickest chamber of the heart, averaging 10-15 mm (0.4-0.6 in.) and forms the apex of the heart
- Blood passes from the left ventricle through the aortic valve (aortic semilunar valve) into the ascending aorta.
- The blood into aorta flows into two branches- ascending aorta (carry blood to the heart wall) and descending aorta (thoracic aorta and abdominal aorta- carry blood throughout the body).
- During fetal life, a temporary blood vessel, called the ductus arteriosus, shunts blood from the pulmonary trunk into the aorta, normally closes shortly after birth, leaving a remnant known as the ligamentum arteriosum, which connects the arch of the aorta and pulmonary trunk.

12.2.5 HEART VALVES :

- As each chamber of the heart contracts, it pushes the blood into a ventricle or out of the heart into an artery, through the valves.
- Valves open and close in response to pressure changes at the time of contraction and relaxation.
- Each of the four valves helps ensure the one-way flow of blood by

opening to let blood through and then closing to prevent its backflow.

Operation of the Atrioventricular Valves :

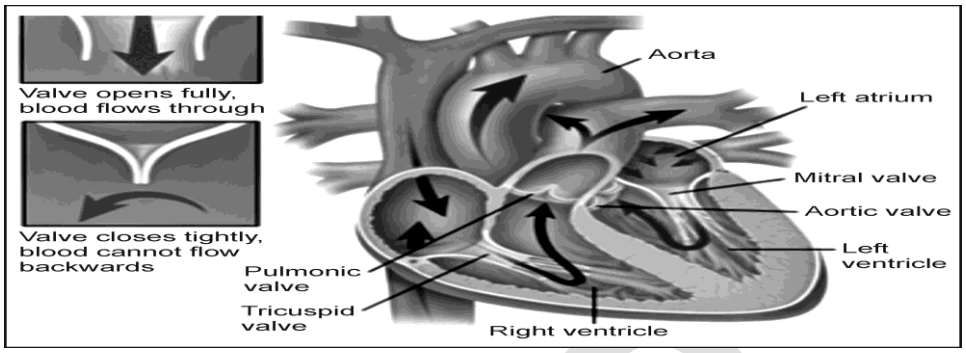


Fig. 12.2.5 Valves of the heat and working

- The tricuspid and bicuspid valves are termed atrioventricular (AV) valves, because they are located between an atrium and a ventricle.
- When an AV valve is open, the rounded ends of the cusps project into the ventricle.
- When the ventricles are relaxed, the papillary muscles are relaxed, the chordae tendineae are slack and blood moves from a higher pressure in the atria to a lower pressure in the ventricles through open AV valves.
- When the ventricles contract,the papillary muscles contract, which pulls on and tightens the chordae tendineae, the pressure of the blood drives the cusps upward until their edges meet and close the opening.
- This prevents the valve cusps from everting (opening into the atria) in response to the high ventricular pressure.

Operation of the Semilunar Valves :

- The aortic and pulmonary valves are known as the semilunar (SL) valves because they are made up of three crescent moon-shaped cusps.
- Each cusp attaches to the arterial wall by its convex outer margin.
- The SL valves allow ejection of blood from the heart into arteries but prevent backflow of blood into the ventricles.
- When the ventricles contract, pressure builds up within the chambers.
- The semilunar valves open when pressure in the ventricles exceeds the

pressure in the arteries, permitting ejection of blood from the ventricles into the pulmonary trunk and aorta.

- As the ventricles relax, blood starts to flow back toward the heart. This back flowing blood fills the valve cusps, which causes the free edges of the semilunar valves to contact each other tightly and close the opening between the ventricle and artery.
- Surprisingly, there are no valves guarding the junctions between the venae cavae and the right atrium or the pulmonary veins and the left atrium.

12.2.6 CARDIAC MUSCLE TISSUE :

- Compared with skeletal muscle fibers, cardiac muscle fibers are shorter in length and less circular in transverse section, it also exhibit branching.
- A typical cardiac muscle fiber is 50-100 μm long and has a diameter of about 14 μm.
- Usually one centrally located nucleus is present, although an occasional cell may have two nuclei.
- The ends of cardiac muscle fibers connect to neighboring fibers by irregular transverse thickenings of the sarcolemma called intercalated discs.
- The discs contain desmosomes, which hold the fibers together and gap junctions, which allow muscle action potentials to conduct from one muscle fiber to its neighbors.
- Gap junctions allow the entire myocardium of the atria or the ventricles to contract as a single, coordinated unit.
- Mitochondria are larger and more numerous in cardiac muscle fibers

than in skeletal muscle fibers.

- Cardiac muscle fibers have the same arrangement of act in and myosin and the same bands, zones and Z discs, as skeletal muscle fibers.
- The transverse tubules of cardiac muscle are wider but less abundant than those of skeletal muscle; the one transverse tubule per sarcomere is located at the Z disc.
- The sarcoplasmic reticulum of cardiac muscle fibers is somewhat smaller than the SR of skeletal muscle fibers, as a result, cardiac muscle has a smaller intracellular reserve of $Ca2^{+}$.

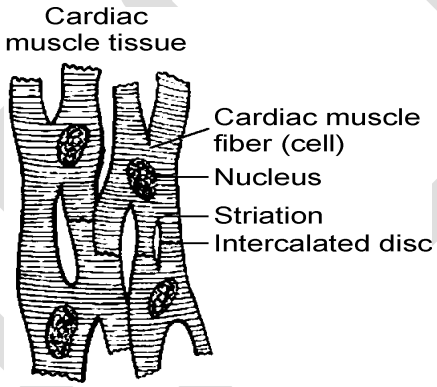


Fig.12.2.6 (b) Cardiac muscle fibre-consist of myofibrils and intercalated disc.

12.3 BLOOD CIRCULATION:

- In postnatal (after birth) circulation, the heart pumps blood into two closed circuits with each beat-systemic circulation and pulmonary circulation.
- The two circuits are arranged in series. The output of one becomes the input of the other.

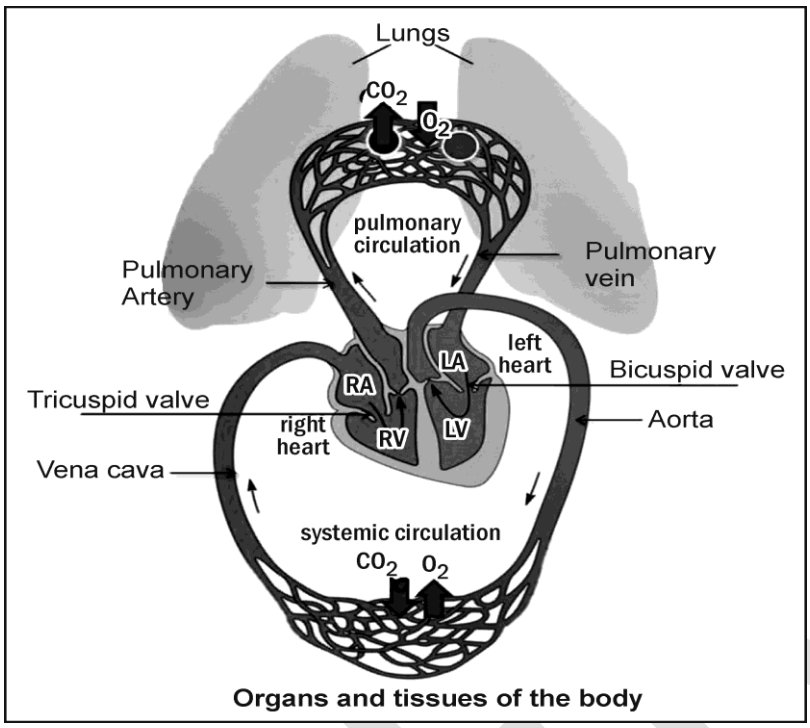


Fig. 12.3 Blood circulation through the heart. RA- Right atrium, RV- Right ventricle, LA- Left atrium, LV- Left ventricle.

12.3.1 SYSTEMIC CIRCULATION :

- The left side of the heart is the pump for systemic circulation; it receives bright red oxygenated (oxygen-rich) blood from the lungs.
- The left ventricle ejects blood into the aorta. From the aorta, the blood divides into separate streams, entering progressively smaller systemic arteries that carry it to all organs throughout the body except for the air sacs (alveoli) of the lungs.
- In systemic tissues, arteries give rise to smaller-diameter arterioles which finally lead into extensive beds of systemic capillaries.
- Exchange of nutrients and gases occurs across the thin capillary walls. Blood unloads O_2 (oxygen) and picks up CO_2 (carbon dioxide).
- In most cases, blood flows through only one capillary and then enters a systemic venule. Venules carry deoxygenated (oxygen-poor) blood away from tissues and merge to form larger systemic veins, ultimately the blood flows back to the right atrium.

12.3.2 PULMONARY CIRCULATION :

- The right side of the heart is the pump for pulmonary circulation; it receives all the dark-red deoxygenated blood returning from the systemic circulation.
- Blood ejected from the right ventricle flows into the pulmonary trunk, which branches into pulmonary arteries that carry blood to the right and left lungs (see Fig.12.3).
- In pulmonary capillaries, blood unloads CO_2, which is exhaled and picks up O_2 from inhaled air. The freshly oxygenated blood then flows into pulmonary veins and returns to the left atrium.

12.3.3 CORONARY CIRCULATION:

- Nutrients are not able to diffuse quickly enough from blood in the chambers of the heart to supply all the layers of cells that make up the heart wall.
- For this reason, the myocardium has its own network of blood vessels, the coronary or cardiac circulation.
- The coronary arteries branch from the ascending aorta and encircle the heart like a crown encircles the head.
- While the heart is contracting, little blood flows in the coronary arteries because they are squeezed shut.
- When the heart relaxes, however, the high pressure of blood in the aorta propels blood through the coronary arteries, into capillaries and then into coronary veins.

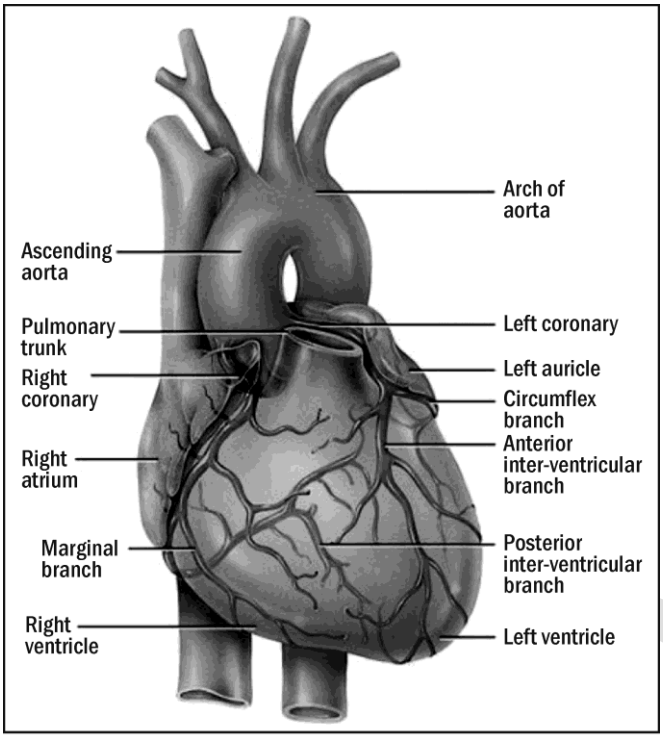


Fig. 12.3.3 (1) Anterior view of coronary arteries- coronary arteries branch from the ascending aorta. 595 596

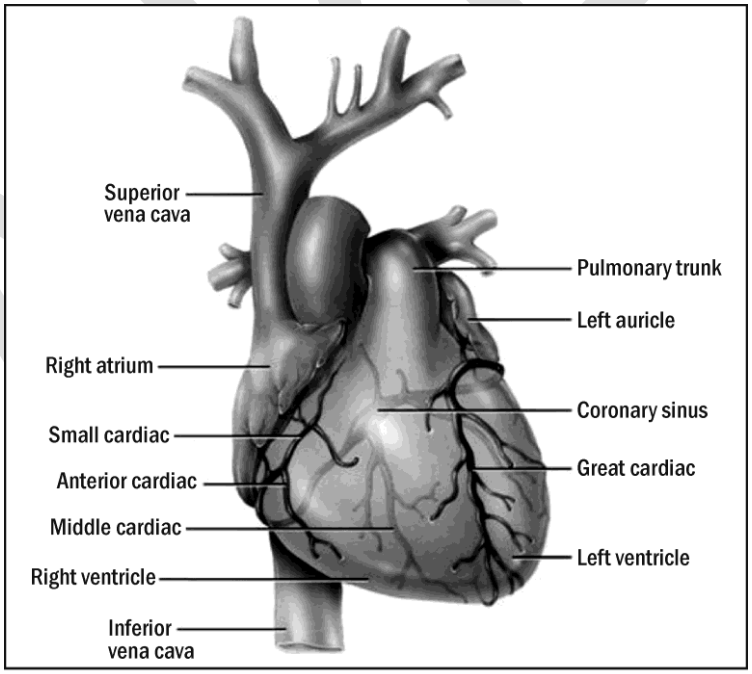


Fig. 12.3.3 (2) Anterior view of coronary veins-aorta propels blood through the coronary arteries, into capillaries followed by coronary vein.

Coronary Arteries :

- Two coronary arteries, the right and left coronary arteries, branch from the ascending aorta and supply oxygenated blood to the myocardium.

(i) Left coronary artery : The left coronary artery passes inferior to the left auricle and divides into the anterior interventricular and circumflex branches. The anterior interventricular branch or Left Anterior Descending (LAD) artery supplies oxygenated blood to the walls of both ventricles. The circumflex branch distributes oxygenated blood to the walls of the left ventricle and left atrium.

(ii) Right coronary artery : The right coronary artery supplies small branches (atrial branches) to the right atrium and it continues inferior to the right auricle and ultimately divides into the posterior interventricular (supplies the walls of the two ventricles with oxygenated blood) and marginal branches (supplies oxygenated blood to the myocardium of the right ventricle).

- Most parts of the body receive blood from branches of more than one artery and where two or more arteries supply the same region. These connections, called an astomoses, provide alternate routes, called collateral circulation, for blood to reach a particular organ or tissue.
- They provide detours for arterial blood if a main route becomes obstructed. Thus, heart muscle may receive sufficient oxygen even if one of its coronary arteries is partially blocked.

Coronary Capillaries :

After blood passes through the arteries of the coronary circulation, it flows into capillaries, where it delivers oxygen and nutrients to the heart muscle and collects carbon dioxide and waste.

Coronary Veins :

- After passing through capillaries the blood then moves into coronary veins.
- Most of the deoxygenated blood from the myocardium drains into a large vascular sinus (a thin walled vein that has no smooth muscle to

alter its diameter) in the coronary sulcus on the posterior surface of the heart, called the coronary sinus.

- The deoxygenated blood in the coronary sinus empties into the right atrium.
- The principal tributaries carrying blood into the coronary sinus are the following:

(i) Great cardiac veins : It drains the areas of heart supplied by the left coronary artery (left and right ventricles and left atrium).

(ii) Middle cardiac vein : It drains the areas supplied by the posterior interventricular branch of the right coronary artery (left and right ventricles).

(iii) Small cardiac vein: It drains the right atrium and right ventricle.

(iv) Anterior cardiac veins : It which drain the right ventricle and open directly into the right atrium.

12.4 BLOOD VESSELS:

The five main types of blood vessels are arteries, arterioles, capillaries, venules and veins.

12.4.1 STRUCTURE AND FUNCTIONS OF BLOOD VESSELS:

(1) Arteries :

The wall of an artery has 3 coats or tunics :

(i) Tunica interna (tunica intima) : This innermost coat contains a lining of simple squamous epithelium called endothelium a basement membrane and a layer of elastic tissue called the internal elastic lamina. Tunia interna is closest to the lumen (hollow center) through which blood flows.

(ii) Tunica media : This middle coat is usually the thickest layer. It consist

of elastic fibers and smooth muscle fibers that extend circularly around the lumen. It also has an external elastic lamina composed of elastic tissue. Arteries, thus, have high compliance (stretch without tearing in response to a small increase in pressure).

(iii) Tunica externa :

- It is composed mainly of elastic and collagen fibers.
- Sympathetic neurons of the ANS are distributed to the smooth muscle of the tunia media; their stimulation typically stimulates the smooth muscle to constrict, causing vasoconstriction.
- Depending upon the size they are termed as :

(a) Elastic (conducting) arteries :

- These are the large arteries (diameter > 1 cm); they leave the heart.
- Tunica media of elastic arteries contains a high proportion of elastic fibers.
- Elastic arteries function as a pressure reservoir, helping blood to propel onward. Thus, blood continues to move through the arteries even while the ventricles are relaxed.
- The example of elastic or conducting arteries are the aorta, the brachio-cephalic, common carotid, subclavian, vertebral, pulmonary and common iliac arteries.

(b) Muscular (distributing) arterie :

- These are the medium sized arteries (0.1-10 mm in diameter). Their tunica media contains more smooth muscle and fewer elastic lamina fibres than elastic arteries.
- They are capable of greater vasoconstriction and vasodilation to adjust the rate of blood flow.
- These relatively thick-walled arteries have a thin internal elastic lamina

and a prominent external elastic lamina.

- Muscular arteries (or distributing arteries) distribute blood to various parts of the body.
- Examples include the brachial artery in the arm and radial artery in the forearm.

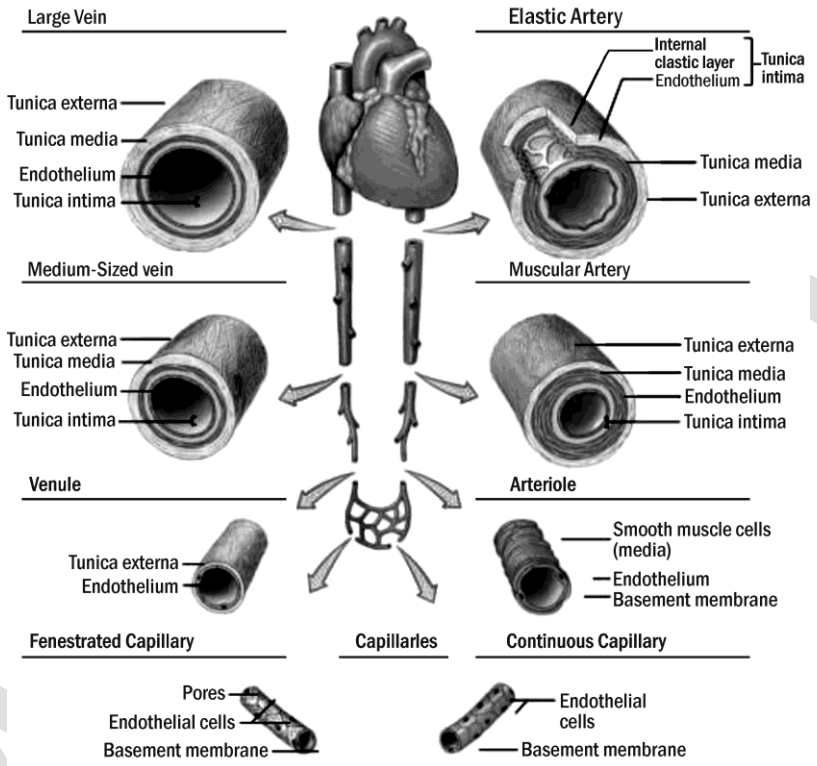


Fig. 12.4.1 Structure of different types of blood vessels

(2) Arteriole :

- An arteriole delivers blood to capillaries.
- Their tunica media is composed of smooth muscle and very few elastic fibers.
- Arterioles are known as resistance vessels because contraction and relaxation of the smooth muscle in arteriole walls can change their diameter.
- Vasoconstriction of arterioles increases vascular resistance and decreases blood flow in capillaries. It also increases blood pressure.

- Vasodilation decreases vascular resistance and increases blood flow; it also decreases blood pressure.

(3) Capillaries :

- Arterioles are branch out into numerous tiny vessels called capillaries.
- The flow of blood from arterioles to venules through capillaries is called microcirculation. High metabolizing tissues (e.g. muscles, the liver, the kidneys and the nervous system) have extensive capillary networks as compared to low metabolizing tissues (e.g. tendons and ligaments).
- Capillaries are absent in a few tissues, e.g. all covering and lining epithelia, the cornea, lens of the eye and cartilage.
- Presence of only a single layer of endothelial cells and a basement membrane (absence of tunica media and tunica externa) and large surface area makes the capillaries suitable for rapid exchange of materials with the interstitial fluid of tissues.
- A network of 10-100 capillaries is called a capillary bed. Precapillary sphincters regulate the flow of blood through capillary beds.
- Three different types of capillaries in the body are :

(i) Continuous capillaries : They have intercellular clefts (gaps between neighbouring endothelial cells) and are found in skeletal and smooth muscle, connective tissues and the lungs.

(ii) Fenestrated capillaries : These (porous; pores 70-100 nm in diameter) are found in kidneys, villi of the small intestine, choroid plex uses of the ventricles in the brain and some endocrine glands.

(iii) Sinusoids : These are wider than fenestrations, with incomplete or absent basement membrane and very large intercellular clefts, are found in the liver, red bone marrow, spleen and some endocrine glands.

(4) Venules :

- Several capillaries unite to form venules (little veins); they collect blood from capillaries and deliver it to veins. These are 10-100 μm in diameter.
- Smallest venules consist of endothelial tunica interna and a tunica media with a few scattered muscle fibers. Their porous wall permits many phagocytic WBCs to migrate from the blood stream into the inflamed or infected tissue.
- Larger venules contain the tunica externa.

(5) Veins :

- The tunica interna of veins is thinner and the tunica media is much thinner than those of arteries. These are 0.1 mm > 1 mm in diameter.
- The tunica extema of veins is the thickest layer and consists of collagen and elastic fibres.
- Veins lack the external or internal elastic laminae found in arteries.
- Many veins, especially those in the limbs, have valves (flap like cusps of tunica interna).
- The valve cusps project into the lumen, pointing towards the heart. The valves aid in venous return by preventing the back flow of blood.
- A vascular (venous) sinus is a vein with thin endothelial wall that has no smooth muscle to alter its diameter.
- The surrounding dense connective tissue replaces the tunica media and tunica extema in providing support, e.g. dural venous sinuses and the coronary sinus.

(6) Anastamoses :

- The union of branches of two or more arteries supplying the same body region is called an anastamoses.
- Anastamoses provide alternative routes for blood to reach a tissue or organ. It is known as collateral circulation.

- Anastomoses may also occur between veins and between arterioles and venules. Obstruction of an end artery blocks theblood supply to a whole segment of an organ, producing necrosis (death) of that segment.

12.5 THE CONDUCTION SYSTEM OF HEART:

- An inherent and rhythmical electrical activity is the reason for the heart's lifelong beat.
- The source of this electrical activity is a network of specialized cardiac muscle fibers called autorhythmic fibers.
- Autorhythmic fibers repeatedly generate action potentials that trigger heart contractions, thus act as a pacemaker, setting the rhythm of electrical excitation that causes contraction of the heart.
- They form the cardiac conduction system, a network of specialized cardiac muscle fibers that provide a path for each cycle of cardiac excitation to progress through the heart.
- The conduction system ensures that cardiac chambers become stimulated to contract in a coordinated manner, which makes the heart an effective pump.

12.5.1 COMPONENTS OF CARDIAC CONDUCTING SYSTEM:

The components of cardiac conducting system consist of SA node, AV node and AV bundle and Purkinje fibres.

(1) Sinus (Sinoatrial) Node :

- The sinus node (also called sinoatrial node) is a small, flattened, ellipsoid strip of specialized cardiac muscle about 3 mm wide, 15 mm long and 1 mm thick.
- It is located in the superior posterolateral wall of the right atrium immediately below and slightly lateral to the opening of the superior vena cava.

- The sinus nodal fibers connect directly with the atrial muscle fibers so that any action potential that begins in the sinus node spreads immediately into the atrial muscle wall.

(2) Atrioventricular (AV) Node :

- The A-V node is located in the posterior wall of the right atrium immediately behind the tricuspid valve.
- The atrial conductive system is organized so that the cardiac impulse does not travel from the atria into the ventricles too rapidly; this delay allows time for the atria to empty their blood into the ventricles before ventricular contraction begins.

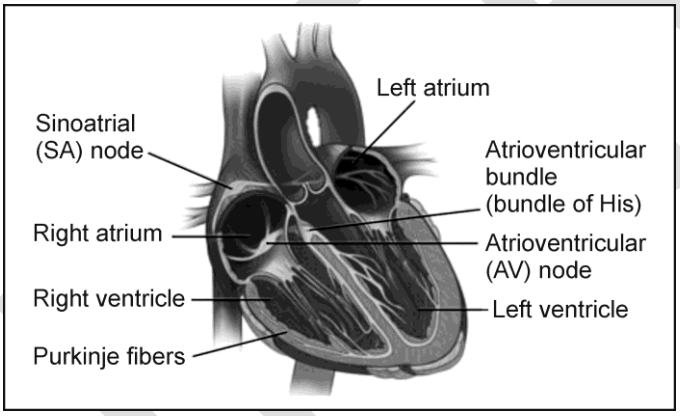


Fig. 12.5.1 Components of conducting system of heart.

(3) Atrioventricular (AV) bundle (bundle of His) :

- AV node, plus its connections with the entering atrial internodal pathway fibers and the exiting A-V bundle.
- A final delay of another 0.04 second occurs mainly in this penetrating A-V bundle, which is composed of multiple small fascicles passing through the fibrous tissue separating the atria from the ventricles.
- The slow conduction in the transitional, nodal and penetrating A-V bundle fibers is caused mainly by diminished numbers of gap junctions between successive cells in the conducting pathways, so there is great resistance to conduction of excitatory ions from one conducting fiber to the next.

(4) Purkinje Fibers :

- After penetrating the fibrous tissue between the atrial and ventricular muscle, the distal portion of the A-V bundle passes downward in the ventricular septum for 5 to 15 mm toward the apex of the heart.
- Then the bundle divides into left and right bundle branches that lie beneath the endocardium on the two respective sides of the ventricular septum. Each branch spreads downward toward the apex of the ventricle, progressively dividing into smaller branches.
- These branches in turn course sidewise around each ventricular chamber and back toward the base of the heart.
- The ends of the purkinje fibers penetrate about one third of the way into the muscle mass and finally become continuous with the cardiac muscle fibers.
- From the time the cardiac impulse enters the bundle branches in the ventricular septum until it reaches the terminations of the purkinje fibers, the total elapsed time averages only 0.03 second.
- Therefore, once the cardiac impulse enters the ventricular Purkinje conductive system, it spreads almost immediately to the entire ventricular muscle mass.

12.5.2 PROPAGATION OF ACTION POTENTIALS:

Cardiac action potentials propagate through the conduction system in the following sequence :

(1) Cardiac excitation normally begins in the sinoatrial (SA) node. SA node cells repeatedly depolarize to threshold spontaneously (a pacemaker potential). When the pacemaker potential reaches threshold, it triggers an action potential. Each action potential from the SA node propagates throughout both atria via gap junctions in the intercalated discs of atrial muscle fibres. Following the action potential, two atria contract at the

same time.

(2) By conducting along atrial muscle fibers, the action potential reaches the atrioventricular (AV) node. At the AV node, the action potential slows considerably as a result of various differences in cell structure in the AV node. This delay provides time for the atria to empty their blood into the ventricles.

(3) From the AV node, the action potential enters the atrioventricular (AV) bundle. This bundle is the only site where action potentials can conduct from the atria to the ventricles.

(4) After propagating along the AV bundle, the action potential enters both the right and left bundle branches. The bundle branches extend through the interventricular septum toward the apex of the heart.

(5) Finally, the purkinje fibers rapidly conduct the action potential beginning at the apex of the heart upward to the remainder of the ventricular myocardium. Then the ventricles contract, pushing the blood upward toward the semilunar valves.

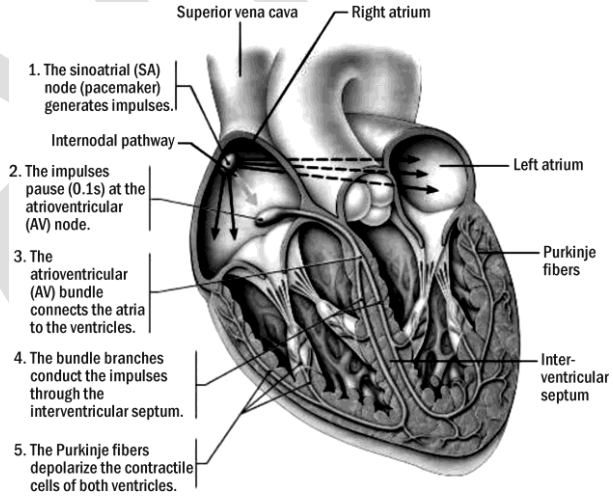


Fig. 12.5.2 Cardiac action potential propagation through different components of conducting system

- On their own, autorhythmic fibers in the SA node would initiate an action potential about every 0.6 second or 100 times per minute.

- Thus, the SA node sets the rhythm for contraction of the heart it is the natural pacemaker. This rate is faster than that of any other autorhythmic fibers.
- Nerve impulses from the autonomic nervous system (ANS) and blood-borne hormones (such as epinephrine) modify the timing and strength of each heartbeat, but they donot establish the fundamental rhythm.

12.5.3 ACTION POTENTIAL AND CONTRACTION OF CONTRACTILE FIBERS:

- The action potential initiated by the SA node travels along the conduction system and spreads out to excite the and ventricular muscle fibers, called contractile fibers.
- An action potential occurs in a contractile fiber as follows:

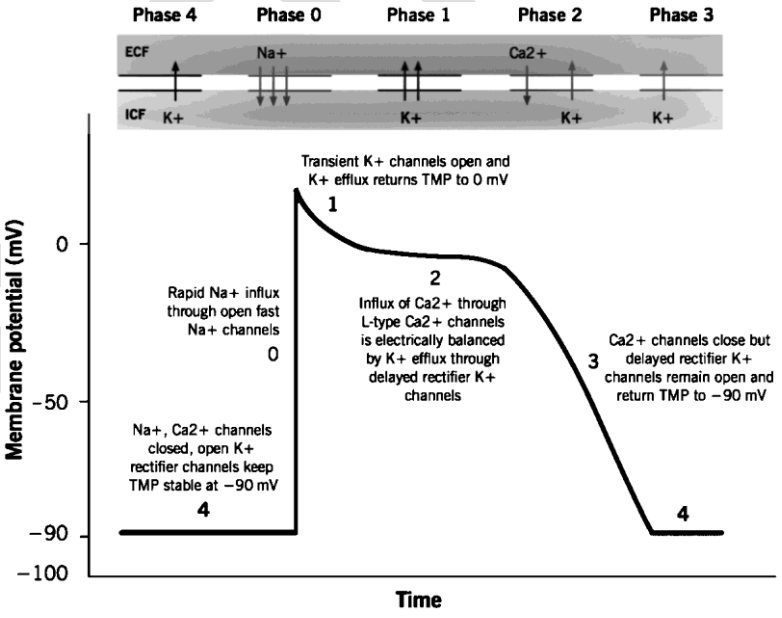


Fig. 12.5.3 Cardiac action potential. ECF- Extracellular fluid, ICF- Intracellular fluid, TMP Threshold membrane potential

(1) Depolarization :

- Unlike autorhythmic fibers, contractile fibers have a stable resting membrane potential that is close to – 90 mV.

- When a contractile fiber is brought to threshold by an action potential from neighbouring fibers, its voltage-gated fast Na^+ channels open. These sodium ion channels are referred to as "fast" because they open very rapidly in response to a threshold-level depolarization.
- Opening of these channels allows Na^+ inflow, which down the electrochemical gradient produces a rapid depolarization (Phase 0).
- Within a few milliseconds, the fast Na^+ channels automati-cally inactivate and Na^+ inflow decreases.

(2) Plateau :

- The next phase of an action potential is the plateau, a period of maintained depolarization. It is due in part to opening of voltage-gated slow Ca^{2+} channels in the sarcolemma (Phase 2).
- When these channels open, calcium ions move from the interstitial fluid which causes even more Ca^{2+} to pour out of the sarcoplasmic reticulum into the cytosol through additional Ca^{2+} channels in the sarcoplasmic reticulum membrane.
- The increased Ca^{2+} concentration in the cytosol ultimately triggers contraction.
- Several different types of voltage-gated K^+ channels are also found in the sarcolemma of a contractile fiber.
- Just before the plateau phase begins, some of these K^+ channels open, allowing potassium ions to leave the contractile fiber. (Phase 1).
- Therefore, depolarization is sustained during the plateau phase because Ca^{2+} inflow just balances K^+ outflow.
- The plateau phase lasts for about 0.25 sec and the membrane potential of the contractile fiber is close to 0 mV.

(3) Repolarization :

- The recovery of the resting membrane potential during the repolarization phase of a cardiac action potential resembles that in other excitable cells.
- After a delay (which is particularly prolonged in cardiac muscle), additional voltage-gated K^+ channels open.
- Outflow of K^+ restores the negative resting membrane potential (–90 mV) (Phase 3).
- At the same time, the calcium channels in the sarcolemma and the sarcoplasmic reticulum are closing, which also contributes to repolarization.

(4) Refractory period :

- In muscle, the refractory period is the time interval during which a second contraction cannot be triggered (Phase 4). The refractory period of a cardiac muscle fiber lasts longer than the contraction itself.
- As a result, another contraction cannot begin until relaxation is well under way. For this reason, tetanus (maintained contraction) cannot occur in cardiac muscle as it can in skeletal muscle.

(5) Mechanism of contraction :

- As Ca^{2+} concentration rises inside a contractile fiber, Ca^{2+} binds to the regulatory protein troponin, which allows the actin and myosin filaments to begin sliding past one another and tension starts to develop.
- Substances that alter the movement of Ca^{2+} through slow Ca^{2+} channels influence the strength of heart contractions. Epinephrine, for example, increases contraction force by enhancing Ca^{2+} flow into the cytosol.

12.6 CARDIAC CYCLE:

A single cardiac cycle includes all the events associated with one heartbeat. Thus, a cardiac cycle consists of systole and diastole of the atria and the ventricles.

12.6.1 PHASES OF THE CARDIAC CYCLE :

- In each cardiac cycle, the atria and ventricles alternately contract and relax, forcing blood from areas of higher pressure to areas of lower pressure.
- As a chamber of the heart contracts, blood pressure within it increases.
- Figure shows the relation between the heart's electrical signals (ECG) and changes in atrial pressure, ventricular pressure, aortic pressure and ventricular volume during the cardiac cycle.
- When heart rate is 75 beats/min, a cardiac cycle lasts 0.8 sec.
- The different phases of the cardiac cycle are :

(1) Atrial systole :

- During atrial systole the atria are contracting. At the same time, the ventricles are relaxed and it lasts about 0.1 sec.
- Depolarization of the SA node causes atrial depolarization, marked by the P wave in the ECG.
- Atrial depolarization causes atrial systole. As the atria contract, they exert pressure on the blood within, which forces blood through the open AV valves into the ventricles.
- Atrial systole contributes a final 25 mL of blood to the volume already in each ventricle (about 105 mL). The end of atrial systole is also the end of ventricular diastole (relaxation).
- Thus, each ventricle contains about 130 mL at the end of its relaxation period (diastole). This blood volume is called the End-Diastolic Volume (EDV).

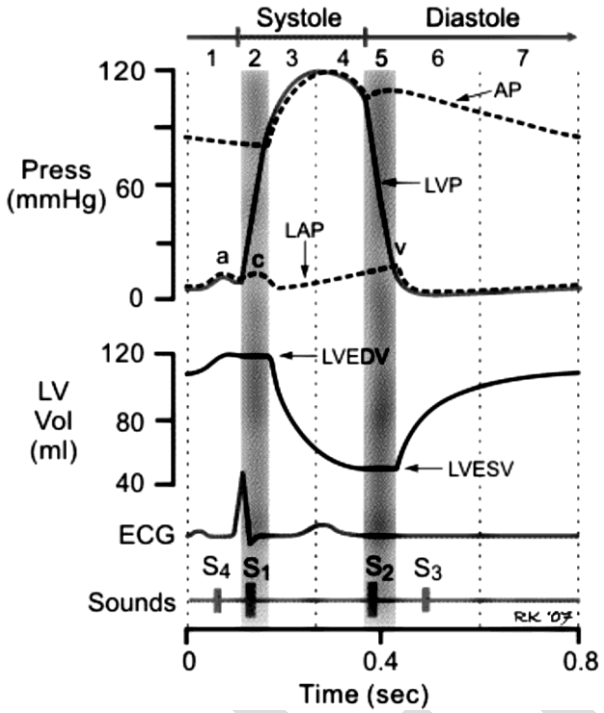


Fig. 12.6.1 (1) Pressure and volume changes during cardiac cycle. LAP- left atrial pressure, LVP- left ventricular pressure, LVEDV- left ventricular end diastolic volume.

(2) Ventricular Systole :

- During ventricular systole the ventricles are contracting. At the same time, the atria are relaxed in atrial diastole and it which lasts about 0.3 sec. The QRS complex in the ECG marks the onset of ventricular depolarization.
- Ventricular depolarization causes ventricular systole. As ventricular systole begins, pressure rises inside the ventricles and pushes blood up against the atrioventricular (AV) valves, forcing them shut. Last for about 0.05 seconds. This is the period of isovolumetric contraction. During this interval, the muscle contraction is isometric (same length) and ventricular volume remains the same (isovolumic).
- Continued contraction of the ventricles increases the pressure inside the chambers, when left ventricular pressure surpasses aortic pressure (about 80mmHg) and right ventricular pressure rises above the pressure in the pulmonary trunk (about 20 mmHg), both SL valves open, which ejects the blood from the heart. The period lasts for about 0.25 sec.

- The left ventricle ejects about 70 mL of blood into the aorta and the right ventricle ejects the same volume of blood into the pulmonary trunk. The volume remaining in each ventricle at the end of systole, about 60 mL, is the end-systolic volume (ESV).
- Stroke volume (SV), the volume ejected per beat from each ventricle, equals end-diastolic volume minus end-systolic volume :

  SV = EDV – ESV

  At rest, the stroke volume is about (130 mL - 60 mL) 70 mL.

(3) Relaxation Period :

During the relaxation period the atria and the ventricles are both relaxed and it lasts about 0.4 sec. The T wave in the ECG marks the onset of ventricular repolarization.

- Ventricular repolarization causes ventricular diastole. As the ventricles relax, pressure within the chambers falls, thus the blood in the aorta and pulmonary trunk begins to flow backward which closes the SL valves. After the SL valves close, there is a brief interval when ventricular blood volume does not change, this is the period of isovolumetric relaxation.
- As the ventricles continue to relax, the pressure falls quickly. When ventricular pressure drops below atrial pressure, the AV valves open and ventricular filling begins.
- The major part of ventricular filling occurs just after the AV valves open. At the end of the relaxation period, the ventricles are about three-quarters full. The P wave appears in the ECG, signalling the start of another cardiac cycle.

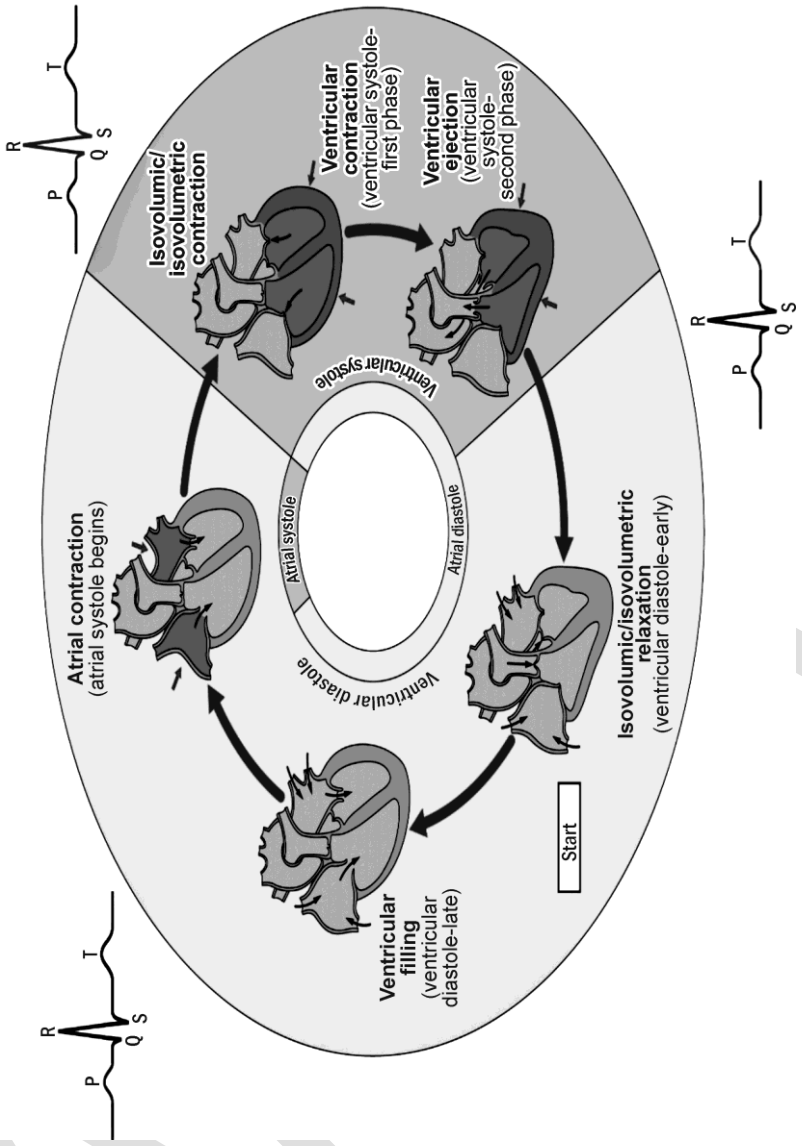


Fig. 12.6.1 (2) Different phases of the cardiac cycle

12.6.2 CORRELATION OF ECG WAVES WITH ATRIAL AND VENTRICULAR SYSTOLE :

- The term systole refers to the phase of contraction; the phase of relaxation is diastole.
- The ECG waves predict the timing of atrial and ventricular systole and diastole :

(1) A cardiac action potential arises in the SA node and it propagates throughout the atrial muscle and down to the AV node in about 0.03 sec. As the atrial contractile fibers depolarize, the P wave appears in the ECG.

After the P wave begins, the atria contract (atrial systole).

(2) Conduction of the action potential slows at the AV node because the fibers at this place have much smaller diameters and fewer gap junctions and thus the resulting 0.1 sec delay gives the atria time to contract.

(3) About 0.2 sec after onset of the P wave, the action potential propagates through the bundle branches, Purkinje fibers and the entire ventricular myocardium, producing the QRS complex due to progressive depolarization. At the same time, atrial repolarization is occurring, but it is not usually evident in an ECG because the larger QRS complex masks it.

(4) Contraction of ventricular contractile fibers (ventricular systole) begins shortly after the QRS complex appears and continues during the S-T segment.

(5) Repolarization of ventricular contractile fibers begins at the apex and spreads throughout the ventricular myocardium. This produces the T wave in the ECG about 0.4 sec after the onset of the P wave.

(6) Shortly after the T wave begins, the ventricles start to relax (ventricular diastole). By 0.6 sec, ventricular repolarization is complete and ventricular contractile fibers are relaxed.

- During the next 0.2 sec, contractile fibers in both the atria and ventricles are relaxed. At 0.8 sec, the P wave appears again in the ECG, the atria begin to contract and the cycle repeats.

12.6.3 HEART SOUNDS :

- The sound of the heartbeat comes primarily from blood turbulence caused by the closing of the heart valves.
- During each cardiac cycle, there are four heart sounds, but in a normal heart only the first and second heart sounds (S1 and S2) are loud enough

to be heard through a stethoscope. The timing of heart sounds relative to other events in the cardiac cycle.

- The first sound (S1), which can be described as a lubb sound, is louder and a bit longer, which is caused by blood turbulence associated with closure of the AV valves soon after ventricular systole begins.
- The second sound (S2), which is shorter and not as loud as the first, can be described as a dupp sound, caused by blood turbulence associated with closure of the SL valves at the beginning of ventricular diastole.
- Normally not loud enough to be heard, S3 is due to blood turbulence during rapid ventricular filling and S4 is due to blood turbulence during atrial systole.
- Heart sounds provide valuable information about the mechanical operation of the heart.
- A heart murmur is an abnormal sound consisting of a clicking, rushing or gurgling noise that either is heard before, between or after the normal heart sounds or may mask the normal heart sounds, which indicates a valve disorder.

12.7 CARDIAC OUTPUT (CO) :

- Cardiac Output (CO) is the volume of blood ejected from the left ventricle (or the right ventricle) into the aorta (or pulmonary trunk) each minute.
- Cardiac output equals the stroke volume(SV) multiplied by the Heart Rate (HR), the number of heartbeats per minute :

  CO (mL/min) = SV (mL/beat) X HR (beats/min)
- In a typical resting adult male, stroke volume averages 70 mL/ beat and heart rate is about 75 beats/min. Thus, average cardiac output is 5.25 L/min.

12.8 REGULATION OF STROKE VOLUME AND HEART RATE :

- ~~Factor~~s that increase stroke volume or heart rate normally increase CO.
- Cardiac reserve is the difference between a person's maximum cardiac output and cardiac output at rest. The average person has a cardiac reserve of four or five times the resting value. People with severe heart disease may have little or no cardiac reserve.

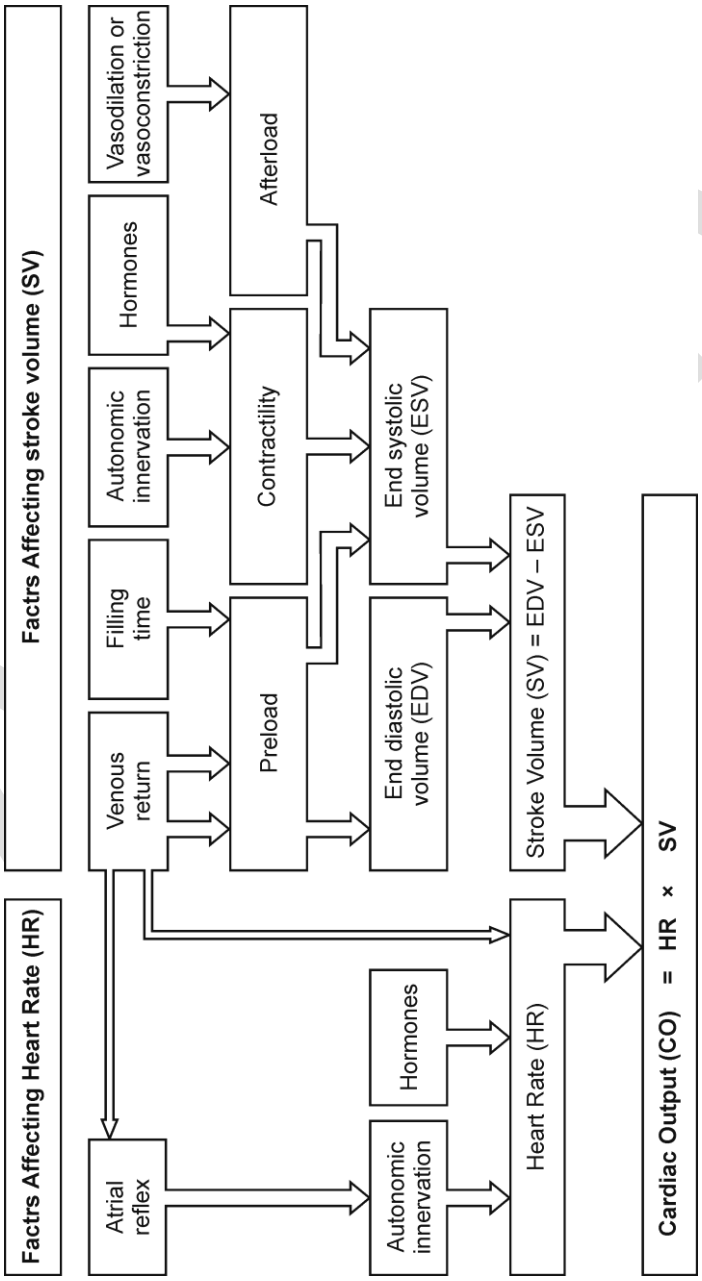


Fig. 12.8 Factors affecting cardiac output

12.8.1 REGULATION OF STROKE VOLUME :

Three factors regulating stroke volume are as follows :

(1) Preload (the degree of stretch on the heart before it contracts).

- The preload is proportional to the End-Diastolic Volume (EDV). Normally, the greater the EDV, the more forceful the next contraction.
- A greater preload (stretch) on cardiac muscle fibers prior to contraction increases their force of contraction. Within limits, the more the heart fills with blood during diastole, the greater the force of contraction during systole. This relationship is known as the Frank-Starling law of the heart. The Frank-Starling law of the heart equalizes the output of the right and left ventricles and keeps the same volume of blood flowing to both the systemic and pulmonary circulations.
- If the left side of the heart pumps a little more blood than the right side, the volume of blood returning to the right ventricle (venous return) increases. The increased EDV causes the right ventricle to contract more forcefully on the next beat, bringing the two sides back into balance.

- **Two key factors determine EDV :**

(a) The duration of ventricular diastole : When heart rate increases, the duration of diastole is shorter means a smaller EDV and the ventricles may contract before they are adequately filled.

(b) Venous return : It is the volume of blood returning to the right ventricle, when venous return increases, a greater volume of blood flows into the ventricles and the EDV is increased.

(2) Contractility (the forcefulness of contraction of individual ventricular muscle fiber) :

- The second factor that influences stroke volume is myocardial contractility, the strength of contraction at any given preload.

- Positive inotropic substance (substances that increase contra-ctility), promote Ca^{2+} inflow during cardiac action potentials, which strengthens the force of the next contraction.
- Stimulation of the sympathetic division of the autonomic nervous system (ANS), hormones such as epinephrine and norepinephrine, increased Ca^{2+} level in the interstitial fluid and the drug digitalis all have positive inotropic effects.
- In contrast, inhibition of the sympathetic division of the ANS, anoxia, acidosis, some anaesthetics and increased K^{+} level in the interstitial fluid have negative inotropic effects.

(3) Afterload (the pressure that must be exceeded before ejection of blood from the ventricles can occur) :

- The pressure that must be overcome before a semilunar valve can open is termed the afterload.
- An increase in afterload causes stroke volume to decrease, so that more blood remains in the ventricles at the end of systole.
- Conditions that can increase afterload include hypertension (elevated blood pressure) and narrowing of arteries by atherosclerosis.

12.8.2 REGULATION OF HEART RATE :

- Adjustments in heart rate are important in the short-term control of cardiac output and blood pressure.
- The sinoatrial (SA) node initiates contraction and, if left to itself, would set a constant heart rate of about 100 beats/min.
- However, tissues require different volumes of blood flow under different conditions. During exercise, for example, cardiac output rises to supply working tissues with increased amounts of oxygen and nutrients. Stroke volume may fall if the ventricular myocardium is damaged or if blood volume is reduced by bleeding. In these cases,

homeostatic mechanisms maintain adequate cardiac output by increasing the heart rate and contractility.

- Among the several factors that contribute to regulation of heart rate, the most important are the autonomic nervous system and hormones released by the adrenal medullae (epinephrine and norepinephrine).

(1) Autonomic Regulation of Heart Rate :

- Nervous system regulation of the heart originates in the cardiovascular center in the medulla oblongata, it receives input from a variety of sensory receptors and from higher brain centres, such as the limbic system and cerebral cortex.
- The cardiovascular center then directs appropriate output by increasing or decreasing the frequency of nerve impulses in both the sympathetic and parasympathetic branches of the ANS.
- Sensory receptors that provide input to the cardiovascular center include :

(i) Proprioceptor (major stimulus for the quick rise in heart rate that occurs at the onset of physical activity).

(ii) Chemoreceptors : Monitor chemical changes in the blood.

(iii) Baroreceptors :

- Monitor the stretching of major arteries and veins caused by the pressure of the blood, Located in the arch of the aorta and in the carotid arteries.
- Before physical activity begins, especially in competitive situations, heart rate may climb. This anticipatory increase occurs because the limbic system sends nerve impulses to the cardiovascular center in the medulla.
- As physical activity begins, proprioceptors that are moni-toring the position of limbs and muscles send nerve impulses at an increased

frequency to the cardiovascular center.

Regulation by sympathetic system :

- Sympathetic neurons extend from the medulla oblongata into the spinal cord. From the thoracic region of the spinal cord, sympathetic cardiac accelerator nerves extend out to the SA node, AV node and most portions of the myocardium.
- Impulses in the cardiac accelerator nerves trigger the release of norepinephrine, which binds to beta-1 (β1) receptors on cardiac muscle fibers.
- This interaction has two separate effects:

(i) In SA (and AV) node fibers, norepinephrine speeds the rate of spontaneous depolarization so that these pacemakers fire impulses more rapidly and heart rate increases.

(ii) In contractile fibers throughout the atria and ventricles, norepinephrine enhances Ca^{2+} entry through the voltage-gated slow Ca^{2+} channels, thereby increasing contractility. As a result, a greater volume of blood is ejected during systole.

- With a moderate increase in heart rate, stroke volume does not decline because the increased contractility offsets the decreased preload.
- With maximal sympathetic stimulation, however, heart rate may reach 200 beats/min in a 20-year old person. At such a high heart rate, stroke volume is lower than at rest due to the very short filling time.

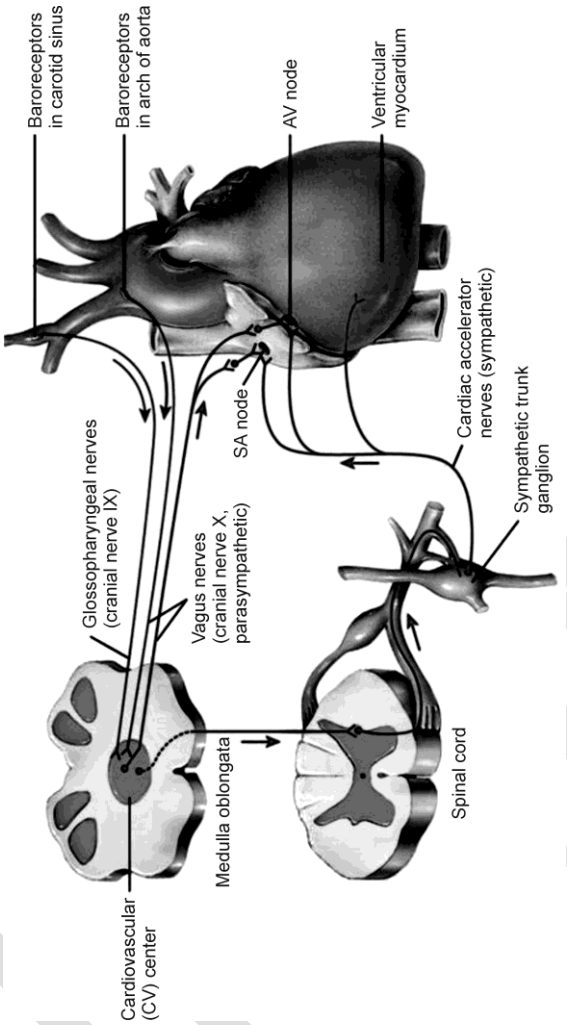


Fig. 12.8.2 Autonomic Regulation of Heart Rate

Regulation by parasympathetic system :

(i) Parasympathetic nerve impulses reach the heart via the right and left vagus (X) nerves.

(ii) Vagal axons terminate in the SA node, AV node and atrial myocardium.

(iii) They release acetylcholine, which decreases heart rate by slowing the rate of spontaneous depolarization in autorhythmic fibers.

(iv) As only a few vagal fibers innervate ventricular muscle, changes in parasympathetic activity have little effect on contractility of the ventricles.

- A continually shifting balance exists between sympathetic and parasympathetic stimulation of the heart.

- At rest, parasympathetic stimulation predominates. The resting heart rate-about 75 beats/min-is usually lower than the autorhythmic rate of the SA node (about 100 beats/min). With maximal stimulation by the parasympathetic division, the heart can slow to 20 or 30 beats/min or can even stop momentarily.

(2) Chemical Regulation of Heart Rate :

- Certain chemicals influence both the basic physiology of cardiac muscle and the heart rate. For example, hypoxia (lowered oxygen level), acidosis (low pH) and alkalosis (high pH) all depress cardiac activity.
- Several hormones and cations have major effects on the heart :

(i) Hormone :

- Epinephrine and norepinephrine (from the adrenal medullae) enhance the heart's pumping effectiveness. These hormones increase both heart rate and contractility. Exercise, stress and excitement cause the adrenal medullae to release more hormones.
- Thyroid hormones also enhance cardiac contractility and increase heart rate. One sign of hyperthyroidism (excessive thyroid hormone) is tachycardia, an elevated resting heart rate.

(ii) Cations :

- Intracellular and extracellular concentrations of several cations (for example, Na^+ and K^+) are important for action potentials in all nerve and muscle fibers, as a result the relative concentrations of three cations – K^+, Ca^{2+} and Na^+ have a large effect on cardiac function.
- Elevated blood levels of K^+ or Na^+ decrease heart rate and contractility.
- Excess Na^+ blocks Ca^{2+} inflow during cardiac action potentials, thereby decreasing the force of contraction, whereas excess K^+ blocks generation of action potentials.

  A moderate increase in interstitial (and thus intracellular) Ca^{2+} level

speeds heart rate and strengthens the heartbeat.

(3) Other Factors in Heart Rate Regulation :

- Age, gender, physical fitness and body temperature also influence resting heart rate.
- A newborn baby is likely to have a resting heart rate over 120 beats/min; the rate then gradually declines throughout life.
- Adult females often have slightly higher resting heart rates than adult males, although regular exercise tends to bring resting heart rate down in both sexes.
- A physically fit person may even exhibit bradycardia, a resting heart rate under 50 beats/min. This is a beneficial effect of endurance-type training because a slowly beating heart is more energy efficient than one that beats more rapidly.
- Increased body temperature, as occurs during a fever or strenuous exercise, causes the SA node to discharge impulses more quickly, thereby increasing heart rate. Decreased body temperature decreases heart rate and strength of contraction, because it slows metabolism, which reduces the oxygen needs of the tissues, allowing the heart and brain to withstand short periods of interrupted or reduced blood flow during the procedure.

12.9 HEMODYNAMICS :

- Hemodynamics is the dynamics of blood flow.
- Hemodynamics ultimately begins with the heart which supplies the driving force for all blood flow in the body.
- Cardiac output propels blood through the arteries and veins as a function of ventricular contraction.

- Ventricular motion results from the shortening of cardiac myocytes concentrically. This squeezing motion is translated into the cardiac output which is a function of both heart rate and ejection fraction (the starting volume after diastolic filling minus the final ventricular volume after systole).
- Hemodynamics represents the governing principles of this blood flow and its behaviour in the blood vessels.

12.9.1 BLOOD FLOW :

- Blood flow is the volume of blood that flows through any tissue in a given time period (in mL/min). Total blood flow is cardiac output (CO), the volume of blood that circulates through systemic (or pulmonary) blood vessels each minute.
- The cardiac output becomes distributed into circulatory routes that serve various body tissues depends on two more factors :

(i) The pressure difference that drives the blood flow through a tissue.

(ii) The resistance to blood flow in specific blood vessels.

- Blood flows from regions of higher pressure to regions of lower pressure; the greater the pressure difference, the greater the blood flow.

12.9.2 BLOOD PRESSURE:

- Blood pressure (BP) is the hydrostatic pressure exerted by blood on the walls of a blood vessel.
- Contraction of the ventricles generates blood pressure.
- BP is determined by cardiac output, blood volume and vascular resistance.
- Systolic blood pressure is the highest pressure attained in arteries during systole and diastolic blood pressure is the lowest arterial pressure during diastole.

- As blood leaves the aorta and flows through the systemic circulation, its pressure falls progressively as the distance from the left ventricle increases.
- Mean Arterial Pressure (MAP) is the average blood pressure in arteries and is roughly one-third of the way between the diastolic and systolic pressures.

  It can be estimated as follows :

  MAP = diastolic BP + 1/3 (systolic BP - diastolic BP)
- Thus, in a person whose BP is 110/70 mmHg, MAP is about 83 mmHg [70 + 1/3(110 -70)].
- Another way to calculate cardiac output is to divide mean arterial pressure (MAP) by resistance (R) :

  CO = MAP/R

12.9.3 VASCULAR RESISTANCE :

- Vascular resistance is the opposition to blood flow due to friction between blood and the walls of blood vessels.
- Vascular resistance depends on following factors:

(i) Size of the lumen :

Resistance is inversely proportional to the fourth power of the diameter (d) of the blood vessel's lumen (R 1/d4). The smaller the lumen of a blood vessel, the greater its resistance to blood flow.

(ii) Blood viscosity :

The viscosity of blood depends mostly on the ratio of red blood cells to plasma (fluid) volume and to a smaller extent on the concentration of proteins in plasma. The higher the blood's viscosity, the higher the resistance.

(iii) Total blood vessel length :

Resistance to blood flow through a vessel is directly proportional to the length of the blood vessel. The longer a blood vessel, the greater the resistance.

(iv) Total Peripheral Resistance (TPR) :

Also known as Systemic vascular resistance (SVR), refers to all the vascular resistances offered by systemic blood vessels. The smallest vessels-arterioles, capillaries and venules-contribute the most resistance.

12.9.4 VENOUS RETURN :

- It is the volume of blood flowing back to the heart through the systemic veins, occurs due to the pressure generated by contractions of the heart's left ventricle.
- Besides the heart, two other mechanisms "pump" blood from the lower body back to the heart and it depend on the presence of valves in veins.

The skeletal muscle pumps :

(i) While we are standing at rest, both the proximal valve (venous valve closer to the heart) and the distal valve (one farther from the heart in this part of the leg) are open and blood flows upward toward the heart. Contraction of leg muscles, compresses the vein which pushes blood through the proximal valve, an action called milking. At the same time, the distal valve in the uncompressed segment of the vein closes as some blood is pushed against it.

(i) Just after muscle relaxation, pressure falls in the previously compressed section of vein, which causes the proximal valve to close. The distal valve now opens because blood pressure in the foot is higher than in the leg and the vein fills with blood from the foot. The proximal valve then reopens.

The respiratory pump :

- During inhalation, the diaphragm moves downward, which causes a

decrease in pressure in the thoracic cavity and an increase in pressure in the abdominal cavity. As a result, abdominal veins are compressed and a greater volume of blood moves from the compressed abdominal veins into the decompressed thoracic veins and then into the right atrium.

- When the pressures reverse during exhalation, the valves in the veins prevent backflow of blood from the thoracic veins to the abdominal veins.

12.9.5 VELOCITY OF BLOOD FLOW :

- The speed or velocity of blood flow (in cm/sec) is inversely related to the cross-sectional area.
- Each time an artery branches, the total cross-sectional area of all its branches is greater than the cross-section area of the original vessel, so blood flow becomes slower and slower as blood moves further away from the heart and is slowest in the capillaries.
- Conversely, when venules unite to form veins, the total cross-sectional area becomes smaller and flow becomes faster.
- Thus, the velocity of blood flow decreases as blood flows from the aorta to arteries to arterioles to capillaries and increases as it leaves capillaries and returns to the heart.

12.10 CONTROL OF BLOOD PRESSURE AND BLOOD FLOW :

Several interconnected negative feedback systems control blood pressure by adjusting heart rate, stroke volume, systemic vascular resistance and blood volume.

12.10.1 ROLE OF THE CARDIOVASCULAR CENTER :

- The cardiovascular (CV) center in helps to controls neural, hormonal and local negative feedback systems that regulate blood pressure and blood flow to specific tissues.
- Groups of neurons scattered within the CV center regulate heart rate,

contractility (force of contraction) of the ventricles and blood vessel diameter.

- Some neurons stimulate the heart (cardio stimulatory center); others inhibit the heart (cardioinhibitory center). Still others control blood vessel diameter by causing constriction (vasoconstrictor center) or dilation (vasodilator center); these neurons are referred to collectively as the vasomotor center.
- The cardiovascular center receives input both from higher brain regions and from sensory receptors.
- Nerve impulses descend from the cerebral cortex, limbic system and hypothalamus to affect the cardiovascular center.
- The three main types of sensory receptors that provide input to the cardiovascular center are proprioceptors, baroreceptors and chemoreceptors.
- Output from the cardiovascular center flows along sympathetic and parasympathetic neurons of the ANS.
- Sympathetic impulses reach the heart via the cardiac accelerator nerves. An increase in sympathetic stimulation increases heart rate and contractility and decrease in sympathetic stimulation decreases heart rate and contractility.
- Parasympathetic stimulation, conveyed along the vagus (X) nerves, decreases heart rate.
- The cardiovascular center also continually sends impulses to smooth muscle in blood vessel walls via vasomotor nerves.
- The vasomotor region of the cardiovascular center continually sends impulses to arterioles throughout the body, but especially to those in the skin and abdominal viscera.
- The result is a moderate state of tonic contraction or vasoconstriction, called vasomotor tone, which sets the resting level of systemic vascular resistance.

- Sympathetic stimulation of most veins causes constriction that moves blood out of venous blood reservoirs and increases blood pressure.

12.10.2 NEURAL REGULATION OF BLOOD PRESSURE:

The nervous system regulates blood pressure via negative feedback loops that occur as two types of reflexes :

(1) Baroreceptor Reflexes :

- Baroreceptors, pressure-sensitive sensory receptors, are located in the aorta, internal carotid arteries (arteries in the neck that supply blood to the brain) and other large arteries in the neck and chest.
- They send impulses to the cardiovascular center to help regulate blood pressure.
- The two most important baroreceptor reflexes are :

(a) The carotid sinus reflex :

(i) The carotid sinuses are small widenings of the right and left internal carotid arteries just above the point where they branch from the common carotid arteries.

(ii) Blood pressure stretches the wall of the carotid sinus, which stimulates the baroreceptors. Nerve impulses propagate from the carotid sinus baroreceptors over sensory axons in the glossopharyngeal (IX) nerves to the cardiovascular center in the medulla oblongata.

(b) The aortic reflex :

(i) Baroreceptors in the wall of the ascending aorta and arch of the aorta initiate the aortic reflex, which regulates systemic blood pressure.

(ii) Nerve impulses from aortic baroreceptors reach the cardio-vascular center via sensory axons of the vagus (X) nerves.

- When blood pressure falls, the baroreceptors are stretched less and they send nerve impulses at a slower rate to the cardiovascular center. In response, the CV center decreases parasympathetic stimulation of the heart by way of motor axons of the vagus nerves and increases

sympathetic stimulation of the heart via cardiac accelerator nerves. Another consequence of increased sympathetic stimulation is increased secretion of epinephrine and norepinephrine by the adrenal medulla.

- As the heart beats faster and more forcefully and as systemic vascular resistance increases, cardiac output and systemic vascular resistance rise and blood pressure increases to the normal level.
- Conversely, when an increase in pressure is detected, the baroreceptors send impulses at a faster rate. The CV center responds by increasing parasympathetic stimulation and decreasing sympathetic stimulation. The resulting decreases in heart rate and force of contraction reduce the cardiac output.
- The cardiovascular center also slows the rate at which it sends sympathetic impulses along vasomotor neurons that normally cause vasoconstriction. The resulting vasodilation lowers systemic vascular resistance.

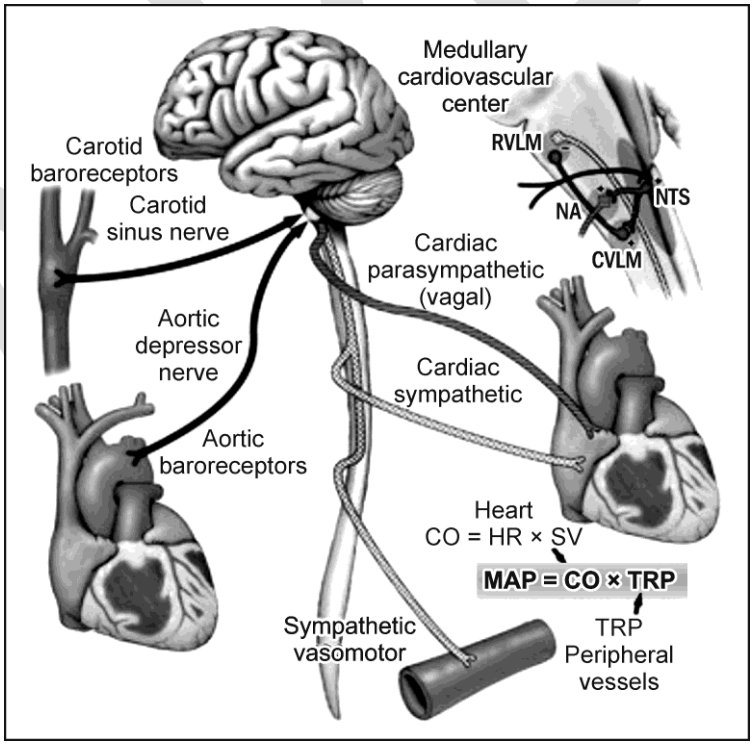


Fig. 12.10.2 Regulation of blood pressure

(2) Chemoreceptor Reflexes :

- Chemoreceptors, sensory receptors that monitor the chemical

composition of blood and are located close to the baroreceptors of the carotid sinus called carotid bodies and arch of the aorta in small structures called aortic bodies.

- These chemoreceptors detect changes in blood level of O_2, CO_2 and H^+.
- Hypoxia (lowered O_2 availability), acidosis (an increase in H^+ concentration) or hypercapnia (excess CO_2) stimulates the chemoreceptors to send impulses to the cardiovascular center, which increases sympathetic stimulation to arterioles and veins, producing vasoconstriction and an increase in blood pressure.

12.10.3 HORMONAL REGULATION OF BLOOD PRESSURE:

Several hormones help regulate blood pressure and blood flow by altering cardiac output, changing systemic vascular resistance or adjusting the total blood volume :

(1) Renin-angiotensin-aldosterone (RAA) system :

- When blood volume falls or blood flow to the kidneys decreases, juxtaglomerular cells in the kidneys secrete renin into the bloodstream.
- Renin is converted into angiotensin II by Angiotensin Converting Enzyme (ACE), which raises blood pressure in two ways.

(i) First angiotensin II is a potent vasoconstrictor; it raises blood pressure by increasing systemic vascular resistance.

(ii) It also stimulates secretion of aldosterone, which increases reabsorption of sodium ions (Na^+) and water by the kidneys. The water reabsorption increases total blood volume, which increases blood pressure.

(2) Epinephrine and norepinephrine :

- In response to sympathetic stimulation, the adrenal medulla releases epinephrine and increasing the rate and force of heart contractions.
- They also cause vasoconstriction of arterioles and veins in the skin and abdominal organs and vasodilation of arterioles in cardiac and skeletal muscle, which helps increase blood flow to muscle during exercise.

(3) Antidiuretic hormone (ADH) :

- ADH is produced by the hypothalamus and released from the posterior pituitary in response to dehydration or decreased blood volume. ADH causes vasoconstriction, which increases blood pressure. For this reason ADH is also called vasopressin.
- ADH also promotes movement of water from the lumen of kidney tubules into the bloodstream. This results in an increase in blood volume and a decrease in urine output.

(4) Atrial natriuretic peptide (ANP) :

Released by cells in the atria of the heart, ANP lowers blood pressure by causing vasodilation and by promoting the loss of salt and water in the urine, which reduces blood volume.

12.10.4 AUTOREGULATION OF BLOOD PRESSURE :

- The ability of a tissue to automatically adjust its blood flow to match its metabolic demands is called autoregulation.
- Two general types of stimuli cause autoregulatory changes in blood flow :

(1) Physical changes :

- Warming promotes vasodilation and cooling causes vasocon-striction.
- In addition, smooth muscle in arteriole walls exhibits a myogenic response i.e. it contracts more forcefully when it is stretched and relaxes when stretching lessens.

(2) Vasodilating and vasoconstricting chemicals :

- Several types of cells including white blood cells, platelets, smooth muscle fibers, macrophages and endothelial cells release a wide variety of chemicals that alter blood-vessel diameter.
- Vasodilating chemicals released by metabolically active tissue cells include K^+, H^+, lactic acid (lactate), adenosine (from ATP) and nitric oxide (NO), kinins and histamine.
- Vasoconstrictors include thromboxane A2, superoxide radicals, serotonin (from platelets) and endothelins (from endothelial cells).

12.11 ELECTROCARDIOGRAM :

- As action potentials propagate through the heart, they generate electrical currents that can be detected at the surface of the body. An electrocardiogram (ECG), is used to record these electrical signals.
- The ECG is a composite record of action potentials produced by all the heart muscle fibers during each heartbeat.
- The instrument used to record the changes is an electrocardiograph.
- In clinical practice, electrodes are positioned on the arms and legs (limb leads) and at six positions on the chest (chest leads) to record the ECG.
- The electrocardiograph amplifies the heart's electrical signals and produces 12 different tracings from different combinations of limb and chest leads. Each limb and chest electrode records slightly different electrical activity because of the difference in its position relative to the heart.
- By comparing these records with one another and with normal records, it is possible to determine defects in heart or conducting system.

12.11.1 NORMAL ECG :

In a typical record, three clearly recognizable waves appear with each heartbeat.

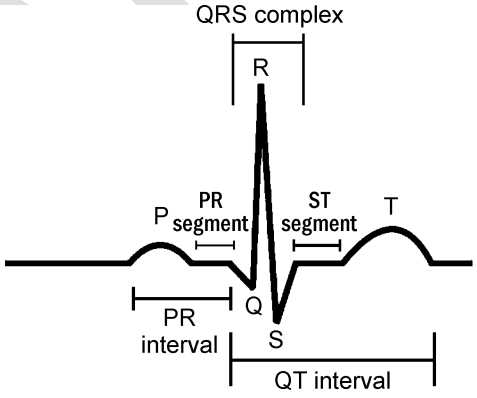


Fig. 12.11.1 Normal electrocardiogram or ECG

(1) P wave :

- It is a small upward deflection on the ECG.
- The P wave represents atrial depolarization, which spreads from the SA

node through contractile fibers in both atria.

(2) QRS complex :

- It begins as a downward deflection, continues as a large, upright, triangular wave and ends as a downward wave.
- The QRS complex represents rapid ventricular depolarization, as the action potential spreads through ventricular contractile fibers.

(3) T wave :

- It is a dome-shaped upward deflection called the T wave.
- It indicates ventricular repolarization and occurs just as the ventricles are starting to relax.
- The T wave is smaller and wider than the QRS complex because repolarization occurs more slowly than depolarization.

Abnormalities in ECG :

- In reading an ECG, the size of the waves can provide clues to abnormalities.
- Larger P waves indicate enlargement of an atrium; an enlarged Q wave may indicate a myocardial infarction; and an enlarged R wave generally indicates enlarged ventricles.
- The T wave is flatter than normal when the heart muscle is receiving insufficient oxygen.
- The T wave may be elevated in hyperkalemia.

12.11.2 INTERVALS (SEGMENTS) IN ECG :

Analysis of an ECG also involves measuring the time spans between

waves, which are called intervals or segments.

P-Q segment :

- It is the time from the beginning of the P wave to the beginning of the QRS complex.
- It represents the conduction time from the beginning of atrial excitation to the beginning of ventricular excitation.
- In other words it is the time required for the action potential to travel through the atria, atrioventricular node and the remaining fibers of the conduction system.

S-T segment :

It begins at the end of the S wave and ends at the beginning of the T wave, represents the time when the ventricular contractile fibers are depolarized during the plateau phase of the action potential.

Q-T segment :

- The Q-T interval extends from the start of the QRS complex to the end of the T wave.
- It is the time from the beginning of ventricular depolarization to the end of ventricular repolarization.

Abnormal heart rhythms and inadequate blood flow to the heart may occur only briefly or unpredictably. To detect these problems, continuous ambulatory electrocardiographs are used. For the purpose electrodes are attached to the chest are connected to the monitor and information on the heart's activity is stored in the monitor and retrieved later by medical personnel.

12.12 PULSE :

- The alternate expansion and recoil of elastic arteries after each systole of the left ventricle create a traveling pressure wave that is called the pulse. It may be felt in any artery that lies near the surface or over a hardtissue (e.g. bone). The pulse rate in terms of beats per minute varies considerably with age and in different circumstances.
- The pulse rate is normally the same as the heart rate, about 70-80 beats per minute at rest. Tachycardia is a rapid resting heart or pulse rate over 100 beats/min. Bradycardia is a slow resting heart or pulse rate under 50 beats/min.
- Endurance-trained athletes normally exhibit bradycardia. A brief bout of exercise may increase the rate from 70 to 150 beats/min.
- Sudden abnormal and scaring noise, anger, fear and any such excitement results in sudden increase in the heart beat and pulse rate.

12.13 DISORDERS OF CARDIOVASCULAR SYSTEM :

- Cardiovascular disorders is a class of disease that involves the heart or blood vessels.
- These are the conditions which affects structures and function of heart. They are as follows :

12.13.1 CORONARY ARTERY DISEASE :

- Coronary Artery Disease (CAD) is a serious medical problem that affects about 7 million people annually.
- CAD results from the effects of the accumulation of atherosclerotic plaques. in coronary arteries, which leads to a reduction in blood flow

to the myocardium.

- Some individuals have no signs or symptoms; others experience angina pectoris (chest pain) and still others suffer heart attacks.

12.13.2 CONGENITAL HEART DEFECTS :

- A defect that is present at birth and usually before, is called a congenital defect.
- Among the several congenital defects that affect the heart are the following.

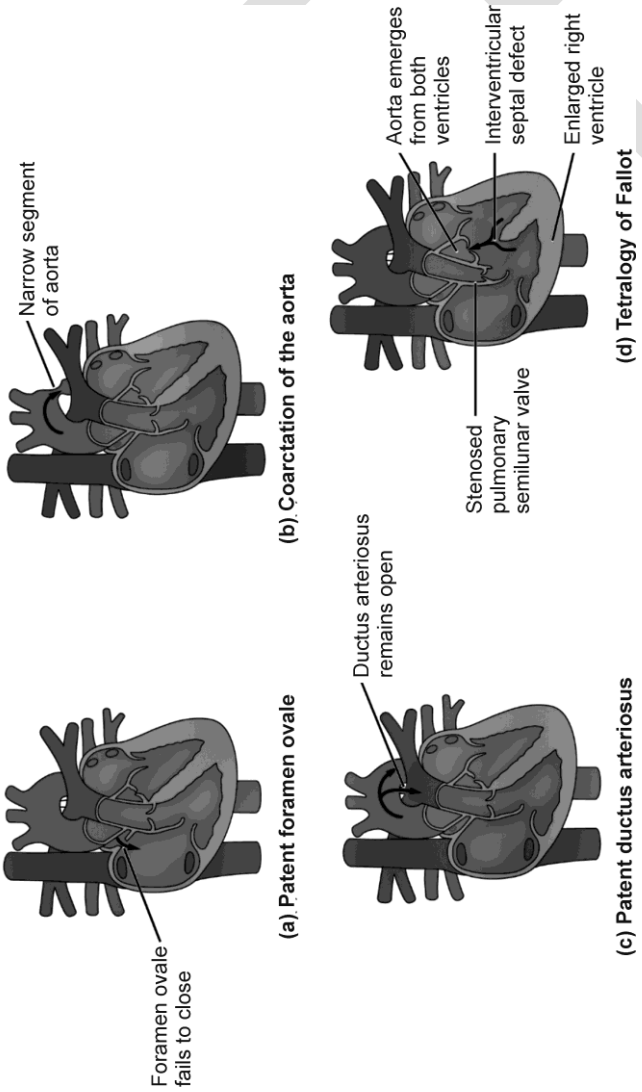


Fig. 12.13.2 Congenital heart defects

(a) Patent foramen ovale : In an atrial septal defect the fetal foramen ovale between the two atria fails to close after birth.

(b) Coarctation of the aorta : A segment of the aorta is too narrow and thus the flow of oxygenated blood to the body is reduced, the left ventricle is forced to pump harder and high blood pressure develops.

(c) Patent Ductus Arteriosus (PDA) : In some babies, the ductus arteriosus, a temporary blood vessel between the aorta and the pulmonary trunk, remains open rather than closing shortly after birth. As a result, aortic blood flows into the lower-pressure pulmonary trunk, thus increasing the pulmonary trunk blood pressure and overworking both ventricles.

(d) Tetralogy of Fallot : Condition is a combination of four developmental defects: an interventricular septal defect, an aorta that emerges from both ventricles, a stenosed pulmonary valve and an enlarged right ventricle.

12.13.3 ARRHYTHMIAS :

- The term arrhythmia or dysrhythmia refers to an abnormal rhythm as a result of a defect in the conduction system of the heart. The heart may beat irregularly, too quickly or too slowly.
- Symptoms include chest pain, shortness of breath, lightheadedness, dizziness and fainting.
- Arrhythmias are categorized by their speed, rhythm and origination of the problem.

(i) Bradycardia refers to a slow heart rate (below 50 beats per minute).

(ii) Tachycardia refers to a rapid heart rate (over 100 beats per minute)

(iii) Fibrillation refers to rapid, uncoordinated heartbeats.

(iv) Arrhythmias that begin in the atria are called supraventricular or atrial arrhythmias; those that originate in the ventricles are called ventricular arrhythmias.

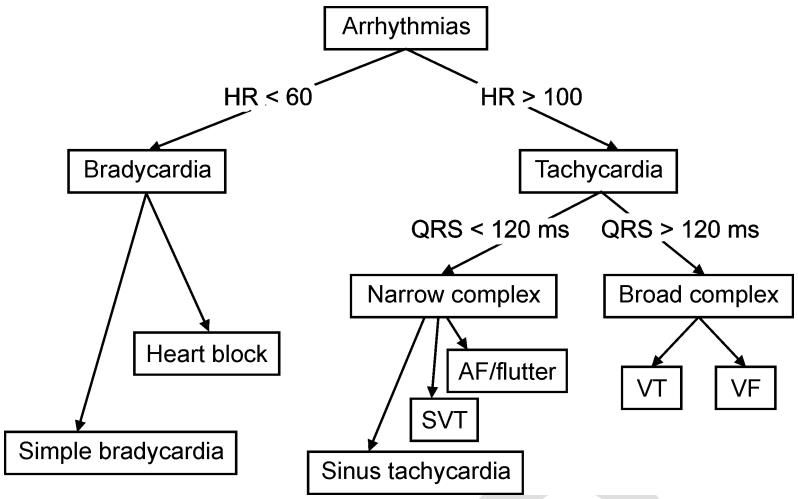


Fig. 12.13.3 Different types of arrhythmia

12.13.4 HYPERTENSION :

- Hypertension is a long-term medical condition in which the blood pressure in the arteries is persistently elevated.

Hypertension is generally classified into 2 types :

(1) Primary or essential hypertension in which the cause of increase in blood pressure is unknown.

(2) Secondary hypertension, in which the increase in blood pressure is caused by diseases of the kidneys, endocrines or some other organs.

- According to the clinical course, both essential and secondary hypertension may be benign or malignant.

(i) Benign hypertension is moderate elevation of blood pressure and the rise is slow over the years. About 90-95% patients of hypertension have benign hypertension.

(ii) Malignant hypertension is marked and sudden increase of blood pressure to 200/140 mmHg or more in a known case of hypertension or in a previously normotensive individual; the patients develop papilloedema, retinal haemorrhages and hypertensive encephalopathy.

12.13.5 ANGINA PECTORIS :

- Angina pectoris is resulting from transient myocardial ischaemia. It is

characterised by paroxysmal pain in the substernal or precordial region of the chest which is aggravated by an increase in the demand of the heart and relieved by a decrease in the work of the heart. Often, the pain radiates to the left arm, neck, jaw or right arm.

- There are 3 overlapping clinical patterns of angina pectoris with some differences in their pathogenesis :

  (i) Stable or typical angina

  (ii) Prinzmetal's variant angina

  (iii) Unstable or crescendo angina

(i) Stable or typical angina :

- This is the most common pattern. Stable or typical angina is characterized by attacks of pain following physical exertion or emotional excitement and is relieved by rest.
- The pathogenesis of condition lies in chronic stenosing coronary atherosclerosis that cannot perfuse the myocardium adequately when the workload on the heart increases.
- During the attacks, there is depression of ST segment in the ECG due to poor perfusion of the subendocardial region of the left ventricle but there is no elevation of enzymes in the blood as there is no irreversible myocardial injury.

(ii) Prinzmetal's variant angina:

- This pattern of angina is characterized by pain at rest and has no relationship with physical activity.
- The exact pathogenesis of Prinzmetal's angina is not known. It may occur due to sudden vasospasm of a coronary trunk induced by coronary atherosclerosis or may be due to release of humoral vasoconstrictors by mast cells in the coronary adventitia.
- ECG shows ST segment elevation due to transmural ischaemia. These

patients respond well to vasodilators like nitroglycerin.

(iii) Unstable or crescendo angina:

- Also referred to as 'pre-infarction angina' or 'acute coronary insufficiency', this is the most serious pattern of angina.
- It is characterized by more frequent onset of pain of prolonged duration and occurring often at rest.
- It is thus indicative of an impending acute myocardial infarction.
- Distinction between unstable angina and acute MI is made by ST segment changes on ECG- acute MI characterised by ST segment elevation while unstable angina may have non-ST segment elevation MI.

12.14 POINTS TO REMEMBER:

(1) The heart is located in the mediastinum; about two-thirds of its mass is to the left of the midline. Its apex is the pointed, inferior part; its base is the broad, superior part.

(2) The pericardium is the membrane that surrounds and protects the heart

(3) Three layers make up the wall of the heart: epicardium (visceral layer of the serous pericardium), myocardium and endocardium.

(4) The heart chambers include two superior chambers, the right and left atria and two inferior chambers, the right and left ventricles.

(5) The right atrium receives blood from the superior vena cava, inferior vena cava and coronary sinus. Blood exits the right atrium through the tricuspid valve.

(6) The right ventricle receives blood from the right atrium. It pumps blood through the pulmonary valve into the pulmonary trunk.

(7) Oxygenated blood enters the left atrium from the pulmonary veins and exits through the bicuspid (mitral) valve.

(8) The left ventricle pumps oxygenated blood through the aortic valve into the aorta.

(9) Heart valves prevent backflow of blood within the heart. The atrioventricular (AV) valves are the tricuspid valve on the right side of the heart and the bicuspid (mitral) valve on the left. The semilunar (SL) valves are the aortic valve, at the entrance to the aorta and the pulmonary valve, at the entrance to the pulmonary trunk.

(10) The left side of the heart is the pump for systemic circulation. The left ventricle ejects blood into the aorta and blood then flows into systemic arteries, arterioles, capillaries, venules and veins, which carry it back to the right atrium.

(11) The right side of the heart is the pump for pulmonary circulation, the circulation of blood through the lungs. The right ventricle ejects blood into the pulmonary trunk and blood then flows into pulmonary arteries, pulmonary capillaries and pulmonary veins, which carry it back to the left atrium.

(12) The coronary circulation provides blood flow to the myocardium. The main arteries of the coronary circulation are the left and right coronary arteries; the main veins are the cardiac veins and the coronary sinus.

(13) Blood vessels consist of arteries, arterioles, capillaries, venules and veins.

(14) Components of the conduction system are the sinoatrial (SA) node (pacemaker), atrioventricular (AV) node, atrioventri-cular (AV) bundle (bundle of His), bundle branches and Purkinje fibers.

(15) Phases of an action potential in a ventricular contractile fiber include rapid depolarization, a long plateau and repolari-zation.

(16) The phases of the cardiac cycle are (a) atrial systole, (b) ventricular systole and (c) relaxation period. With an average heartbeat of 75 beats/min, a complete cardiac cycle requires 0.8 sec.

(17) Cardiac Output (CO) is the amount of blood ejected per minute by the left ventricle into the aorta (or by the right ventricle into the pulmonary trunk). It is calculated as follows: CO (mL/min) = Stroke volume (SV) in mL/beat × heart rate (HR) in beats/min. Stroke volume (SV) is the amount of blood ejected by a ventricle during each systole.

(18) Stroke volume is related to preload (stretch on the heart before it contracts), contractility (forcefulness of contraction) and after load (pressure that must be exceeded before ventricular ejection can begin).

(19) Nervous control of the cardiovascular system originates in the cardiovascular center in the medulla oblongata.

(20) Sympathetic impulses increase heart rate and force of contraction; parasympathetic impulses decrease heart rate.

(21) Heart rate is affected by hormones (epinephrine, nor-epinephrine, thyroid hormones), ions (Na^+, K^+, Ca^{2+}), age, gender, physical fitness and body temperature.

(22) The record of electrical changes during each cardiac cycle is called an electrocardiogram (ECG).

(23) Disorders of cardiovascular system includes, coronary Artery Disease, congenital Heart Defect, arrhythmias and angina pectoris, hypertension.