General Physiology Lect. 1

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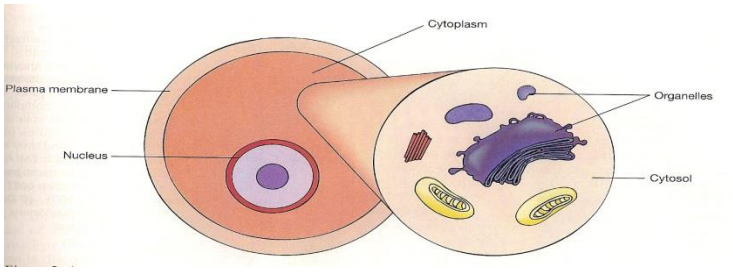
Function organization of the human body

The goal of physiology is to explain the physical and chemical factors that are responsible for the origin development and progression of life. Each life from the very simple virus up to the latest tree or the complicated human being has its own functional characteristics. Therefore, the vast field of physiology can be divided into viral physiology, plant physiology, human physiology and many more subdivisions

In human physiology we attempt to explain the specific characteristics and mechanisms of the human body that make it living being.

The basic living unit of the body is the cell. All cells use oxygen as one of the major substances from which energy is divided; the oxygen combines with carbohydrates, fat or protein to release the energy required for cell function.



About 60% of the adult human body is fluid, most of this fluid is inside the cells and is called intracellular fluid, about one-third of it is in the spaces outside the cells and is called extracellular fluid. This E.C.F is in constant motion throughout the body. It is rapidly mixed by the blood and the tissue fluids, and E.C.F are the ions and nutrients needed by the cells for maintenance of cellular function. Therefore all cells live in essentially the same environment, that is the E.C.F, and for this reason is often called the internal environment of the body.

Although there is a constant change between E.C.F. and I.C.F., but there is a significant difference between the constituents of the two fluids.

The E.C.F. contains large amounts of sodium, chloride and bicarbonate ions, plus nutrients for cells, such as oxygen, glucose, fatty acids and amino acids …etc.

The I.C.F. differs significantly from the E.C.F. particularly, it contains large amount of potassium, magnesium and phosphate ions instead of the sodium and chloride found in E.C.F.

Homeostasis:

The term of homeostasis mean maintenance of state or constant conditions in the internal environment. Essentially all of the organs and tissues of the body perform functions. That helps to maintain constant conditions.

The process of homeostasis can be understood through the followings:

1. The E.C.F. is transported through all parts of the body in two different stages. The first entails movement of blood around the circulatory system & the second , movement of fluid between the blood capillaries and the cells. All the blood in the circulation transverses the entire of the circulation in an average once each minute when the body is at rest and as six times during activity. In general , no cell is located more than 25-50 micrometers from a capillary.

2. Origin of nutrients in the E.C.F. :

a. ***Respiratory system:*** the blood passes through the body and also flows through the lungs. The blood picks up oxygen in the alveoli, thus acquiring the oxygen needed by the cells.
The membrane between the alveoli and the lumen of the pulmonary capillaries is only 0.4-2.0 micrometers in thickness.

b. ***Gastrointestinal track:*** here, different dissolved nutrients including carbohydrates, fatty acids, amino acids and others are absorbed into the E.C.F.

c. The liver changes the chemical composition of many of these to more usable forms.

d. The muscloskeletal provides motility and energy.

3. Removal of metabolic end products:

a. Removal of carbon dioxide by the lungs.

b. Kidney, regulation of blood fluid and excretion of excess substances.

4. Regulation of body functions:

a. ***Nervous system:*** The nervous system is composed of three major parts:

1. Sensory input portion.
2. Central nerve system.
3. Motor output portion.

b. ***Hormonal system:***

Located in the body, are eight major endocrine glands that secrete chemical substances called hormones. Hormones are transported in the E.C.F. to all parts of the body to help regulate cellular function.

C. ***Reproduction:***

Help to maintain static condition by generating new beings to take the phase of those that are dying.

The human body has literally thousands of control systems in it. The most important of these are genetic control systems that operate in all cells to control I.C. function as well as E.C. function.

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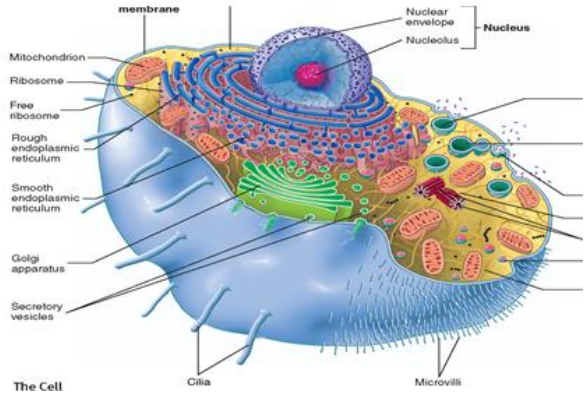
Cell

Cell is defined as the structural and functional unit of the living body because it has all the characteristics of life



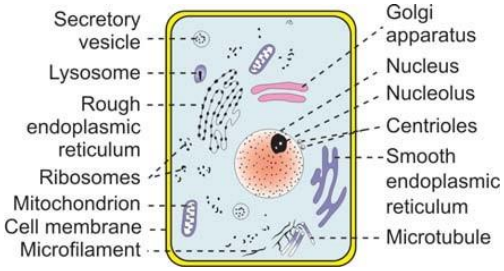
The cell membrane is a protective sheath that envelops the cell body. It separates the fluid outside the cell called extracellular fluid (ECF) and the fluid inside the cell called intracellular fluid (ICF). It is a semipermeable membrane and allows free exchange of certain substances between ECF and ICF

The cell membrane is composed of three types of substances

1. Proteins (55%)
2. Lipids (40%)
3. Carbohydrates (5%).

Each cell is formed by a cell body and a cell membrane or plasma membrane that covers the cell body. The important parts of the cell are

a. Cell membrane
b. Nucleus
c. Cytoplasm with organelles



The cell membrane is a unit membrane having the 'fluid mosaic model' i.e., the membrane is a fluid with mosaic of proteins (mosaic means pattern formed by arrangement of different colored pieces of stone, tile, glass or other such materials , lipids and carbohydrates. The electron microscopic study reveals three layers in the cell membrane namely, one electron lucent lipid layer in the center and two electron dense layers on either side of the central layer. Carbohydrate molecules are found on the surface of the cell membrane.

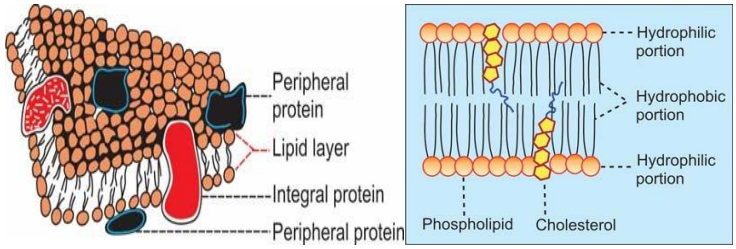
FUNCTIONS OF CELL MEMBRANE

1. Protective function: Cell membrane protects the cytoplasm and the organelles present in the cytoplasm.
2. Selective permeability: Cell membrane acts as a semipermeable membrane which allows only some substances to pass through it and acts as a barrier for other substances.
3. Absorptive function: Nutrients are absorbed into the cell through the cell membrane.
4. Excretory function: Metabolites and other waste products from the cell are excreted out through the cell membrane.
5. Exchange of gases: Oxygen enters the cell from the blood and carbon dioxide leaves the cell and enters the blood through the cell membrane.
6. Maintenance of shape and size of the cell: Cell membrane is responsible for the maintenance of shape and size of the cell.

Lipid Layer of Cell Membrane

It is a bilayered structure formed by a thin film of lipids. It is fluid in nature and the portions of the membrane along with the dissolved substances move to all areas of the cell membrane. The major lipids are:

a. Phospholipids
b. Cholesterol



Functions of lipid layer

The lipid layer is semi permeable in nature and allows only the fat soluble substances like oxygen, carbon dioxide and alcohol to pass through it. It does not allow the water soluble materials like glucose, urea and electrolytes to pass through it.

Protein Layers of the Cell Membrane

The protein layers of the cell membrane are the electron dense layers situated on either side of the central lipid layer. The protein substances present in these layers are mostly glycoproteins. These protein molecules are classified into two categories:

a. Integral proteins
b. Peripheral proteins.

Functions of protein layers

Functionally, the proteins in the cell membrane exist in different forms such as integral proteins, channel proteins, carrier proteins etc.

1. *Integral proteins* provide structural integrity of the cell membrane
2. *Channel proteins* provide route for diffusion of water soluble substances like glucose and electrolytes
3. *Carrier proteins* help in transport of substances across the cell membrane
4. *Receptor proteins* serve as receptor sites for hormones and neurotransmitters
5. *Enzymes:* some of the protein molecules form the enzymes which control

chemical reactions within the cell membrane

6. *Antigens:* Some proteins act as antigens and induce the process of antibody formation.

Carbohydrate of the Cell Membrane

Carbohydrate molecules form a thin loose covering over the entire surface of the cell membrane called glycocalyx. Some carbohydrate molecules are attached with proteins and form glycoproteins and some are attached with lipids and form glycolipids.

Functions of carbohydrates

1. The carbohydrate molecules are negatively charged and do not permit the negatively charged substances to move in and out of the cell.
2. The glycocalyx from the neighboring cells helps in the tight fixation of cells with one another.
3. Some of the carbohydrate molecules form the receptors for some hormones.

CYTOPLASM

The cytoplasm is the fluid present inside the cell. It contains a clear liquid portion called cytosol which contains various substances like proteins, carbohydrates, lipids and electrolytes. Apart from these substances, many organelles are also present in cytoplasm. The cytoplasm is distributed as peripheral ectoplasm just beneath the cell membrane and inner endoplasm between the ectoplasm and the nucleus.

ORGANELLES IN CYTOPLASM

All the cells in the body contain some common structures called organelles in the cytoplasm. Some organelles are bound by limiting membrane and others do not have limiting membrane .

1. ENDOPLASMIC RETICULUM

Endoplasmic reticulum is made up of tubules and microsomal vesicles. These structures form an interconnected network which acts as the link between the organelles and cell membrane.

The endoplasmic reticulum is of two types namely, rough endoplasmic reticulum and smooth endoplasmic reticulum.

Functions of rough endoplasmic reticulum

It is concerned with the protein synthesis in the cell, especially those secreted from the cell such as insulin from □ cells of islets of Langerhans in pancreas and antibodies in leukocytes.

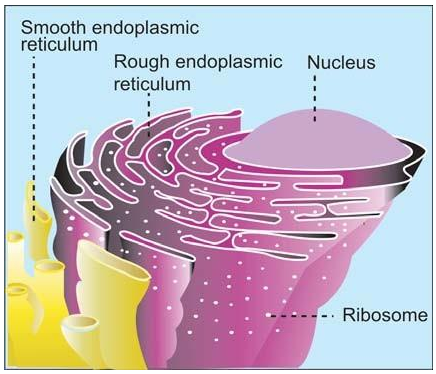
It also plays an important role in degradation of worn out cytoplasmic organelles like mitochondria. It wraps itself around the worn out organelles and forms a vacuole which is often called the autophagosome. It is digested by lysosomal enzymes

Functions of smooth endoplasmic reticulum

i. It is responsible for synthesis of cholesterol and steroid
ii. It is concerned with various metabolic processes of the cell because of the presence of many enzymes on the outer surface
iii. It is concerned with the storage and metabolism of calcium

iv. It is also concerned with catabolism and detoxification of toxic substances like some drugs and carcinogens (cancer producing substances) in liver.

Rough endoplasmic reticulum and smooth endoplasmic reticulum are interconnected and continuous with one another. Depending upon the activities of the cells, the rough endoplasmic reticulum changes to smooth endoplasmic reticulum and *vice versa*.

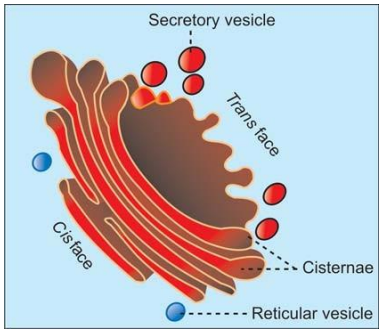


GOIGI APPARATUS

The Golgi apparatus is situated near the nucleus. It has two ends or faces namely, *cis* face and *trans* face. The *cis* face is positioned near the endoplasmic reticulum. The reticular vesicles from endoplasmic reticulum enter the Golgi apparatus through *cis* face. The *trans* face is situated near the cell membrane. The processed substances make their exit from Golgi apparatus through *trans* face.

Functions of Golgi Apparatus

i. It is concerned with the processing and delivery of substances like proteins and lipids to different parts of the cell.
ii. It functions like a post office because, it packs the processed materials into the secretory granules, secretory vesicles, and lysosomes
iii. It also functions like a shipping department of the cell because it sorts out and labels the materials for distribution to their proper destinations.



Lysosomes

These are small globular structures filled with enzymes. These enzymes are synthesized in rough endoplasmic reticulum and transported to the Golgi apparatus.

Lysosomes are of two types:

i. Primary lysosome which is pinched off from Golgi apparatus. It is inactive in spite of having the hydrolytic enzymes.
ii. Secondary lysosome which is active lysosome formed by the fusion of a primary lysosome with phagosome or endosome.

Functions of Lysosomes

i. Digestion of unwanted substances

With the help of hydrolytic enzymes like proteases, lipases, amylases and nucleases, lysosome digests and removes the unwanted substances.

ii. Removal of excess secretory products in the cells

Lysosomes in the cells of the secretory glands play an important role in the removal of excess secretory products by degrading the secretory granules.

iii. Secretory function – Secretory lysosomes

Recently, lysosomes having secretory function called secretory lysosomes are found in some of the cells, particularly in the cells of immune system. The conventional lysosomes are modified into secretory lysosomes by combining with secretory granules

Peroxisomes

Peroxisomes are otherwise called as microbodies. These are pinched off from endoplasmic reticulum. Peroxisomes contain some oxidative enzymes such as catalase, urate oxidase and D-amino acid oxidase.

Functions of Peroxisomes

i. Degrade the toxic substances like hydrogen peroxide and other metabolic products by means of detoxification
ii. Form the major site of oxygen utilization in the cells
iii. Break down the excess fatty acids
iv. Accelerate gluconeogenesis from fats
v. Degrade purine to uric acid
vi. Participate in the formation of myelin and bile acids.

Centrosome AND CENTRIOLES

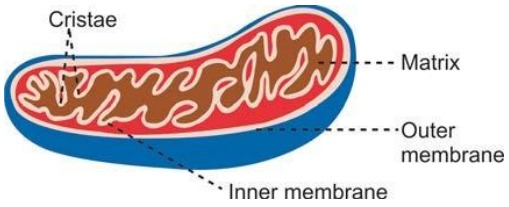
The centrosome is situated near the center of the cell close to the nucleus. It consists of two cylindrical structures called centrioles which are responsible for the movement of chromosomes during cell division.

Secretory VESICLES

The secretory vesicles are globular structures, formed in the endoplasmic reticulum, and processed and packed in Golgi apparatus. When necessary, the secretory vesicles rupture and release the secretory substances into the cytoplasm.

MITOCHONDRION

The mitochondrion is a rod or oval shaped structure with a diameter of 0.5 to 1 µ. It is covered by a double layered membrane .



Functions of Mitochondrion

i. The mitochondrion is called the 'power house of the cell' because it produces the energy required for the cellular functions. The energy is produced by oxidation of the food substances like proteins, carbohydrates and lipids by the oxidative enzymes in cristae. During oxidation, water and carbon dioxide are produced with release of energy. The released energy is stored in mitochondria and used later for synthesis of ATP.

ii. The components of respiratory chain in the mitochondrion are responsible for the synthesis of ATP by utilizing the energy through oxidative phosphorylation. The ATP molecules defuse throughout the cell from mitochondrion. Whenever energy is needed for cellular activity, the ATP molecules are broken down

iii.Apoptosis

ORGANELLES WITHOUT LIMITING MEMBRANE

RIBOSOMES

The ribosomes are small granular structures with a diameter of 15 nm. The ribosomes are made up of proteins (35%) and RNA (65%). The RNA present in ribosomes is called ribosomal RNA (rRNA).

Functions of Ribosomes

Ribosomes are called protein factories because of their role in the synthesis of proteins. Messenger RNA (mRNA) passes the genetic code for protein synthesis from nucleus to the ribosomes. The ribosomes, in turn arrange the amino acids into small units of proteins. The ribosomes attached with endoplasmic reticulum are involved in the synthesis of proteins like the enzymatic proteins, hormonal proteins, lysosomal proteins and the proteins of the cell membrane. The free ribosomes are responsible for the synthesis of proteins in hemoglobin, peroxisome and mitochondria.

Cytoskeleton

The cytoskeleton of the cell is a complex network that gives shape, support and stability to the cell. It is also essential for the cellular movements and the response of the cell to external stimuli. The cytoskeleton consists of three major protein components viz.

a. Microtubules
b. Intermediate filaments
c. **Microfilaments**

Microtubules

Microtubules are straight and hollow tubular structures formed by bundles of globular protein called □ and □ tubulin

Functions of microtubules

Microtubules:

i. Determine the shape of the cell
ii. Give structural strength to the cell
iii. Responsible for the movements of centrioles and the complex cellular structures like cilia
iv. Act like conveyer belts which allow the movement of granules, vesicles, protein molecules and some organelles like mitochondria to different parts of the cell
v. Form the spindle fibers which separate the chromosomes during mitosis

Intermediate Filaments

The intermediate filaments form a network around the nucleus and extend to the periphery of the cell. These filaments are formed by fibrous proteins and help to maintain the shape of the cell. The adjacent cells are connected by intermediate filaments by desmosomes.

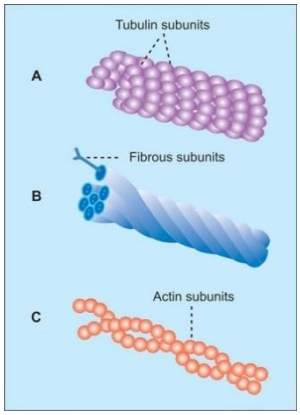
Microfilaments

Microfilaments are long and fine thread like structures which are made up of non tubular contractile proteins called actin and myosin. Actin is more abundant than myosin.

Functions of microfilaments

Microfilaments:

i. Give structural strength to the cell
ii. Provide resistance to the cell against the pulling forces
iii. Responsible for cellular movements like contraction, gliding and cytokinesis (partition of cytoplasm during cell division).



NUCLEUS

Nucleus is present in those cells which divide and produce enzymes. The cells with nucleus are called eukaryotes and those without nucleus are known as

prokaryotes (e.g. red blood cells). Prokaryotes do not divide or synthesize the enzymes.

Most of the cells have only one nucleus (uninucleated). Few types of cells like skeletal muscle cells have many nuclei (multinucleated). Generally the nucleus is located near the center of the cell. It is mostly spherical in shape. However, the shape and situation of nucleus vary in different cells.

Nuclear Membrane

The nucleus is covered by a double layered membrane called nuclear membrane. It encloses the fluid called nucleoplasm. Nuclear membrane is porous and permeable in nature and it allows nucleoplasm to communicate with the cytoplasm

Nucleoplasm

It is a gel like ground substance and contains large quantities of the genetic material in the form of DNA. The DNA is made up of chromatin threads. These chromatin threads become the rod shaped chromosomes just before the cell division.

Nucleoli

One or more nucleoli are present in each nucleus. The nucleolus contains RNA and some proteins, which are similar to those found in ribosomes. The RNA is synthesized by chromosomes and stored in the nucleolus.

FUNCTIONS OF NUCLEUS

1. Controls all the activities of the cell
2. Synthesizes RNA
3. Forms subunits of ribosomes
4. Sends genetic instruction to the cytoplasm for protein synthesis through mRNA
5. Controls the cell division through genes
6. Stores the hereditary information (in genes) and transforms this information from one generation of the species to the next.

Cell Junctions

The connection between the cells or the contact between the cell and extracellular matrix is called the cell junction. It is also called as membrane junction. It is generally classified into three types:

1. Occluding junction
2. Communicating junction
3. Anchoring junction

OCCLUDING JUNCTION

The junction which prevents the movement of ions and molecules from one cell to another cell is called the occluding junction.

Tight junctions belong to this category. It is formed by the tight fusion of the cell membranes from the adjacent cells. The area of the fusion is very tight and forms a ridge. This type of junction is present in the apical margins of epithelial cells in intestinal mucosa, wall of renal tubule, capillary wall and choroid plexus

Functions of Tight Junctions

1. The tight junctions hold the neighboring cells of the tissues firmly and thus provide strength and stability to the tissues.
2. It provides the barrier or gate function by which the interchange of ions, water and macromolecules between the cells is regulated.
3. It acts like a fence by preventing the lateral movement of integral membrane proteinsand lipids from cell membrane

4,By the fencing function, the tight junctions maintains the cell polarity by keeping the proteins in the apical region of the cell membrane.

5..Tight junctions in the brain capillaries form the blood-brain barrier (BBB) which prevents the entrance of many harmful substances from the blood into the brain tissues

COMMUNICATING JUNCTIONS

The junctions, which permit the movement of ions and molecules from one cell to another cell, are called communicating junctions. Gap junction and chemical synapse are the communicating junctions.

GAP JUNCTION OR NEXUS

The gap junction is also called nexus. It is present in heart, basal part of epithelial cells of intestinal mucosa, etc.

Functions of Gap Junction

1. The diameter of the channel in the gap junction is about 1.5 to 3 nm. So, the substances having molecular weight less than 1000 such as glucose also can pass through this junction easily

2. It helps in the exchange of chemical messengers between the cells

3. It helps in rapid propagation of action potential from one cell to another cell

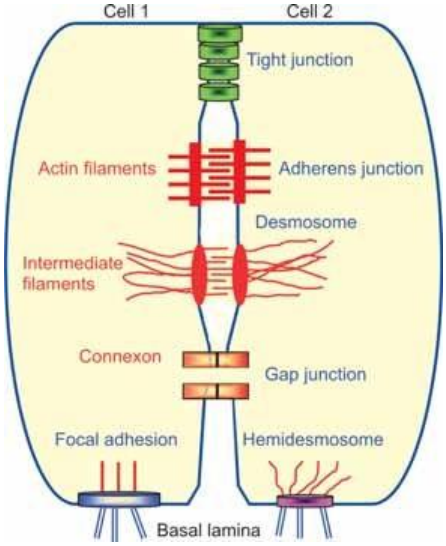
CHEMICAL SYNAPSE

Chemical synapse is the junction between a nerve fiber and a muscle fiber or between two nerve fibers, through which the signals are transmitted by the release of chemical transmitter

ANCHORING JUNCTIONS

Anchoring junctions are the junctions, which provide firm structural attachment between two cells or between a cell and the extracellular matrix. There are four types of anchoring junctions

i. Adherens junctions (cell to cell)
ii. Focal adhesions (cell to matrix)
iii. Desmosomes (cell to cell)
iv. Hemidesmosomes (cell to matrix)


Cell 1
Cell 2
Tight junction
Actin filaments
Adherens junction
Desmosome
Intermediate filaments
Connexon
Gap junction
Focal adhesion
Hemidesmosome
Basal lamina

General physiology Lect. 3

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Homeostasis

Homeostasis" means the maintenance of constant internal environment. For the operation of homeostatic mechanism, the body must recognize the **deviation** of any physiological activity from the normal limits.

Fortunately, body is provided with appropriate detectors or sensors, which recognize the deviation and alert the integrating center. The integrating center immediately sends information to the concerned effectors to either accelerate or inhibit the activity so that the normalcy is restored.

Types of transports

1. Diffusion (passive)
2. Carrier-mediated transport (passive or active)
3. Vesicular transport (active

FACTORS AFFECTING RATE OF DIFFUSION

The rate of diffusion of substances through thecell membrane is directly proportional to the following factors:

1. Permeability of the cell membrane
2. Body temperature
3. Concentration gradient or electrical gradient of the substance across the cell membrane
4. Solubility of the Substance

The rate of diffusion of substances through the cell membrane is inversely proportional to the following factors:

1. Thickness of the cell membrane
2. Charge of the ions
3. Size of the molecule

"Active Transport" of Substances Through Membranes

When a cell membrane moves molecules or ions "uphill" against a concentration gradient (or "uphill" against an electrical or pressure gradient), the process is called active transport. Different substances that are actively transported through at least some cell

membranes include sodium ions, potassium ions, calcium ions, iron ions, hydrogen ions, chloride ions, iodide ions, urate ions, several different sugars, and most of the amino acids.

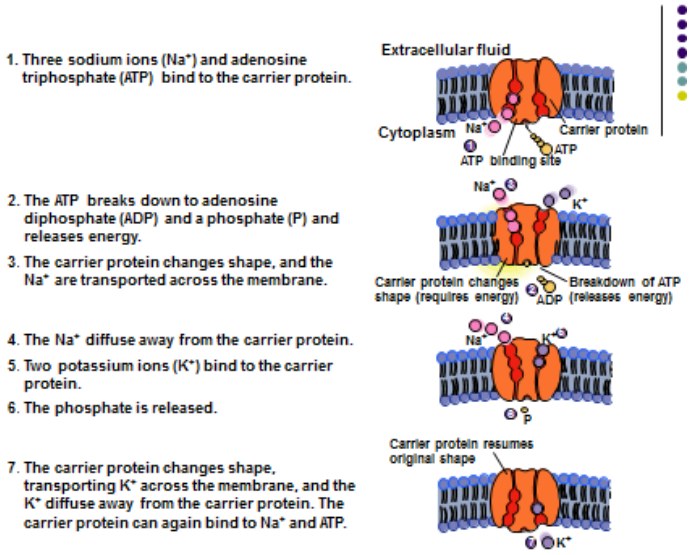
Active transport is divided into two types according to the source of the energy used to cause the transport: **primary active transport** and **secondary active transport**. In **primary active transport**, the energy is derived directly from breakdown of adenosine triphosphate (ATP) or of some other high-energy phosphate compound. In **secondary active transport,** the energy is derived secondarily from energy that has been stored in the form of ionic concentration differences of secondary molecular or ionic substances between the two sides of a cell membrane, created originally by primary active transport. In both instances, transport depends on **carrier proteins** that penetrate through the cell membrane, as is true for facilitated diffusion. However, in active transport, the carrier protein functions differently from the **carrier in facilitated diffusion because it is capable of imparting energy to the transported substance to move it against the electrochemical gradient**.

Sodium-Potassium Pump as an example of Primary Active Transport:

The active transport mechanism that has been studied in greatest detail is the **sodium-potassium (Na+-K+) pump**, a transport process that pumps sodium ions outward through the cell membrane of all cells and at the same time pumps potassium ions from the outside to the inside. This pump is responsible for maintaining the sodium and potassium concentration differences across the cell membrane, as well as for establishing a negative electrical voltage inside the cells. This pump is also the basis of nerve function, transmitting nerve signals throughout the nervous system. The carrier protein is a complex of two separate globular proteins: a larger one called the a subunit, and a smaller one called the b subunit, the larger protein has three specific features that are important for the functioning of the pump:

1. It has three **receptor sites for binding sodium ions** on the portion of the protein that protrudes to the inside of the cell.
2. It has two **receptor sites for potassium ions** on the outside.
3. The inside portion of this protein near the sodium binding sites has **ATPase activity**.

When two potassium ions bind on the outside of the carrier protein and three sodium ions bind on the inside, the ATPase function of the protein becomes activated. This then cleaves one molecule of ATP, splitting it to adenosine diphosphate (ADP) and liberating a high-energy phosphate bond of energy. This liberated energy is then believed to cause a chemical and conformational change in the protein carrier molecule, extruding the three sodium ions to the outside and the two potassium ions to the inside. For some cells, such as electrically active nerve cells, 60 to 70 per cent of the cells' energy requirement may be devoted to pumping Na+ out of the cell and K+ into the cell.



Secondary Active Transport— Co-Transport and Counter-Transport

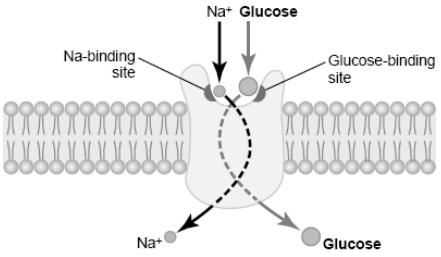
When sodium ions are transported out of cells by primary active transport, a large concentration gradient of sodium ions across the cell membrane usually develops—high concentration outside the cell and very low concentration inside. This gradient represents a storehouse of energy because the excess sodium outside the cell membrane is always attempting to diffuse to the interior. Under appropriate conditions, this diffusion energy of sodium can pull other substances along with the sodium through the cell membrane. This phenomenon is called **co-transport**; it is one form of **secondary active transport.**

For sodium to pull another substance along with it, a coupling mechanism is required. This is achieved by means of still another carrier protein in the cell membrane.

The carrier in this instance serves as an attachment point for both the sodium ion and the substance to be co-transported. Once they both are attached, the energy gradient of the sodium ion causes both the sodium ion and the other substance to be transported together to the interior of the cell. In **counter-transport,** sodium ions again attempt to diffuse to the interior of the cell because of their large concentration gradient. However, this time, the substance to be transported is on the inside of the cell and must be transported to the outside. Therefore, the sodium ion binds to the carrier protein where it projects to the exterior surface of the membrane, while the substance to be counter-transported binds to the interior projection of the carrier protein. Once both have bound, a conformational change occurs, and energy released by the sodium ion moving to the interior causes the other substance to move to the exterior.

Co-Transport of Glucose and Amino Acids Along with Sodium Ions

Glucose and many amino acids are transported into most cells against large concentration gradients; the mechanism of this is entirely by co-transport. Note that the transport carrier protein has two binding sites on its exterior side, one for sodium and one for glucose. Also, the concentration of sodium ions is very high on the outside and very low inside, which provides energy for the transport. A special property of the transport protein is that a conformational change to allow sodium movement to the interior will not occur until a glucose molecule also attaches. When they both become attached, the conformational change takes place automatically, and the sodium and glucose are transported to the inside of the cell at the same time. Hence, this is a **sodium-glucose co-transport** mechanism. **Sodium co-transport of the amino acids** occurs in the same manner as for glucose, except that it uses a different set of transport proteins. Five **amino acid transport proteins** have been identified, each of which is responsible for transporting one subset of amino acids with specific molecular characteristics. **Sodium co-transport of glucose and amino acids occurs especially through the epithelial cells of the intestinal tract and the renal tubules of the kid** **iese substances into the blood**. Other important co-t **ome** cells include co-transport of chloride ions, iodine i



Vesicular Transport

Materials move into or out of the cell by means of vesicl

1. Endocytosis (Clathrin-mediated)
2. Receptor mediated endocytosis
3. Pinocytosis
4. Phagocytosis
5. Exocytosis

ALL are active processes (require ATP) though they are not usually referred to as "active transport"

Endocytosis:

Pinocytosis:

Non specific process.

Plasma membrane invaginates, fuses, vesicle containing ECF pinches off, and vesicle enters cell.

- Phagocytosis:

  Phagocytic cells use pseudopods to surround and engulf particles.
  Pseudopods join, fuse, and surround ingested particle (food vacuole).

Exocytosis:

- Process by which cellular products are secreted into extracellular environment.
- Proteins and other molecules to be secreted are packaged in vesicles by Golgi complex.
- Vesicles fuse with plasma membrane and release contents into extracellular environment.

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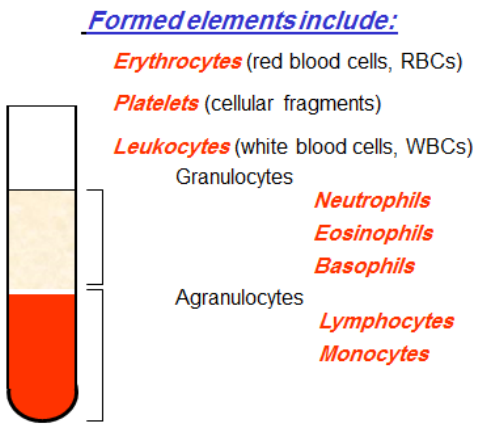
Blood

Blood is a viscous fluid which circulates through a closed system of blood vessels.

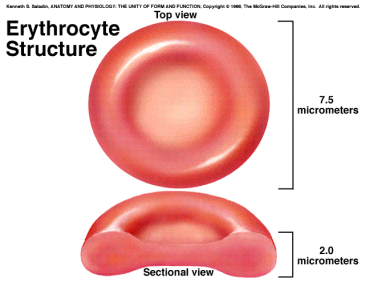
Composition of blood:

It consists of two parts, a fluid portion which is yellow in color called plasma and cellular elements which include different types of cells:

1. Red blood cells (Erythrocytes).
2. White blood cells (Leukocytes) of different types (Neutrophils, Eosinophils, Basophils, Monocytes and Lymphocytes).
3. Platelets (Thrombocytes).



The major function of R.B.C. is to transport hemoglobin which in turn carries oxygen from the lungs to the tissues. R.B.C. are biconcave discs having a mean diameter of about 7.5 micrometers and a thickness at the thickest point of 2.0 micrometers and in the center of 1 micrometers or less. The average volume is 90-95 mm^3.



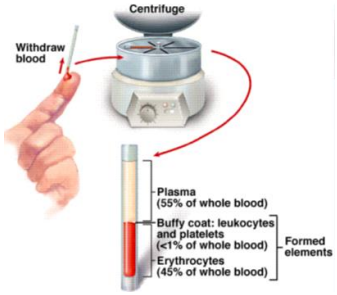
The shapes of R.B.C. , can change remarkably as the cells pass through capillaries. In normal men, the average number of R.B.C., per cubic millimeter is 5.4 millions (± 300,000) and in women is 4.8 millions (±300,000). This difference is due to the presence of testosterone hormone in male, this causes stimulation of the bone marrow which produces the R.B.C.

The concentration of Hb in R.B.C. , is about 34%, every 100 ml of R.B.C. contain 34 gm of Hb. Hemoglobin is a pigment in R.B.C.

The average concentration of Hb in the male is about (13- 18) gm/100 ml blood. In female is about (12-16) gm/100 ml blood, every 1 gm of Hb can combine with 1.39 ml of O2. In male each 100 ml of blood contain over 21 ml of O2 while in female it contains 19 ml of O2.

Hematocrit:

The ratio between plasma and cellular elements is 55% plasma to 45% cellular element (mainly R.B.C.) this ratio is called hematocrit or packed cell volume (P.C.V.) .When the percentage of R.B.C. is below 45% this causes anemia, while the percentage is above 45%, this causes polycythemia.



Plasma:

The fluid of blood, it contains protein, organic and inorganic substances of blood.

There are three types of protein in plasma:

1. Albumin, is present in the concentration of 4.5 gm/dl , its primary function is to cause osmotic pressure at the capillary membrane.
2. Globulin, is present in the concentration 2.5 gm/dl are divide into α , β and γ. α and β function in transporting substances by combining with them , γ to a lesser degree. β globulin play a special role in protecting the body against infection.
3. Fibrinogen, is present in the concentration of (0.3 gm/dl) it's of basic importance in blood clotting.

The total value of plasma protein is about 7 gm/100 ml plasma.

Blood functions:

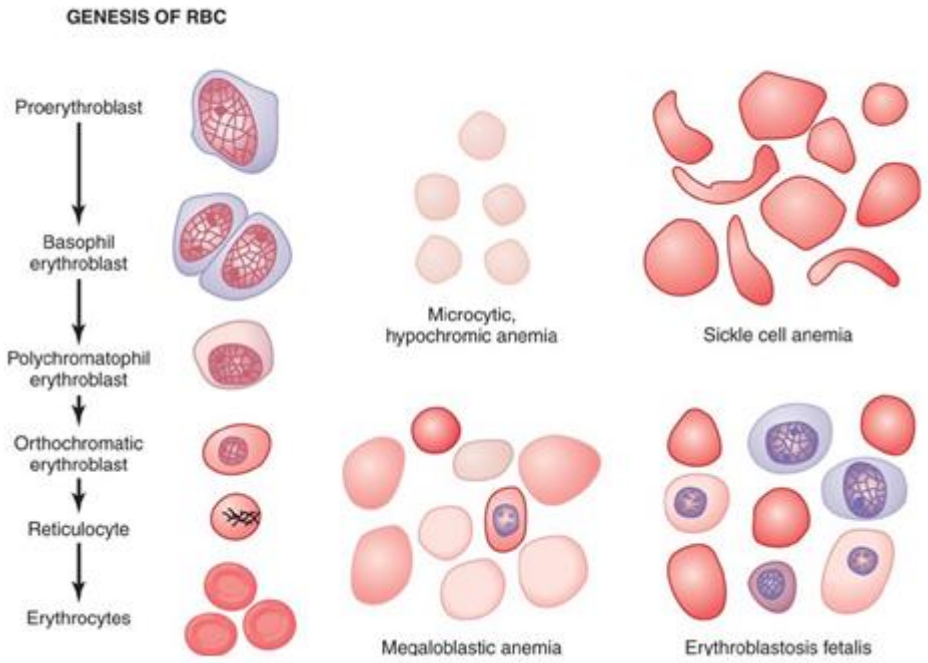
1. The main function of the blood is to transport gases O2 and CO2 . O2 is transported from lungs to the tissue of the body and CO2 is transported in opposite direction that is from the tissue to the lungs.
2. Is the delivery of nutrients, such as glucose, amino acids, fatty acids and vitamins to the tissue.
3. Distribution of heat, heat is generated by deep organs in the body, then it's distributed to all parts of the body.
4. Regulation of ions concentration and PH through the constant exchange of electrolytes between tissue fluids.
5. Protective function.

The W.B.C. play an important role in protection function of the blood in which they defend the body against infection of bacteria, viruses and other foreign bodies.

Genesis of R.B.C. :

R.B.C.s are derived from the cell known as Hemocytoblast which is formed from primodial stem cells located in bone marrow . The Hemocytoblast forms the Basophils erythrocytes (begins the synthesis of Hb). Then it becomes Polychromatophil erythroblast then the nucleus shrinks and the cell becomes Normoblast and then the nucleus extruded. At the same time endoplasmic reticulum reabsorbed and the cell called Reticulocyte when the reticulum is completely reabsorbed the cell then is a mature Erythrocyte.

R.B.C. are produced during early embryonic life by the yolk sac, the spleen and liver begin to produce R.B.C.s , during later embryonic life at age 20 , bone (whether flat or long) begins to produce R.B.C.s and flat bones produce R.B.C., such as bones of the skull, ribs and sternum. The increase of R.B.C.s count under normal value is called Polycythemia.



<u>There are two types of polycythemia:</u>

1. <u>Physiological Polycythemia (secondary)</u> :

   Whenever the tissue becomes hypotoxic because of too little oxygen in the atmosphere, such as at high altitudes, or because of failure of delivery of oxygen to tissues, as occurs in cardiac failure, the blood forming organs automatically produce large quantities of R.B.C.s , the blood count is generally 6-7 million/mm^3

2. <u>Pathological Polycythemia (Vera):</u>

   Which occur during the pathological condition such as cancerous conditions, in which cancer stimulates great number of R.B.C.s to be produced. The R.B.C. count may be 7-8 million/mm and the hematocrit 60-70%.

Anemia :

Anemia means a deficiency of R.B.C.s, which can be caused either by too rapid loss or by too slow production of R.B.C.s , There are different types of anemia:

1.Blood loss anemia: This s caused by loss of large volume of blood usually when there is a blood loss, the plasma is replaced quickly while the R.B.C.s , takes few weeks to be replaced. This is caused in some chronic blood such as (Hemorrhoid).

2.Bone marrow aplasia (aplastic anemia)::

This means the loss of function of bone marrow due to drug poisoning or Gamma-ray irradiation.

3.Hemolysis of R.B.C.s: Resulting from many of causes such as:

a. Drug poisoning.

b. Hereditary diseases such as (sickle cell diseases, spherocytosis, Hbs).

c. Erythroblastosis fetalis, a disease of the newborn in which antibodies from the mother destroy red cells in the baby.

4. Thalasemia (Cooly's anemia):

It's also called Mediterranean anemia, there is a deficiency of globulin, for example: Deficiency of polypeptide chain which causes decrease in concentration of Hb.

5. Maturation failure or (pernicious anemia):

Because of lack of vitamin B12 or folic acid. Vitamin B12 is an essential nutrients for all cells of the body and growth of tissues. Vitamin B12 is required for synthesis of DNA, lack of this causes failure of nuclear marutation and division and therefore inhibits R.B.C.s production.

When the vitamin B12 replaced by intestinal bacteria, is called extrinsic factor and there is other factor called intrinsic factor. B12 should combine with intrinsic factor, if the intrinsic factor is absent, then B12 will not absorbed this disease is called pernicious anemia, in which the

basic abnormality is an atrophic gastric mucosa. In pernicious anemia R.B.C.s are larger than the normal and undergo hemolysis easily.

Destruction of R.B.C.s

R.B.C.s are delivered from the bone marrow into the circulatory system an average of 120days, have no nucleus, endoplasmic reticulum and mitochondria, they have cytoplasmic enzymes that are capable of metabolizing glucose and forming small amount of ATP, which serves the red cell in:

1. Maintaining the pliability of the cell membrane.
2. Maintaining membrane transport of ions.
3. Keeping the iron of the cell hemoglobin in the ferrous form, rather than the ferric form.
4. Preventing oxidation of the proteins in the red cell.

These metabolic system of the red cell become progressively less active with time, and they become more and more fragile, because their life processes wear out.

- **Effect of anemia on circulatory system:**

  It effects the viscosity of the blood from (3-1.5) and decrease resistance of blood flow in the peripheral blood vessels and also cardiac output increase 2 times. Hypoxia cause increase in return of blood to the heart, increasing the cardiac output to a still higher level.

- **Effect of polycythemia on circulatory system:**

  Here, increase blood volume, decrease in the rate of venous return to heart, sluggish blood flow through vessels, increase circulation time and increase in the deoxygenated Hb.

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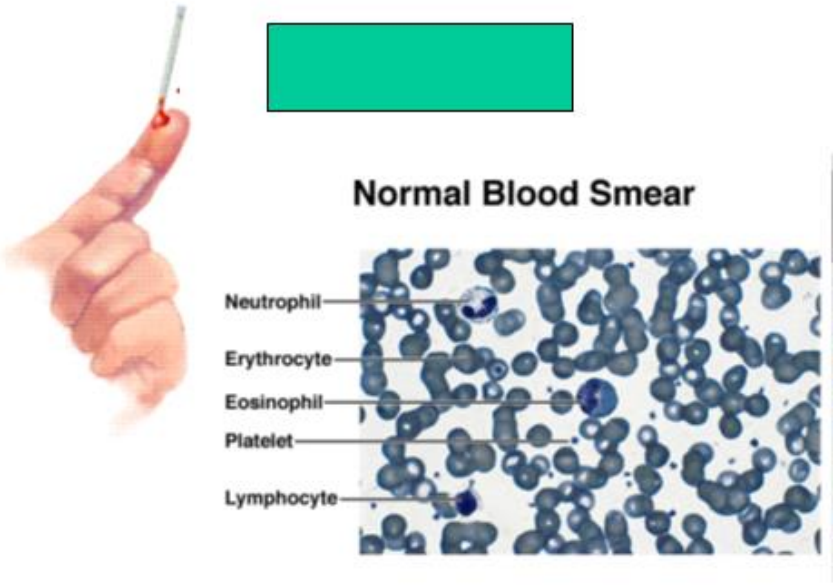
White blood cells

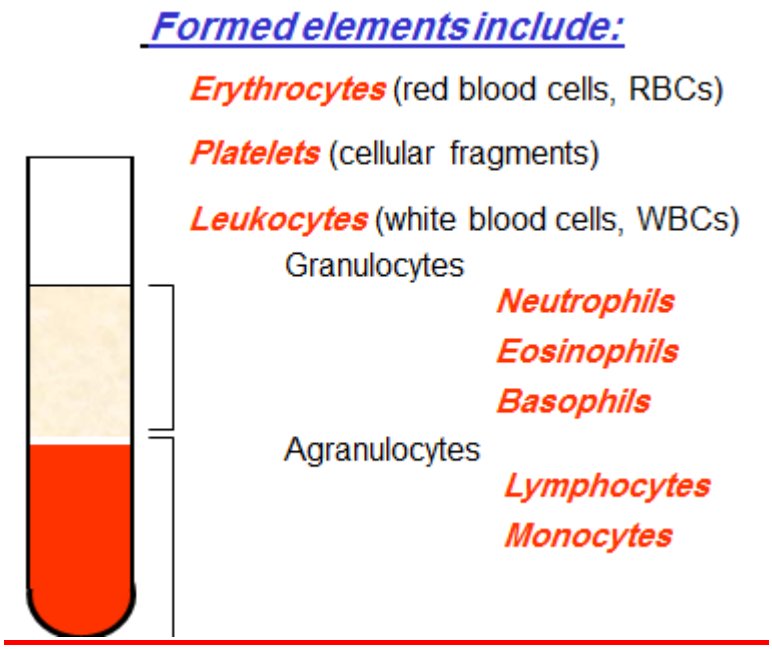
The W.B.C., count is from (4000-11000) cells/mm³, if the count less than 4000, the condition is called leukopenia, if it's more than 11000, the condition is leukocytosis. W.B.C. are involved in the body defense mechanism against mirco-organisms and other foreign materials. W.B.C. are classified according to the type of cytoplasm into the following:



1. ***Granular leukocytes***: in which the cytoplasm contain granules, these are classified into polymorphonuclear leukocytes which include:
   - **A.** ***Neutrophils:*** multilobed nucleus, 2-5 lobes depending on the age of the cell. The percent is 65%.
   - **B.** ***Eosinophils:*** multilobed nucleus (usually bilobed). The percent is 1-3%.
   - **C.** ***Basophils:*** in this type, the nucleus take the (S) shape. The percent less than 1%.

2. ***Agranular leukocytes:*** in which is no granules in the cytoplasm, these are classified into:
   - **A.** ***Monocytes:*** the nucleus is kidney shaped and they are the largest cells in the body. The percent is 7%.
   - **B.** ***Lymphocytes:*** they are large lymphocytes and a small lymphocytes which depend on the age, the percent is 30%.

The granulocytes and monocytes protect the body against invading organisms mainly by ingesting them, that is, by phagocytosis. The lymphocytes and plasma cell function mainly in connection with immune system.



Genesis of the leukocytes

The granulocytes and monocytes are formed only in the bone marrow, lymphocytes and plasma cells are produced mainly in the various lymphogenesis organs, including the lymph gland, spleen, thymus…etc.

Life span of the W.B.C.

The main reason W.B.C., are present in the blood is to be transported from the bone marrow or lymphoid tissue to the areas of the body where they are needed.

The life of the granulocytes, once released from the bone marrow is normally 4-8 hours, circulating in the blood and another 4-5 days in the tissues. In times of serious tissue infection, this total life span is often only a few hours, because the granulocytes proceed rapidly to the infected area.

The monocytes also have a short time, 10-20 hours, in the blood before wandering through the capillary membrane into the tissue. They can live for months or even years unless they

are destroyed by performing phagocytic function. The lymphocytes have life span of weeks, months, or even years, but this depends on the body's need for these cells.

Our bodies have a special system for combating the different infections and toxic agents. This composed of W.B.C., and tissue cells. These cells all work together to prevent diseases by actually destroying invading agents by phagocytosis and by forming antibodies and sensitized lymphocytes.

Phagocytosis:

The most important function of the neutrophils and macrophages is phagocytosis which mean cellular ingestion of the offending agent.

Phagocytes must be selective of the material that is phagocytosed, otherwise, some of the normal cells and structure of the body would be ingested. Whether or not phagocytosis will occur depends especially on three selective procedures:

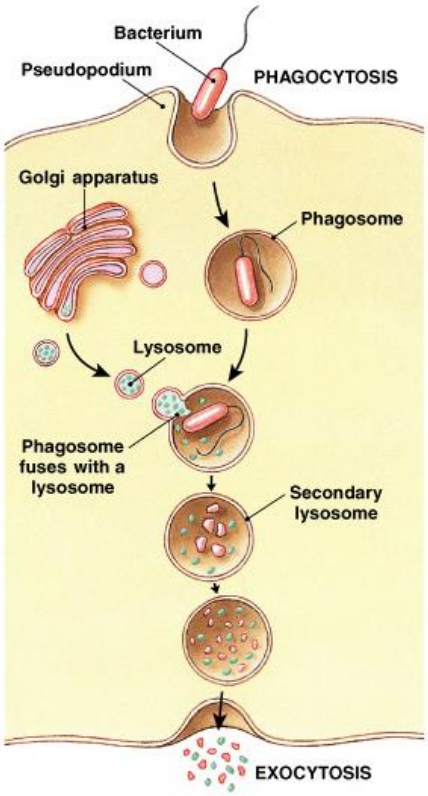
1. Most natural structures in tissue have smooth surface, which resist phagocytosis. But if the surface is rough, the likelihood of phagocytosis is increased.

2. Most natural substances of the body have protective protein coats that they repel the phagocytes, on the other hand, dead tissues and most foreign particles frequently have no protective coats, which also make the subject to phagocytosis.

3. The body has a specific means of recognizing certain foreign materials.

The immune system develops antibodies against infectious agents like bacteria. The antibodies adhere to the bacterial

membrane and there by make the bacteria especially susceptible to phagocytosis.



Inflammation:

When tissue injury occurs, whether caused by bacteria, trauma, chemicals, heat or any other phenomenon, multiple substances that cause dramatic secondary changes in the tissues are released by the injured tissues. The entire complex of tissue changes is called **INFLAMMATION**.

Inflammation is characterized by:

1. Vasodilation of the local blood vessels.
2. Increased permeability of the capillaries.
3. Often clotting of the fluid in the interstitial spaces because of the excessive amounts of fibrinogen and other protein leaking from the capillaries.

4. Migration of large number of granulocytes and monocytes in the tissue.
5. Swelling of the tissue cells.

Leukemias

Uncontrolled production of W.B.C. is caused by cancerous mutation myelogenous and lymphogenous cell.
Leukemias are divided into:
1. Lymphogenous leukemia.
2. Myelogenous leukemia.

The effect of leukemia is metastatic growth of leukemic cells in abnormal areas of the body. Almost all leukemias spread to the spleen, lymph nodes, liver, and other especially vascular regions. In myelogenous leukemia, the cancerous process produces partially differentiated cells, resulting in what might called:

1. Neutrophilic leukemia.
2. Eosinophilic leukemia.
3. Basophilic leukemia.
4. Monocytic leukemia.

More frequently, however, the leukemia cells are bizarre and undifferentiated and not identical to any of the normal W.B.C.. usually the more undifferentiated the cells, the more acute is the leukemia, often leading to death within few months if untreated.

Leukopenia or Agranulocytosis:

A clinical condition known as leukopenia occurs in which the bone marrow stops producing W.B.C. leaving the body unprotected against bacteria and other agents that might invade

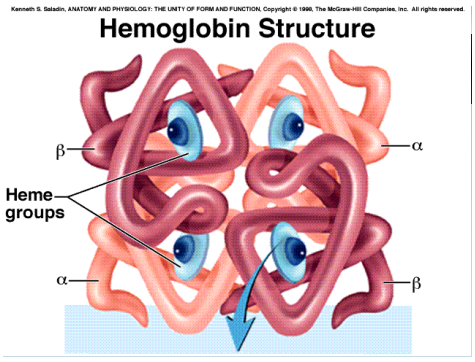
the tissues. Without treatment, death often is less that a week after acute total leukopenia begins. This result from different cases:

1. Irradiation of the body by gamma rays caused by a nuclear explosion.
2. Exposure to drugs and chemical that contain benzene or other is likely to cause aplasia of the bone marrow.

Hemoglobin

Hb is a pigment in R.B.C., it is a protein with molecular weights (64,458). The normal value of Hb is 14-16 gm/100ml blood, every 1 gm of Hb can combine with 1.39 ml O2 . Synthesis of Hb begins in the erythroblasts and continues through the normoblast and reticulocyte stage. Heme portion of Hb is synthesized mainly from acetic acid and glycine and that most of this synthesis occur in mitochondria. The chemical steps in formation of Hb. First, succinyl-CoA binds with glycine to form pyrrole. In turn, four pyrrole combine to form protoporphyrin 1x, which then combine with iron to form heme molecule. Finally, each heme molecule combine with long polypeptide chain, called globin, synthesized by the ribosomes, forming a subunit called Hb chain. Each chain has a molecular weight about 16.000, four of them turn, bind together loosely to form Hb.

1. 2 succinyl-coA+2 glycine → pyrrole
2. 4 pyrrole → protoporphyrin 1x
3. protoporphyrin 1x + Fe → heme
4. heme+polypeptide→hemoglobin chain(α or β)
5. 2 α chains + 2 β chains → hemoglobin A



Formation of Hemoglobin

- Each erythrocyte contains about 280 million molecules of Hb. Hemoglobin consists of four protein chain called globins, two of these, the alpha chain (α), are 141 amino acids long, and other two, the beta (β) chains are 146 amino acids long. Each chain is conjugated with a nonprotein moiety called the heme group. Each heme can carry one molecule of O2, the Hb molecule as a whole can transport up to 4 O2 . About 20% of carbon dioxide in the bloodstream is also transported by Hb.

- Hemoglobin exists in several forms that display slight differences in the globin chains, the form adult Hb (HbA).

- About 2.5% of (HbA), however, is of a form called HbA2, which has a two delta (δ) chains in place of the β chains.

The fetus produces a form called fetal Hb or (HbF), which has two Gamma (γ) chains in the place of the adult β chains. HbF has a higher oxygen-binding capacity than adult HbA and enables the fetus to extract oxygen from the mother's bloodstream. The delta (δ) and gamma (γ) chains are the same length as the (β) chains, but differs in amino acid sequence. HbF is converted into HbA, but in some cases is not converted.

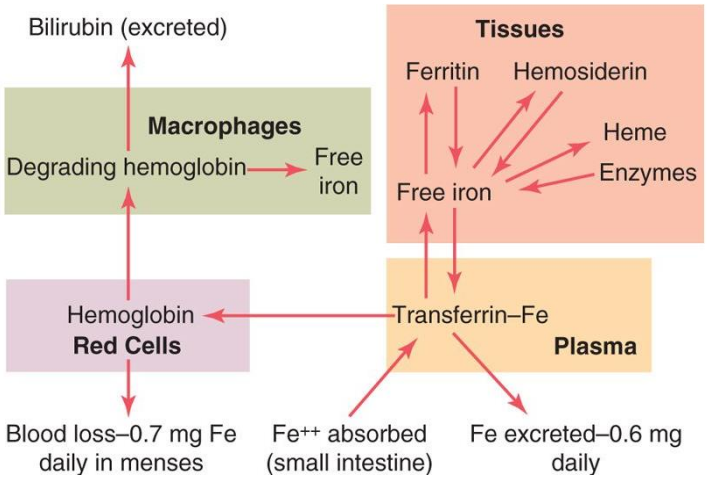
Iron Metabolism

- Because iron is important for formation of Hb, myoglobin and other substances such as cytochromes, cytochrome oxidase, peroxidase, and catalase, it is essential to understand the means by which iron is utilized in the body.
- The total quantity of iron in the body average 4-5 grams, about 65% of which is in the form of Hb.
- About 4% is in the form of myoglobin, 1% is in the form of the various heme compounds that promote intracellular oxidation, 0.1% is combined with the protein transferrin in the blood plasma, and 15-30% is stored mainly in the

reticuloendothelial system and liver parenchymal cells, principally in the form of ferritin. A man excretes about 1 mg of iron each day, mainly into the feces

When iron is absorbed from the small intestine, it immediately combines in the blood plasma with beta globulin, apotransferria to form transferrin, which is then transported in the plasma.

The iron is loosely combined with the globulin molecule and consequently, can be released to any of tissue cells at any point in the body. Excess iron in the blood is deposited in all cells of the body, but especially in liver hepatocytes. In the cell cytoplasm, it combines mainly with a protein, apoferritin to form ferritin. The iron stored as ferritin is called ***storage iron***. Smaller quantities of the iron in the storage pool are stored, insoluble form called ***hemosiderin***. When the quantity of iron in plasma falls very low, iron is removed from ferritin quite easily, but much less easily from hemosiderin. When red blood cells have lived their life span and are destroyed, the Hb released from the cells is ingested by the cells of the monocytes-macrophage system. There free iron is liberated, and it is mainly stored in the ferritin pool or formation of new Hb.



Hb Compounds

There are different compounds of Hb:

1. ***Oxyhemoglobin:*** this results from combination of O2 with Hb.

$$Hb + O2 \rightarrow HbO2$$

2. ***Carboxy Hb:*** this results from union of Co gas with Hb, Co gas is a very poisonous gas even if it is present in very small amount it displaces O2 in OxyHb so that carboxy Hb is produced, this is because of Co gas is about 250 times greater than O2 to Hb.

3. ***Sulfa Hb:*** this compound results from the combination of Hb with sulpher compounds.

4. ***Carbamino Hb:*** this results from the combination of CO2 gas with Hb.

$$Hb + CO2 \rightarrow HbCO2$$

5. ***Methemoglobin:*** if Hb subjected to O2 in the presence of an oxidizing agent, oxidation occurs and a new compound is produced is called Meth Hb.

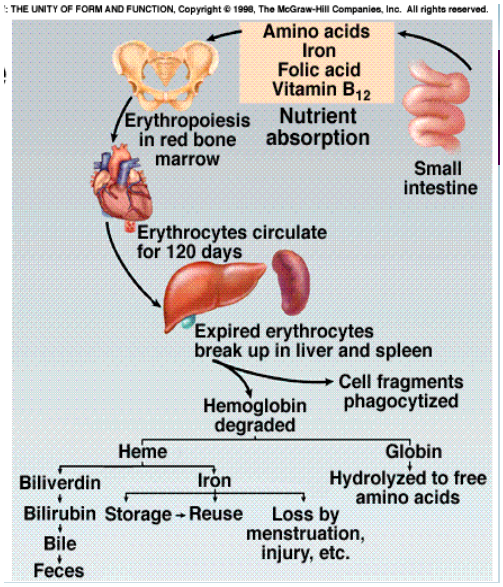
$$\text{Met Hb Fe} \rightarrow Fe + Hb \rightarrow HbFe$$

Destruction of Hb

The Hb released from the cells when they burst is phagocytosed almost immediately by macrophages in many parts of the body, but especially in liver (Kupffer cells), spleen and bone marrow. During the next few hours to days, the macrophage release the iron from the Hb back into the blood to be carried by transferrin either to bone marrow for production of new R.B.C. or to the liver and other tissues for storage in the form of ferritin. The porphyrin portion of the Hb molecule is converted by the macrophages, through a series of stages, into bile pigment bilirubin, which released into the blood and later secreted by the liver into the bile. A high level of bilirubin in the blood causes Jaundice, a yellowish cast in light-colored skin and the whites of eyes. Jaundice may be a sign of rapid hemolysis or a liver diseases. The normal plasma concentration of bilirubin is 0.5 mg/dl. The skin begins to appear jaundiced when concentration rise 1.5 mg/dl .

The common causes of jaundice are:

1. Increased destruction of R.B.C. with rapid release of bilirubin into blood.
2. Obstruction of the bile duct or damage to the liver cells.



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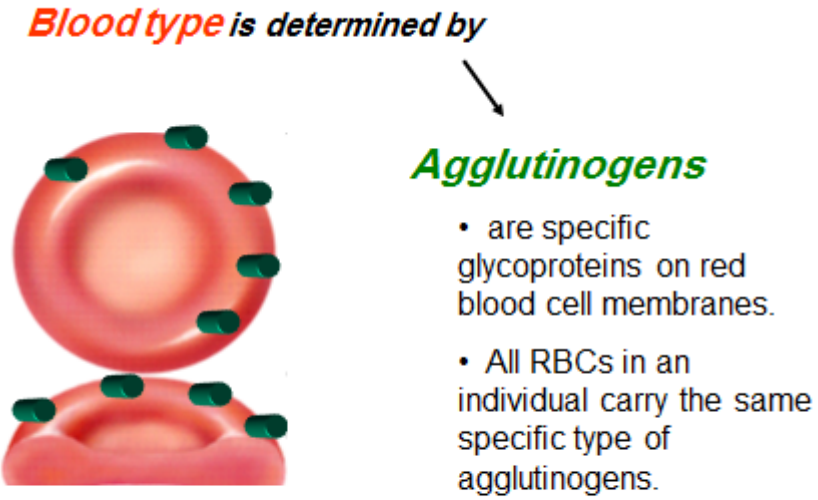
Blood Groups

The ABO blood group consists of blood types A, B, AB and O, depending on the presence or absence of two antigens –type A and type B- occur on the surface of the R.B.C. it is also called (agglutinogens) because they often cause blood cell (agglutination) that cause blood transfusion. Because of the way these agglutinogens are inherited, people may have neither of them on their cells, they may have one, or they may have both simultaneously.

Type A: RBCs carry agglutinogen A.
Type B: RBCs carry agglutinogen B.
Type O: RBCs carry no A nor B agglutinogens.
Type AB: RBCs carry both A and B agglutinogens



Many genes have more than two alleles in a population. The ABO groups afford multiple alleles. Phenotypically, a person may have blood type A,B,AB and O owing to presence of three alleles in the population. Two of alleles are dominant and symbolized with a capital (I) (for immunoglobulin) and a superscript: I and I . there is one recessive allele, symbolized with a lower case i.

Genotype	Phenotype
I I	A
I i	A
I I	B
I i	B
I I	AB
i i	O

The essential function of DNA is to serve as a code for the structure of protein synthesized by a cell. A gene is a sequence of DNA nucleotides that code for a protein.

Agglutinins react against any AB agglutinogen expect those present on a person's own R.B.C. the agglutinin that reacts against antigen A is called α agglutinin, or anti-A, it is present in the plasma of people with type O or type B blood- that is , any one who does not possess agglutinogen A . the agglutinin that reacts against antigen B is β agglutinin, or anti-B, and is present in type O and A individuals – those

who don't possess agglutinogen B. Each agglutinin molecule has 10 binding sites where it can attach to an A or B agglutinogen. An agglutinin can therefore attach to several R.B.C. s at once and bind them together.

Agglutination

Is the process in which R.B.C. s adhere to each other in masses that are bound by these agglutinins.

Agglutinins

The agglutinins are gamma globulins, as other antibodies, and they are produced by the same cells that produce antibodies to any other antigens. Most of them are IgM and IgG immunoglobulin molecules. But why are these agglutinins produced in people who do not have the respective agglutinogens in their R.B.C.s? however, small amount of group A and B antigens enter the body in the food, in bacteria, and in other ways and these substances initiate the development of the anti-A or anti-B agglutinins.

Blood types	***Agglutinogens***	***Agglutinins***
A	**A**	**Anti B**
B	**B**	**Anti A**
AB	**A and B**	**———**
O	**———**	**Anti A and Anti B**

A person's ABO blood type can be determined by placing one drop of blood in a pool of anti-A serum and another drop in a pool of anti-B serum. Blood type AB will exhibit conspicuous agglutination in both antisera; type A or

B will agglutinate only in the corresponding antiserum; and type O will not agglutinate in.

Anti-A	Anti-B	Percentage %
Type A +	–	41%
Type B –	+	9%
Type AB +	+	3%
Type O –	–	47%

In giving transfusion, it is imperative that the donor's blood not agglutinate as it inters the recipient's blood stream. For example, if type B blood were transfused into type A recipient, the recipient's anti-B agglutinins would immediately agglutinate the donor's R.B.C.s. a mismatched transfusion causes a *Transfusion Reaction*. The agglutinated R.B.C.s block small blood vessels, hemolyze, and release their Hb over the next few hours to days. Free Hb can block the kidney tubules and cause death within a week or so from acute renal failure. For this reason, a person with type A (anti-B) blood must never be given a transfusion of type B or AB blood.

Type (AB) called the *Universal Recipient* while (O) *Universal Donor*.

The Rh Group

Along with the O-A-B blood group system, the Rh system is important in the transfusion of blood. In the O-A-B, the agglutinins responsible for causing transfusion reaction develop spontaneously, where as in the Rh system, spontaneous agglutinins almost never occur. There are 6 types of Rh antigens, each of which is called an Rh factor.

These types are C,D,E,c,d and e .A person who has a C antigen doesn't have c, but person missing the C antigen always has the c antigen. The same for D-d and E-e antigens. The type D is widely prevalent in the population. Therefore, anyone who has this type is said to be Rh+, where as a person who does not have type D is said to be Rh– .About 85% of people are Rh+ and 15% are Rh– .

Formation of Anti-Rh agglutinins:

When R.B.C.s containing Rh factor or even protein breakdown products of such cells are injected into a person whose blood does not contain the factor- that is, into the Rh– person anti-Rh agglutinins develop slowly and maximum concentration of agglutinins occurring about 2-4 months. On multiple exposure to Rh factor, the Rh– person become strongly (*sensitized*) to Rh factor.

Erythrobastosis Fetalis (Hemolytic disease of Newborn)

This disease of the fetus is characterized by agglutination and phagocytosis of R.B.C.s . In most instances of this diseases, the mother is Rh– and father is Rh+. The baby has inherited the Rh+ antigen from father, and mother has developed anti-Rh agglutinins from exposure to the baby's Rh antigen , in turn, the mother agglutinins diffuse through the placenta into the fetus to cause R.B.C.s agglutination.

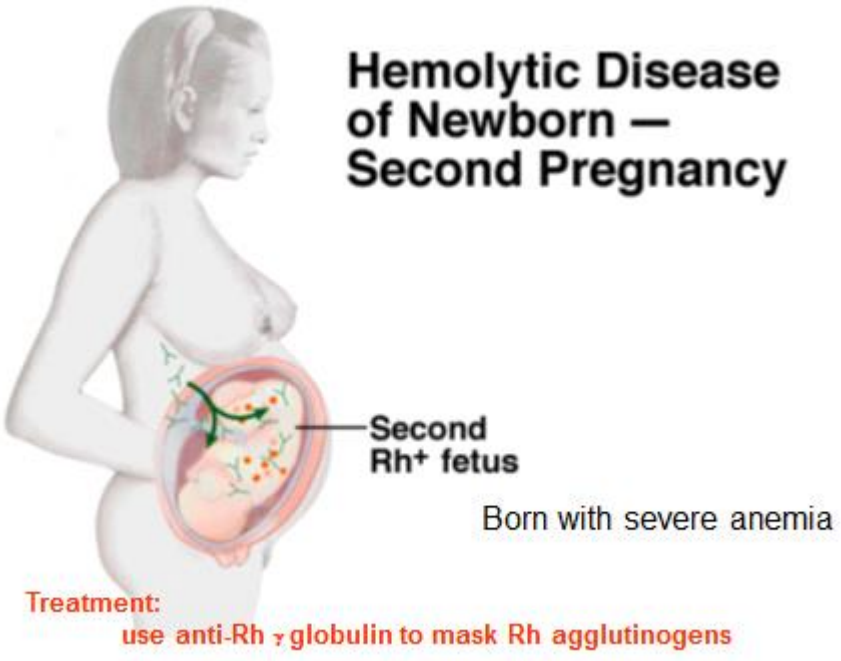
Effect of the Mother's Antibodies on the Fetus:

After anti-Rh antibodies have formed in the mother, they diffuse slowly through the placental membrane into the fetus's blood. There they cause agglutination of fetus's blood. The agglutinated R.B.C.s subsequently hemolyze, releasing Hb into the blood. The macrophages then convert the Hb into *Bilirubin*, which causes the skin to yellow (Jaundice). The antibodies can also attack and damage other cells of the body. The jaundiced erythroblastotic neonate is usually anemic at birth, and anti-Rh agglutinins from mother usually circulate in the infant's blood for 1-2 months after birth, destroying more and more R.B.C.s.

The usual treatment is to replace the neonate's blood with Rh– blood. About 400 milliliters of Rh– blood is infused over a period of 1.5 or more hours while the neonates own Rh+ blood is being removed. The Rh– cells are replaced with the baby own Rh+ cells.

Transfusion Reactions resulting from mismatched Blood Types

If donor's blood of one blood type is transfused to a recipient of another blood type, a transfusion reaction is likely in which the R.B.C.s of donor blood are agglutinated. It is rare that the transfused blood causes agglutination of the recipient's cells, the plasma portion of the donor's blood immediately becomes dilated by all the plasma of recipient, there by decreasing the titir of infused agglutinins to a level low to cause agglutination. On other hand, the infused blood does not dilute the agglutinins in the recipient's plasma to major extent. Therefore, the recipient's agglutinins can still agglutinate the donor's cells.



Nature of Antibodies

The antibodies are gamma globulins called immunoglobulin and they have molecular weights between 160,000-970,000. they always constitute about 20% of all the plasma protein.

It is composed of combinations of light and heavy polypeptide chains, most of combination are 2 light and 2 heavy chains.

This structure of the typical IgG, showing 2 heavy polypeptide chains and 2 light polypeptide chains. The antigen binds as two different sites on the variable portion of the chains. The end of each light and heavy called variable portion, the remainder of each chain is called constant portion.

Each antibody is specific for a particular antigen, this caused by the structural organization of amino acids in variable portion of both light and heavy.

There are many bonding sites that antibody-antigen coupling is nevertheless exceedingly strong, held together by:

1. **Hydrophobic bonding.**
2. **Hydrogen bonding.**
3. **Ionic attractions.**
4. **Van der walls forces.**

There are five general classes of antibodies, respectively IgM, IgG, IgA, IgD and IgE. The antibodies have 10 binding sites that make them exceedingly effective in protecting the body against invaders.

The antibodies acts mainly in two ways to protect the body invading agents by:

1. **direct attack on the invader and.**
2. **by activation of complement system.**

In the direct attack, the antibody like Y-shaped bars, reacting with antigens, because of bivalent nature of the antibodies and multiple antigen sites on most invading agents, the antibodies can inactivate the invading agents in several ways:

1. **Agglutination, in which multiple large particles with antigen on their surface.**
2. **Precipitation, in which the molecular complex of soluble antigen and antibody becomes so large that it is rendered insoluble and precipitates.**
3. **Neutralization, in which the antibodies cover the toxic sites of the antigenic agent.**

4. **Lysis, in which some potent antibodies are occasionally capable of directly attacking membranes of cellular agents and there by causing rupture of the cell.**

The Activation of Complement: **complement is a collective term describes a system of about 20 proteins, many of which are enzyme precursors.**

أ.د.خالد حمدان

Hemostasis and Blood Coagulation

The term hemostasis means prevention of blood loss. This achieved by several mechanisms, including:

1. **Vascular spasm.**
2. **Formation of a platelets plug.**
3. **Formation of blood clot.**
4. **Growth of fibrous tissue into the blood clot to close the whole vessel permanently.**

Vascular Spasm

The most immediate protection against blood loss is vascular spasm, a prompt constriction of the broken vessel. Several things trigger this reaction. An injury stimulates with pain receptors, some of which directly innervate nearby blood vessels and cause them to constrict. Immediately after a blood vessel is cut or ruptured, the stimulus of the trauma to the vessel causes the wall of the vessel to contract due to nervous reflexes, local myogenic spasm and local humoral factors from blood platelets.

Formation of a Platelet Plug.

Platelets are not cells, but small fragments of megakaryote cytoplasm. Although they were once called thrombocytes. Platelets are small round or oval discs 2-4 µm in diameter.

They are formed in the bone marrow from megakaryocytes which are extremely large cells of the hemopoietic series in the bone marrow that fragment into platelets. The normal concentration of platelets in the blood is between 150,000 and 400,000 per µL.

Platelets have many functional, even through these do not have nuclei and can not reproduce. In their cytoplasm are such active factor as:

1. **They secrete growth factors that stimulate mitosis in fibroblasts and smooth muscle and help to maintain the linings of blood vessels.**

2. **They secrete vasoconstrictors that cause vascular spasm in broken vessels.**

3. **They form temporary platelet plugs to stop bleeding.**

4. **They phagocytize and destroy bacteria.**

5. **They secrete chemicals that attract neutrophils and monocytes to sites of inflammation.**

6. **They dissolve blood clots that have outlasted their usefulness.**

The cell membrane of the platelets is also important, on its surface is a coat of glycoproteins that causes it to avoid adherence to normal endothelium and yet to adhere to injured areas of the vessel wall.

Mechanism of the Platelet Plug

Platelet repair of vascular openings is based on several important functions of the platelet itself, when platelets come in contact with a damaged vascular surface, such as the collagen fibers in the vascular wall or damaged endothelial cells, they immediately change their characteristics. They begin to swell, they assume irregular forms and become sticky so that they stick to the collagen fibers, they secrete large quantities of ADP and their enzymes form thromboxane A2 in turn act on nearby platelets to activate them as well forming a platelet plug.

Formation of Blood Clot

The clot begins to develop in 15 seconds, if trauma of the vascular wall has been severe, and in 1-2 minutes if it is minor.

Mechanism of Blood Coagulation

The clotting takes place in three steps:

1. **In response to rupture of the vessel or damage to the blood, the complex of activated substances collectively called prothrombin activator.**
2. **The prothrombin activator catalyzes the conversion of prothrombin into thrombin.**
3. **The thrombin acts an enzyme to convert fibrinogen into fibrin fibers, that enmesh platelets, blood cells and plasma to form the clot.**

Conversion of Prothrombin to Thrombin :

Prothrombin is a plasma protein, an alpha 2- globulin, having a molecular weight of 68,700. it is present in normal plasma in a concentration 15 mg/dl. It is unstable protein that can easily split into thrombin which has a molecular weight 33,700 in presences of prothrombin activator and calcium ions.

Prothrombin is formed by the liver, vitamin K is required by the liver for normal formation of prothrombin.

Conversion of Fibrinogen to Fibrin

Fibrinogen is a high-molecular weight protein (340,000) that occurs in the plasma in quantities of 100-700 mg/dl. It's formed in the liver.
Thrombin is a protein enzyme with proteolytic capabilities, it act on fibrinogen to remove four low-molecular weight peptides from each

molecule of fibrinogen, forming a molecule of fibrin monomer that has the automatic capability of polymerizing with other fibrin molecule forming long fibrin fibers that form the reticulum of clot. There are two reaction pathways to coagulation, one of them, extrinsic mechanism, is initiated by clotting factors released by the damaged blood vessel and perivascular tissues. The reaction pathway it use only clotting factors found in the blood itself called intrinsic mechanim.

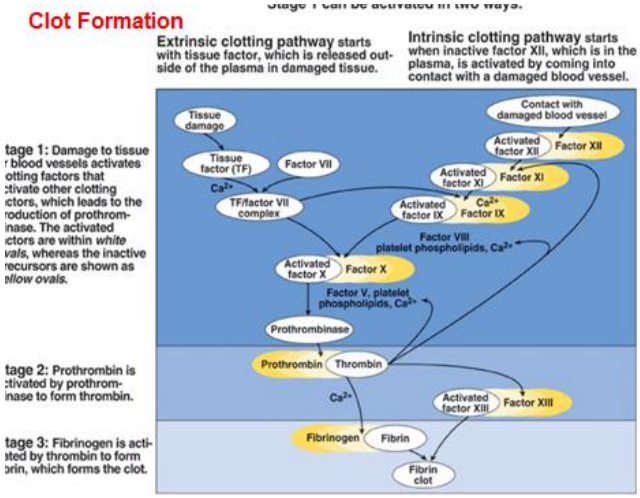
The extrinsic mechanism is the damage of blood vessel release lipoprotein mixture called thromboplastin (factor III) in the presences of Ca , thromboplatin activates factor VII, which then activates factor X. the extrinsic and intrinsic pathways differ only in how they arrive at active factor X.

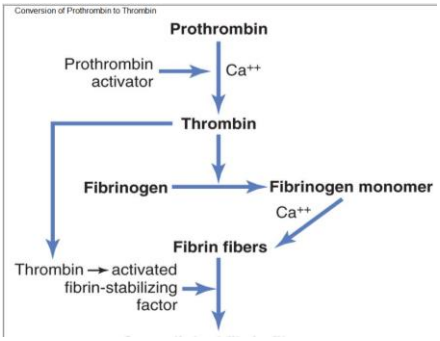
The intrinsic mechanism, when platelets degranulate, they release factor XII (Hageman factor) and then this leads to activated factors XI, IX and VIII, in that order, each serving as an enzyme that catalyzes the next step and finally to factor X. This pathway also requires calcium ions and platelet thomboplastic factor (PF3).

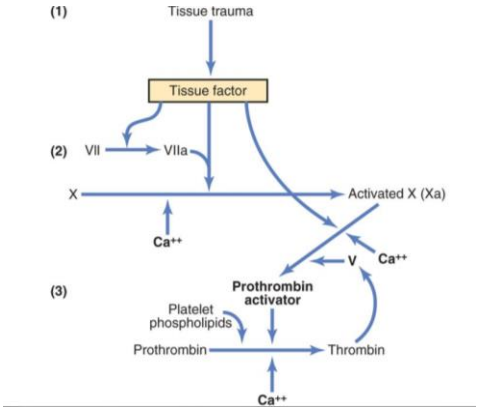
Once factor X is activated, the remaining events are identical in the intrinsic and extrinsic mechanisms. Factor X combines with factors III and V in the presence of (Ca and PF3) to produce an enzyme, prothombin activator, this enzyme acts on a globulin called prothrombin (factor II) , converting it to enzyme thrombin. Thrombin then converts fibrinogen to fibrin. Fibrin forms a loose mesh at first, but factor VIII causes the formation of covalent cross-links that convert this to fibrin polymer – a dense aggregation of fibers that forms the structural basis of the clot.

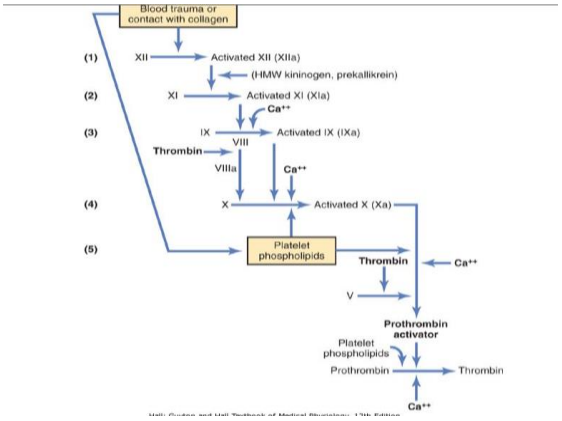
The especially important difference between extrinsic and intrinsic pathway is the extrinsic can explosive nature, once initiated, its speed of occurrence is limited only by the amount of tissue factor released from the traumatized tissues and by the quantities of factor X, VII and V in the blood. With severe trauma, clotting can occur in 15 seconds. While intrinsic usually 1-6 minutes to cause clotting.

Clot Formation









General Physiology Lect.9

أ.د.خالد حمدان

Prevention of Clotting in the Normal Vascular System

The intravascular anticoagulants

1. **<u>Endothelial surface factor:</u>**

   a. **The smoothness of endothelium, which prevents contact activation of the intrinsic clotting system.**
   b. **Layer of glycocalyx, a mucopolysaccharides adsorbed to the inner surface of the endothelium, which repels the clotting factor and platelets.**
   c. **A protein bound with endothelial membrane, thrombin which bind thrombomodulin, this dulin-thrombin not only slows the clotting process, but also activates a plasma protein, protein C, that acts as an anticoagulant by inactivating activated factors V and VIII.**

2. **<u>Antithrombin factor:</u> the most important anticoagulants in the blood itself that remove thrombin from blood, the most powerful**

   1. **The fibrin fibers that themselves are formed during the process of clotting and**
   2. **an alpha- globulin called antithrombin III or antithrombin – heparin co factor, about 85-90% of thrombin formed adsorbed to the fibrin fibers as they develop. The thrombin that does not adsorb to fibrin fibers, soon combines with antithrombin III, which block the effect of the thrombin on the fibrinogen and inactivates it within 12-20 minutes.**

3. **<u>Heparin:</u> is a conjugated polysaccharide, formed by the basophilic mast cells located in the pericapillary connective tissue throughout the body. It prevents blood coagulation by combining with antithrombin-heparin co factor which makes this factor combine with thrombin. The antithrombin heparin complex removes several other activated coagulation factors in addition to thrombin from circulating blood, the others include factors XII, XI, IX and X.**

Prevention of Blood Coagulation outside the Body:

1. **Heparin: it prevents the blood coagulation when added to the sample of blood outside the body as well as in the body.**

2. **Calcium-deionizing agent used for preventing coagulation is sodium, ammonium, or potassium citrate. The citrate ion combines with Ca in the blood to cause an un-ionized Ca compound, and lack of Ca prevents coagulation.**

3. **Collecting of the blood in siliconized containers, which prevents contact activation of platelets and factor XII, which are effects that initiate the intrinsic clotting mechanism.**

4. **Coumarine derivates: these are used internally to prolong the coagulation time from the normal range of about 2-3 minutes to 10 minutes. Vitamin K is essential for the formation of prothrombin by the liver, these substances when given they interfere with action of Vit. K and this cause a decrease in the formation of prothrombin by the**

liver and this causes prolongation of coagulation time, and this prevents the occur of blood clots.

Blood Disease

1. **Decreased prothrombin, factor VII, IX and X caused by Vitamin K.**

Hepatitis , cirrhosis (replacement of liver cells by fibrous tissue), acute yellow atrophy and the presence of a stone in the common bile duct (in which bile does not reach the duodenum) and this effect on the absorption of vit. K . all these factors cause a severe tendency to bleed.
These liver diseases often cause decreased production of prothrombin and the other factor both because of poor vitamin K absorption and because of the diseased liver cells.

2. ***Hemophilia:*** **it is a hereditary disease which affects the male only, the female is not affected by the disease, because at least one of her two X chromosomes will have the appropriate genes. If one of her X chromosomes is deficient, she will be a hemophilia carrier.**

There are three types of Hemophilia:
1. **Classical hemophilia (hemophilia A):**

This is caused by the deficiency of factor VIII.
2. **Hemophilia B: this caused by deficiency of factor IX.**
3. **Hemophilia C: this caused by the deficiency of factor XI.**

The treatment by giving the patient deficient factor.

3. **Thrombocytopenia: this means the presence of a very low quantity of platelets in the circulating system, this caused**

by drugs, chemicals and sometimes due to unknown reason, in this case it's called idiopathic thrombocytopenia.

The treatment by giving the patient blood containing fresh blood platelets. (ordinary, bleeding does not occur until the number of platelets in the blood below 50,000 µl rather than normal 150,000-300,000 levels as low as 10,000 µl are frequently lethal.

Oral cavity Lec.10

Functional anatomy of mouth

The mouth is known as oral cavity or buccal cavity. It is formed by cheeks, lips and palate. It encloses the teeth, tongue and salivary glands. It opens anteriorly to the exterior through lips and posteriorly into the pharynx. Digestive juice present in the mouth is saliva which is secreted by the salivary glands.

Functions of mouth

The primary function of mouth is eating. It has few other important functions also. The functions of the mouth are:

1. Ingestion of food materials.
2. Chewing the food and mixing it with saliva.
3. Appreciation of the taste.
4. Transfer of food (bolus) to the esophagus by swallowing.
5. Role in speech.
6. Social functions such as smiling and other expressions.

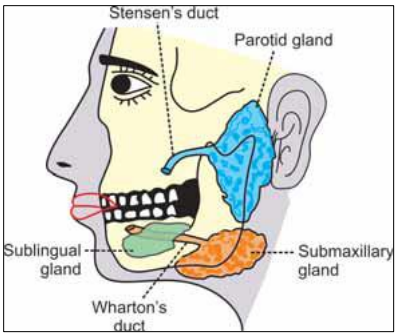
Salivary Glands

In humans, the saliva is secreted by three pairs of major (larger) salivary glands and some minor (small) salivary glands in the oral and pharyngeal mucous membrane. The major glands are:

1. Parotid glands
2. Submaxillary or submandibular glands
3. Sublingual glands.

Parotid glands

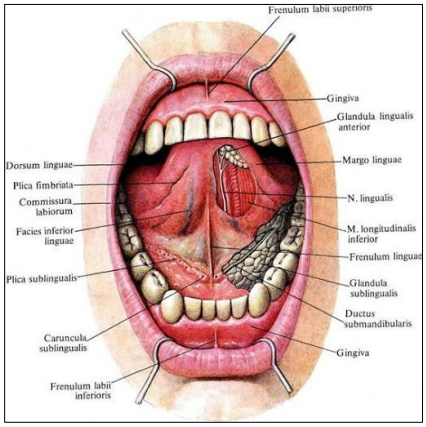
Parotid glands are the largest of all salivary glands situated at the side of the face just below and in front of the ear. Secretions from these glands are emptied into the oral cavity by Stensen's duct that opens inside the cheek against the upper second molar tooth.



Major salivary glands

Submaxillary glands

Submaxillary glands or submandibular glands are located in submaxillary triangle medial to mandible. Saliva from these glands is emptied into the oral cavity by Wharton's duct. The duct opens at the side of frenulum of tongue by means of a small opening on the summit of papilla called caruncula sublingualis.



Sublingual glands

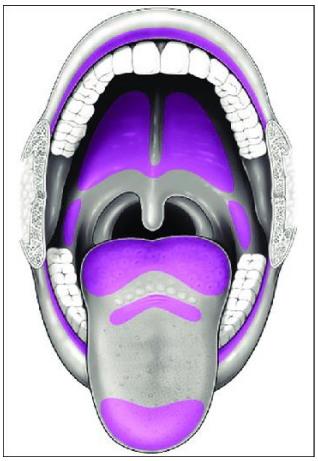
Sublingual glands are the smallest salivary glands situated in the mucosa at floor of mouth. Saliva from these glands is poured into 5-15 small ducts called ducts of Ravinus. These ducts open on small papillae beneath the tongue. One of the ducts is larger and it is called Bartholin's duct (Table 1). It drains the anterior part of the gland and opens on caruncula sublingualis near the opening of submaxillary duct.

Table 1: Ducts of major salivary glands

Gland	Duct
Parotid gland	Stensen's duct
Submaxillary gland	Wharton's duct
Sublingual gland	Ducts of Ravinus/Bartholin's duct

Minor salivary glands

1. Lingual mucus glands situated in posterior 1/3 of the tongue, behind circumvallate papillae and at the tip and margins of tongue.
2. Lingual serous glands located near circumvallate papillae and Filiform papillae.
3. Buccal glands present between the mucous membrane and buccinator muscle. Four to five of these are larger and situated outside buccinator around terminal part of parotid duct. These glands are called molar glands.
4. Labial glands situated beneath the mucous membrane around the orifice of mouth.
5. Palatal glands found beneath the mucous membrane of the soft palate.



Minor salivary gland position

Classification of salivary glands

Salivary glands are classified into three types based on the type of secretion.

1. Serous Glands

This type of gland is predominantly made up of serous cells. These glands secrete thin and watery saliva. Parotid glands and lingual serous glands are serous glands.

2. Mucus Glands

This type of glands is made up of mainly the mucus cells. These glands secrete thick, viscus saliva with high mucin content. Lingual mucus glands, buccal glands and palatal glands belong to this type.

3. Mixed Glands

Mixed glands are made up of both serous and mucus cells. Submandibular, sublingual and labial glands are the mixed glands.

Structure and duct system of salivary glands

Salivary glands are made up of acini or alveoli. Each acinus is formed by a small group of cells which surround a central globular cavity. The central cavity of each acinus is continuous with the lumen of the duct. The fine duct draining each acinus is called intercalated duct. Many intercalated ducts join together to form intralobular duct. Few intralobular ducts join to form interlobular ducts, which unite to form the main duct of the gland (Fig. 3).

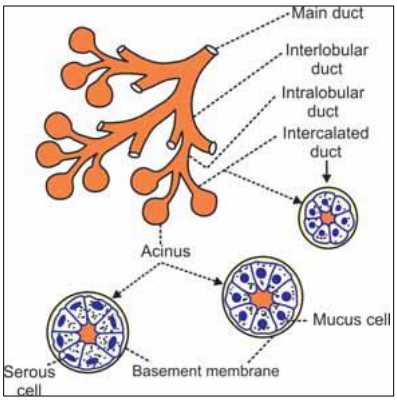


Figure 3: Diagram showing acini and duct system in salivary glands

Mastication

Mastication is the act of chewing food, and it consists of the coordinated function of various parts of the oral cavity to prepare the food for swallowing and digestion.

Structures involved in mastication

Teeth are the most important structures involved in mastication, but other structures such as lips, cheeks, tongue, palate, gingiva and periodontium, muscles of mastication and the temporomandibular joint, along with the lubricating and enzymatic action of saliva, are important for mastication. Food taken into the mouth is crushed by the grinding action of the teeth, which makes it suitable for swallowing. Breakdown of food into smaller particles increases the surface area of the food particles. This in turn increases the enzymatic action leading to effective digestion. Mastication also removes the cellulose covering of some food particles. During chewing, the tongue plays an essential role in controlling the movement of the food and forming the bolus. For food to be broken down, it has to be positioned by the tongue in conjunction with the buccinator muscles of the cheek between the occlusal surfaces of the teeth. The tongue transports solid and liquid foods within the oral cavity.

The pattern of the individual cycle varies depending on the state of breakdown of the food. The masticatory sequence can be divided into three consecutive periods:

1. **Preparatory**: Initial period where food is transported back to the posterior teeth.
2. **Reduction:** Intermediate period where food is ground up.
3. **Pre-swallowing:** Final period where bolus is formed for swallowing

Muscles Involved in Mastication

The muscles which are involved in the process of closing the mouth are masseter, medial pterygoid and temporalis. They are known as elevators. The muscles involved in the process of opening the mouth (depression) are the lateral pterygoid muscles along with the digastric, mylohyoid and geniohyoid muscles. They are known as depressors. Medial pterygoid, lateral pterygoid and masseter are helpful in the protrusion of the mandible. Retraction of the mandible is brought about by the temporalis. Medial and lateral pterygoids of both the sides act alternatively for the side-to-side movement of the mandible.

Bolus formation for swallowing

• The moistening nature of the saliva helps to make the food into a bolus and thus lubricates the oral cavity and pharynx in easy swallowing. When a person secretes less amount of saliva, additional water may be needed to push the food into the stomach.

• Adequate amounts of saliva in the oral cavity is also needed to initiate the digestive process. Saliva helps in chewing as well as mixing of food within the mouth and will assists in swallowing the food.

Deglutition (swallowing)

Deglutition (swallowing) is the process by which food is passed into the stomach from the oral cavity. Swallowing is a reflex activity consisting of muscle contractions and relaxations that help push the ingested food and saliva from the mouth to the stomach. This reflex activity occurs in coordination with numerous motor neurons. The swallowing reflex is pre-programmed as well as initiated in the region of the brainstem known as the swallowing center. Although swallowing can be initiated voluntarily, much of the swallowing occurs without any conscious effort. The swallowing rate is highest during eating and least during sleep, and swallowing occurs around 600 times per day. The volume of a swallow in drinking, and probably in bolus transport, varies from 5 mL in a child to 10–14 mL in adult women and 15–20 mL in adult men.

Phases of Swallowing

Swallowing can be divided into preparatory, oral, pharyngeal and esophageal phases.

1- Preparatory Phase

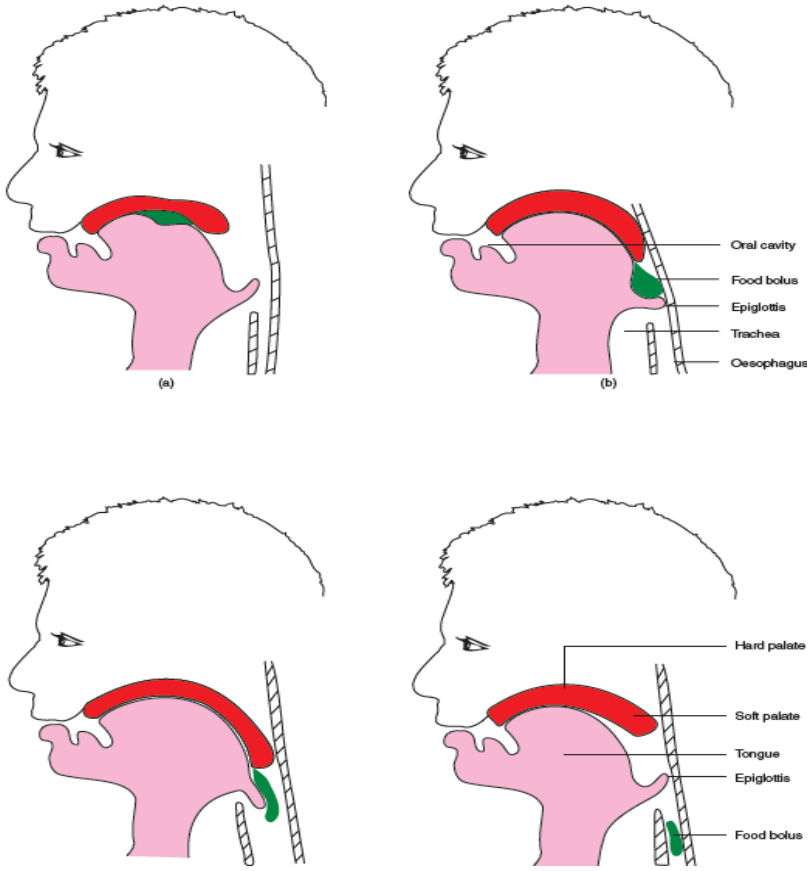
Formation of food bolus occurs during this phase. Food bolus is a round or oval-shaped mass of food formed in the mouth after thorough chewing. The food bolus is formed as a preparatory event for swallowing.

2- Oral Phase (Buccal Phase)

Once the bolus is positioned on the tongue dorsum, the oral phase begins. The lips close and the maxillary and mandible incisors come closer together. The anterior two-third of the tongue elevate against the maxillary alveolar ridge and the anterior hard palate, propelling the bolus towards the pharynx. The nasopharynx is shut off by the upward movement of the soft palate and the forward movement of the posterior pharyngeal wall to prevent regurgitation of food through the nose. This is a voluntary phase and respiration is stopped for a while in this phase.

3- Pharyngeal Phase

At the beginning of the pharyngeal phase, the posterior part of the tongue makes a rapid piston-Like movement to propel the bolus through the oropharynx into the hypopharynx. The pharyngeal constrictors move upwards and forwards and begin propelling the bolus through the pharynx by sequential contractions. The upper esophageal sphincter opens, and the bolus enters the esophagus. During the pharyngeal phase, the laryngeal vestibule closes because of the movement of the epiglottis. The epiglottis first moves from an upright to a horizontal position (**Fig. b**) because of the elevation of the hyoid bone and larynx and the contraction of the thyrohyoid muscles. Further muscle contraction causes the tip of the epiglottis to rotate over the laryngeal vestibule. The epiglottis does not have to cover the laryngeal opening to prevent aspiration of food. Aspiration of food generally does not occur in individuals with an excised epiglottis. However, the epiglottis does direct the bolus into the piriform sinuses and, therefore, around the opening of the airway into the esophagus (**Fig. c** and **d**).



Applied Physiology

Forcing food and liquids into the nasal cavity is known as nasal regurgitation. It can occur in patients with palatal clefts or paralysis of soft palate where the nasal cavity cannot be sealed off from the oropharynx.

4- Esophageal Phase

After the food is placed in the upper end of esophagus, the upper esophageal sphincter contracts, causing peristaltic contractions (wave-like movements) that can send the bolus to the stomach with the help of gravity. The lower esophageal sphincter opens to allow the bolus into the stomach.

Cardiovascular physiology

Cardiovascular physiology

Cardiovascular system (CVS)consists of:

- ✓ Heart

Is the pump which circulates the blood round the body.

- ✓ Blood vessels

Flow blood from the heart to cells & back to the heart.

Functions Cardiovascular system:

I -primary main functions of the heart:

- Acts as a muscular pump:

In order to maintain adequate level of blood flow throughout CVS by pumping blood under pressure into vascular system.

- responsible for the mass movement of fluid in body.

Functions Cardiovascular system:

II -Secondary functions:

I – Transportation:

- delivers O2 to tissues & brings back CO2 to lungs.
- carries absorbed digestion products to liver & tissues.
- Carries metabolic wastes to kidneys to be excreted.
- Distribution of body fluid.

2-Regulation:

- Hormonal: carries hormones to target tissues to produce their effects.
- Immune: carries antibodies, leukocytes(WBC),cytokines& complement to aid body defense mechanism against pathogens.
- Protection: carries platelets & clotting factors to aid protection of body in blood clotting mechanism.
- Temperature: helps in regulation of body temperature by diverting blood to cool or warm the body

Anatomy of the heart

Right Side of the heart
Left side of the heart

Anatomy of the heart

Consists of 2 separated pumps that maintain unidirectional flow of blood: the left & right hearts

- ✓ Lt heart pumps oxygenated blood from the lung to the tissues- Systemic circulation
- ✓ Rt heart pumps deoxygenated blood which has returned from the tissues to the lungs- Pulmonary circulation

The heart contains 4 chambers, each pump contains 2 chambers: an atrium & a ventricle.

Chambers of the heart

2 Atria:

The upper two chambers of the heart (atria) are thin-walled chambers, are divided by a wall-like structure called the interatrial septum.

receive blood returning back to the heart.

2 Ventricles:

The lower two chambers of the heart (ventricles), are thicker, muscular walls.

Pump blood from heart.

Each has same capacity & pumps same volume of blood in a given period of time. Atria & ventricles are separated into 2 functional units by a sheet of fibrous connective tissue, which gives attachment to the valves.

Valves of the heart

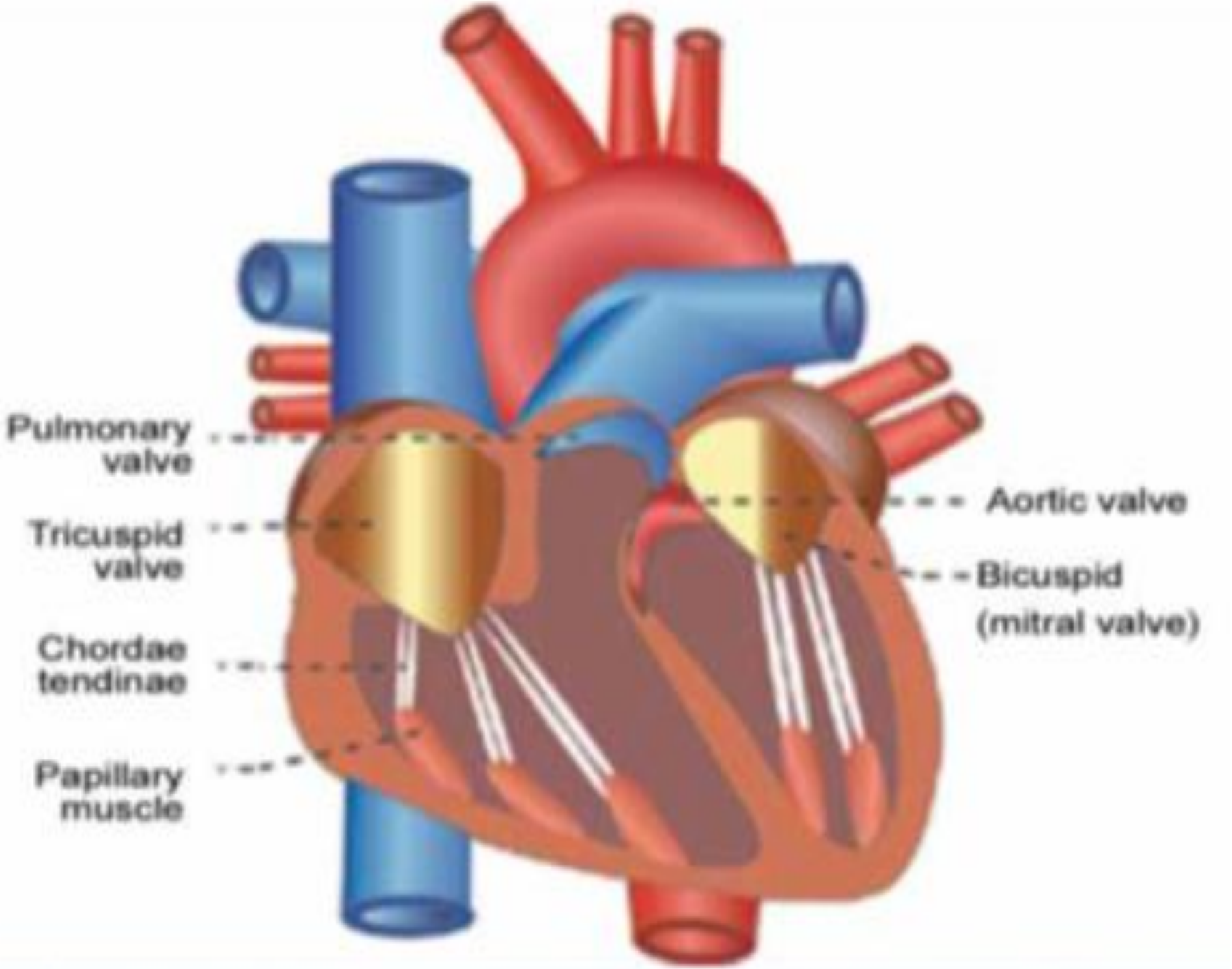
are structures which allow the blood to flow in one direction only, they do not contain any muscle tissue.

- ❑ Each ventricle has a valve at its inlet & valve at its outlet:
- ✓ The inlet valves are termed= atrioventricular (AV)valves, allow blood to flow from atria into ventricles.
  - on the left side it is known as the Mitral valve.
  - On right side it is known as the Tricuspid valve.

- ✓ The outlet valves are known as = the Semilunar valves. At origin of pulmonary artery & aorta.

The valve on left side of the heart is known as aortic valve, on the right side it is also known as pulmonary valve.

Two of the valves are in between the atria and the ventricles called atrioventricular valves. The other two are the semilunar valves, placed at the opening of the blood vessels arising from the ventricles, i.e. systemic aorta and pulmonary artery. The valves of the heart permit the flow of blood through the heart in only one direction


Pulmonary valve
Tricuspid valve
Chordae tendinae
Papillary muscle
Aortic valve
Bicuspid (mitral valve)

Layers of Wall of the heart

Pericardium: outer covering of the heart. made up of two layers These two layers are separated by a space called pericardial cavity which contains a thin film of fluid.

Myocardium:: is the middle layer of the wall of the heart, formed by cardiac muscle fibers. it is responsible for the pumping action of the heart. is formed by three types of cardiac muscle fibers:

i**. muscle Fibers which Form the Contractile Unit of the Heart:**

These cardiac muscle fibers are striated fibers , similar to the skeletal muscles in structure. But, unlike the skeletal muscle fibers,
(involuntary in nature.
The cardiac muscle fiber is covered by sarcolemma. has a centrally placed nucleus. The myofibrils are embedded in the sarcoplasm.

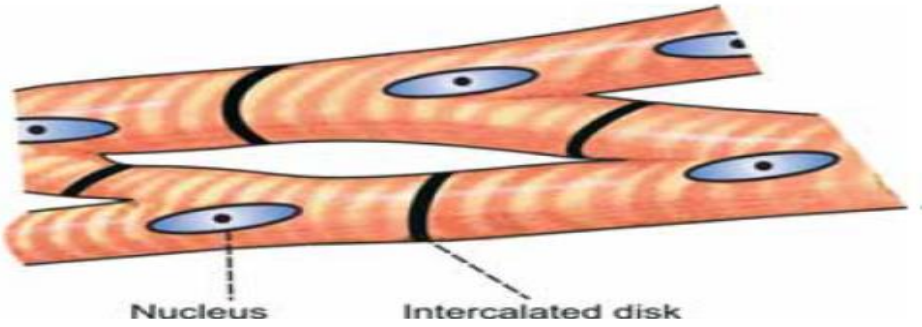
The sarcomere of the cardiac muscle has muscle proteins namely, actin, myosin, troponin and tropomyosin.

The cardiac muscle also have sarcotubular system like that of skeletal muscle.
The important difference between skeletal muscle and cardiac muscle is that the cardiac muscle fiber is branched .

Intercalated disk

is a tough double membranous structure situated at the junction between the branches of neighboring cardiac muscle fibers.

- form adherens junctions which play an important role in contraction of the muscle as a single unit .



Syncytium

The structure of cardiac muscle is considered as a syncytium.

the adjacent muscle fibers fuse together to form gap junctions which facilitates the rapid conduction of electrical activity from one fiber to another.
This makes the cardiac muscle fibers act like a single unit referred as physiological syncytium.

The syncytium in human heart has two portions, atrial syncytium and ventricular syncytium which are connected by atrioventricular ring.

ii. . Muscle Fibers which Form the Pacemaker:

Some of the muscle fibers of the heart are modified into a specialized structure known as pacemaker.

The muscle fibers forming pacemaker have less striation.

Pacemaker:

is structure in the heart that generates the impulses for heart beat. It is formed by the pacemaker cells called P cells. Sinoatrial(SA) node forms the pacemaker in human heart.

iii. Muscle Fibers which Form the Conductive System

The conductive system of the heart is formed by the modified cardiac muscle fibers. The impulses from SA node are transmitted to the atria directly, the impulses are transmitted to the ventricles, through various components of conducting system

ENDOCARDIUM

is the inner layer of the heart wall. wall. It is a thin, smooth and glistening membrane. It is formed by a single layer of endothelial cells lining the inner surface of the heart. Endocardium continues as endothelium of the blood vessels.

BLOOD VESSELS

The vessels of circulatory system divided into arterial and venous systems.

 Arterial System:comprises the aorta, arteries and arterioles

The arterioles are continued as capillaries which are small, thin walled vessels having a(5 to 8 μ.)

The capillaries are functionally very important because, the exchange of materials between the blood and the tissues occurs through these vessels.

VENOUS SYSTEM

From the capillaries venous system starts and it includes the venules, veins and vena cavae.

The venules are smaller vessels with thin muscular wall than the arterioles.

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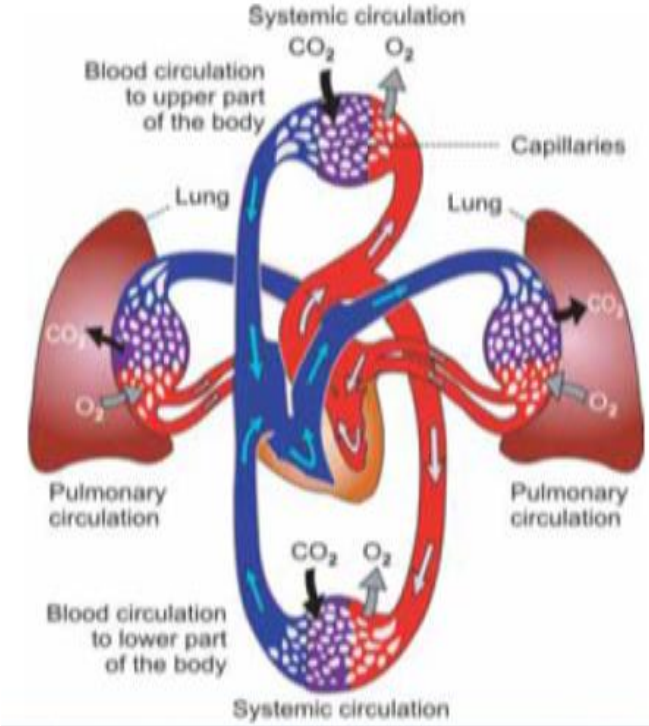
Pulmonary and Systemic Circulations--DIVISIONS OF CIRCULATION

Blood flows through two divisions of circulating system:

1. Systemic circulation
2. Pulmonary circulation.



Arteries include the right and left coronary arteries, marginal arteries, anterior and posterior interventricular arteries, and the circumflex artery.

Pulmonary circulation: blood pumped from RV through lungs & back to the heart

Systemic circulation: oxygen- rich blood pumped by the LV to all organ systems to supply nutrients.

Rate of blood flow through systemic circulation= flow rate through pulmonary circulation.

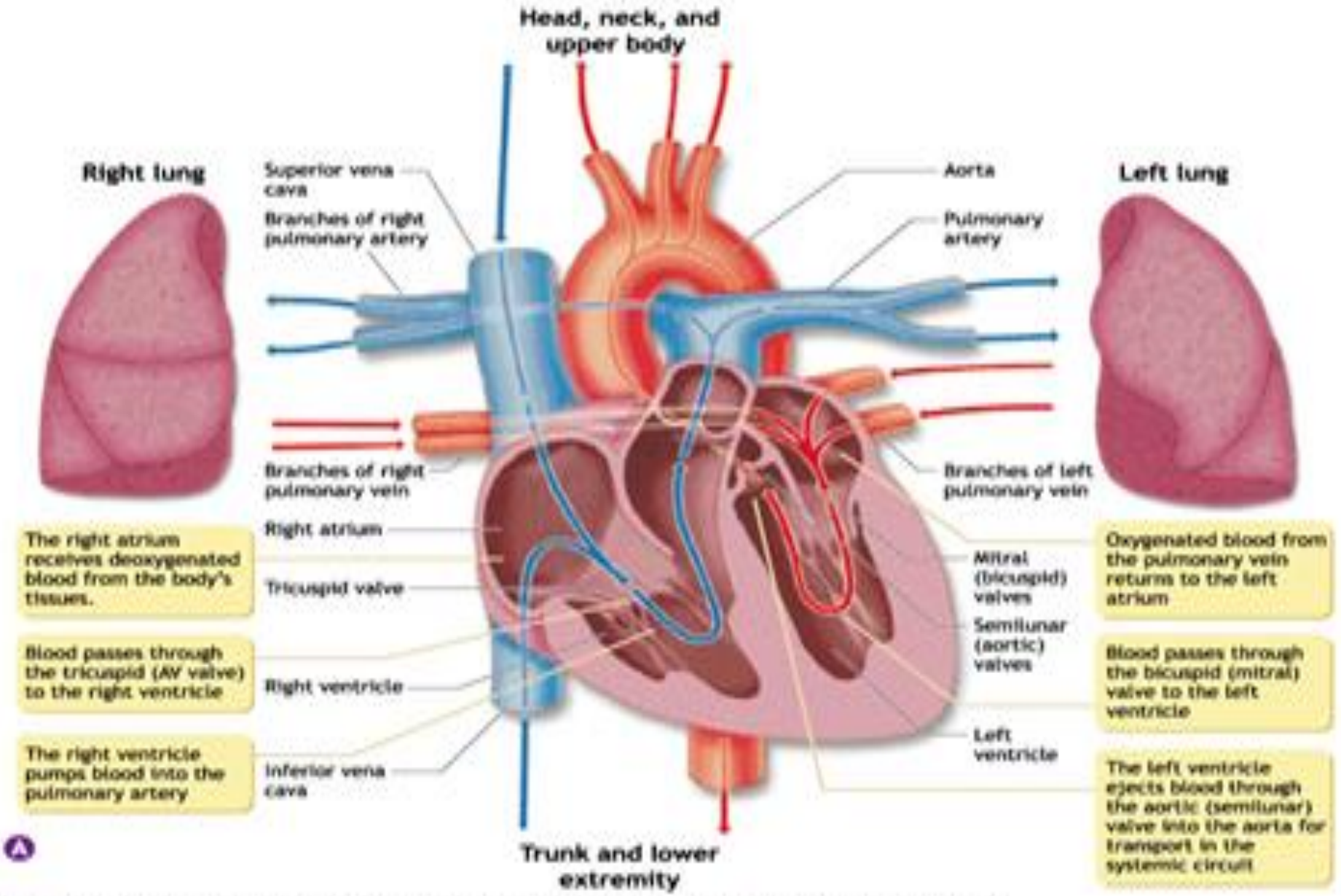


Figure 15.3. A. The heart, its great vessels, and the action of its valves. The valves provide for the one-way flow of blood as indicated by the *arrows*.

Properties of Cardiac Muscle

Physiology of cardiac muscle:

The heart is composed of 2 major types of cardiac muscle:

I- Contractile tissue (compsed of 2 types of muscles: atrial& ventricular muscles) contract when stimulated, in same way as skeletal muscles except for longer duration.

- ✓ Autorhythmic (or automatic) tissue.

- specialized or modified cardiac tissues, that contract only feebly as they contain few contractile fibrils.

- self stimulating with/out any external stimulation.

- initiate repetitive action potentials, that exhibit ''Pacemaker'' potentials, rhythmicity & varying rates of conduction.

- provide an excitatory system for the heart.

- ✓ EXCITABILITY
  is defined as the ability of a living tissue to give response to a stimulus. In all the tissues, the initial response to a stimulus is the electrical activity in the form of action potential. It is followed by mechanical activity in the form of contraction, secretion

- ✓ **RHYTHMICITY**

  is the ability of a tissue to produce its own impulses regularly. It is more appropriately named as autorhythmicity. It is also called self excitation.

  The property of rhythmicity is present in all the tissues of the heart. However, heart has a specialized excitatory structure from which the discharge of impulses is rapid. This specialized structure is called pacemaker. From this, the impulses spread to other parts through the specialized conductive system.

  - **PACEMAKER**

  Though the SA node is the pacemaker in mammalian heart.

- ✓ **Contractility** is ability of the tissue to shorten in length (contraction) after receiving a stimulus.

  Various factors affect the contractile properties of the cardiac muscle.

  The contractile properties are:

  - **ALL OR NONE LAW**

- ❑ **STAIRCASE PHENOMENON**

When the ventricle is stimulated successively without changing the strength, the force of contraction increases gradually for the first few contractions & then it remains same. Gradual increase in the force of contraction is called staircase

❑ SUMMATION OF SUBLIMINAL STIMULI

When a stimulus with a subliminal strength is applied, the heart does not show any response. When few stimuli with same subliminal strength are applied in succession, the heart shows response by contraction. It is due to the summation of the stimuli.

❑ REFRACTORY PERIOD

is the period in which the muscle does not show any response to a stimulus. It is of two types:

1. Absolute refractory period

Absolute refractory period is the period during which the muscle does not show any response at all, whatever may be the strength of the stimulus.

2. Relative Refractory Period

The relative refractory period is the period during which the muscle shows response if the strength of stimulus is increased to maximum. It is the stage at which the muscle is in repolarizing state.

Refractory Period in Cardiac Muscle

Cardiac muscle has a long refractory period compared to that of skeletal muscle. The absolute refractory period extends through out contraction period of cardiac muscle

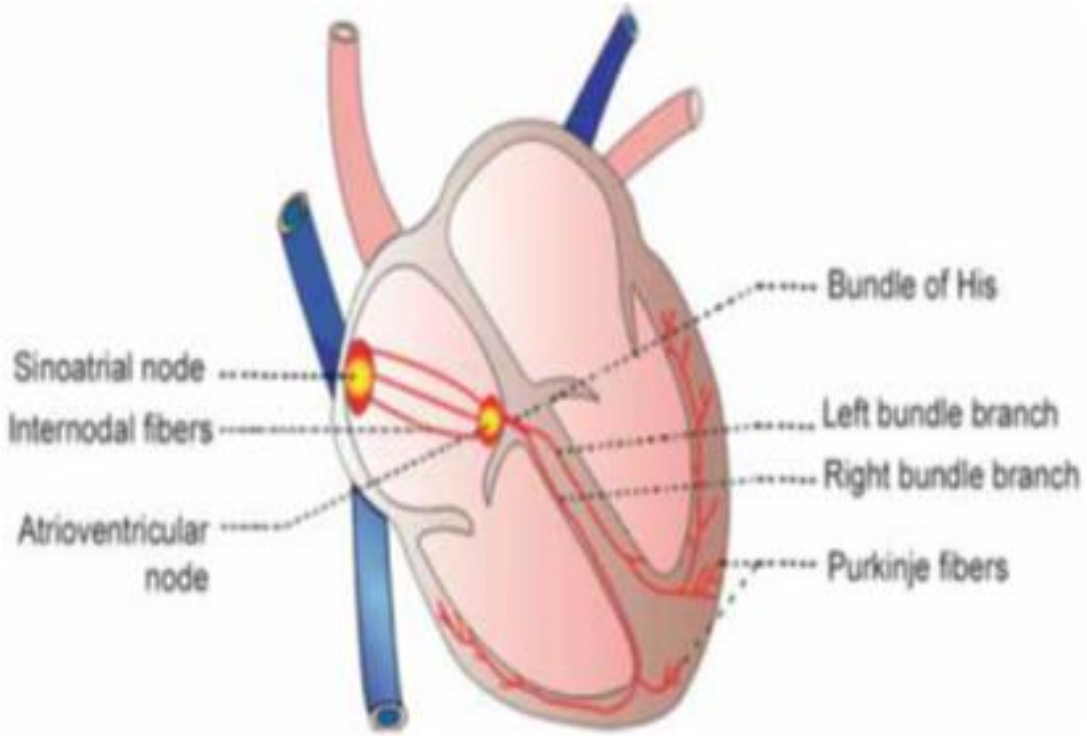
CONDUCTIVITY

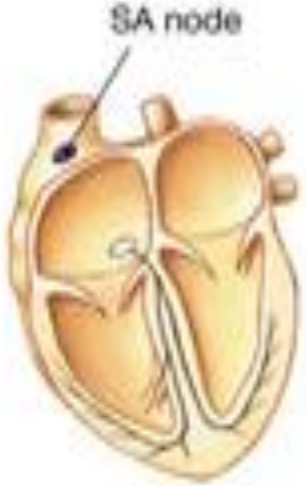
Human heart has a specialized conductive system through which the impulses from SA node are transmitted to all other parts of the heart

CONDUCTIVE SYSTEM IN HUMAN HEART

The conductive system of the heart is formed by the modified cardiac muscle fibers. The conductive tissues of the heart are also called the junctional tissues. The conductive system inhuman heart comprises:

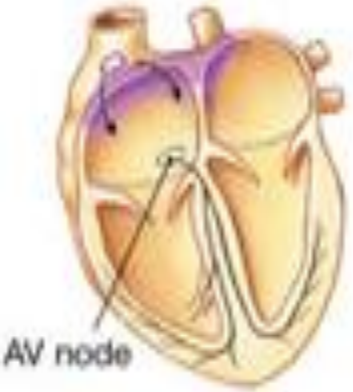
1. AV node
2. Bundle of His
3. Right and left bundle branches
4. Purkinje fibers.





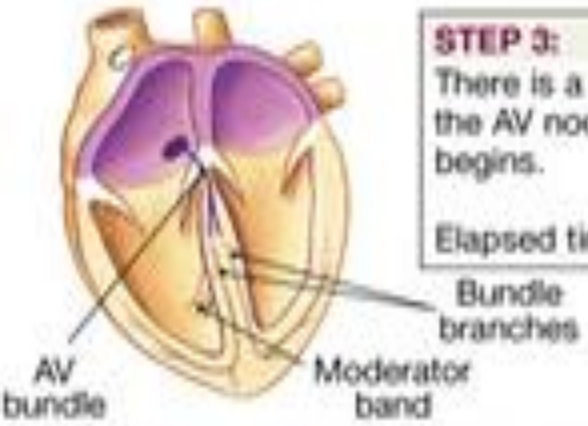
STEP 1:
SA node activity and atrial activation begin.

Time = 0



STEP 2:
Stimulus spreads across the atrial surfaces and reaches the AV node.

Elapsed time = 50 msec



STEP 3:
There is a 100-msec delay at the AV node. Atrial contraction begins.

Elapsed time = 150 msec

STEP 4:
The impulse travels along the interventricular septum within the AV bundle and the bundle branches to the Purkinje fibers and, via the moderator band, to the papillary muscles of the right ventricle.

Elapsed time = 175 msec

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

Elapsed time = 225 msec

Impulse Conduction through the heart

- ✓ SA node begins the action potential
- ✓ Stimulus spreads to the AV node
- ✓ Impulse is delayed at AV node
- ✓ Impulse then travels through ventricular conducting cells
- ✓ Then distributed by Purkinje fibers

Atrial conducting cells are found in internodal pathways

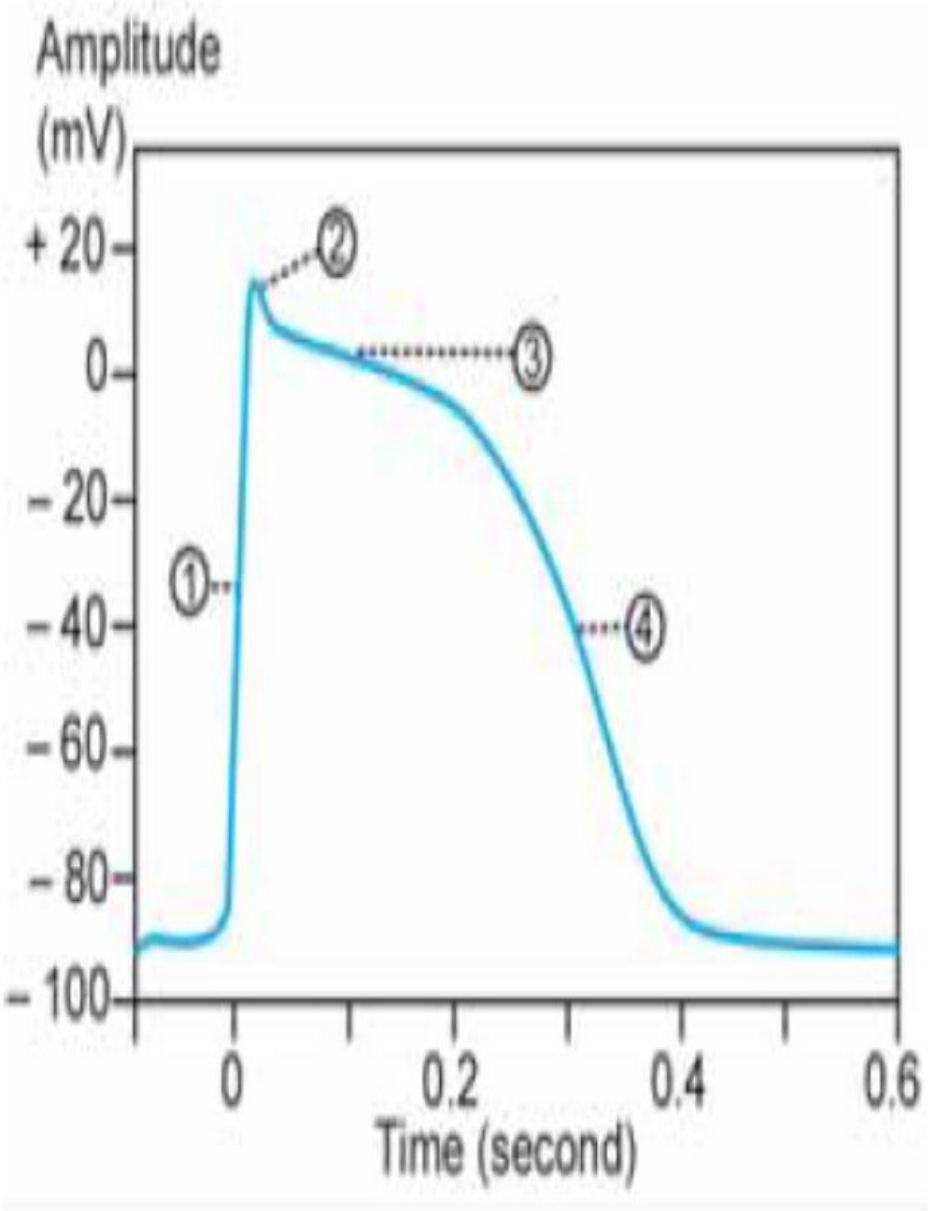
Ventricular conducting cells consist of the AV bundle, bundle branches, and Purkinje fibers. The impulses from SA node are conducted throughout right and left atria. The impulses also reach the AV node via some specialized fibers called intermodal fibers. There are three types of intermodal fibers, All these fibers from SA node converge on AV node and interdigitate with fibers of Av node.

From AV node, the bundle of His arises. It divides into right and left bundle branche swhich run on either side of the interventricular septum. From each branch of Bundle of His

Action potential in a single cardiac muscle fiber occurs in 4 phases:

1. Initial depolarization
2. Initial repolarization
3. A plateau – final depolarization
4. Final repolarization.

duration of action potential in cardiac muscle is (0.25 to0.35 sec).



Nervous system
NEURON

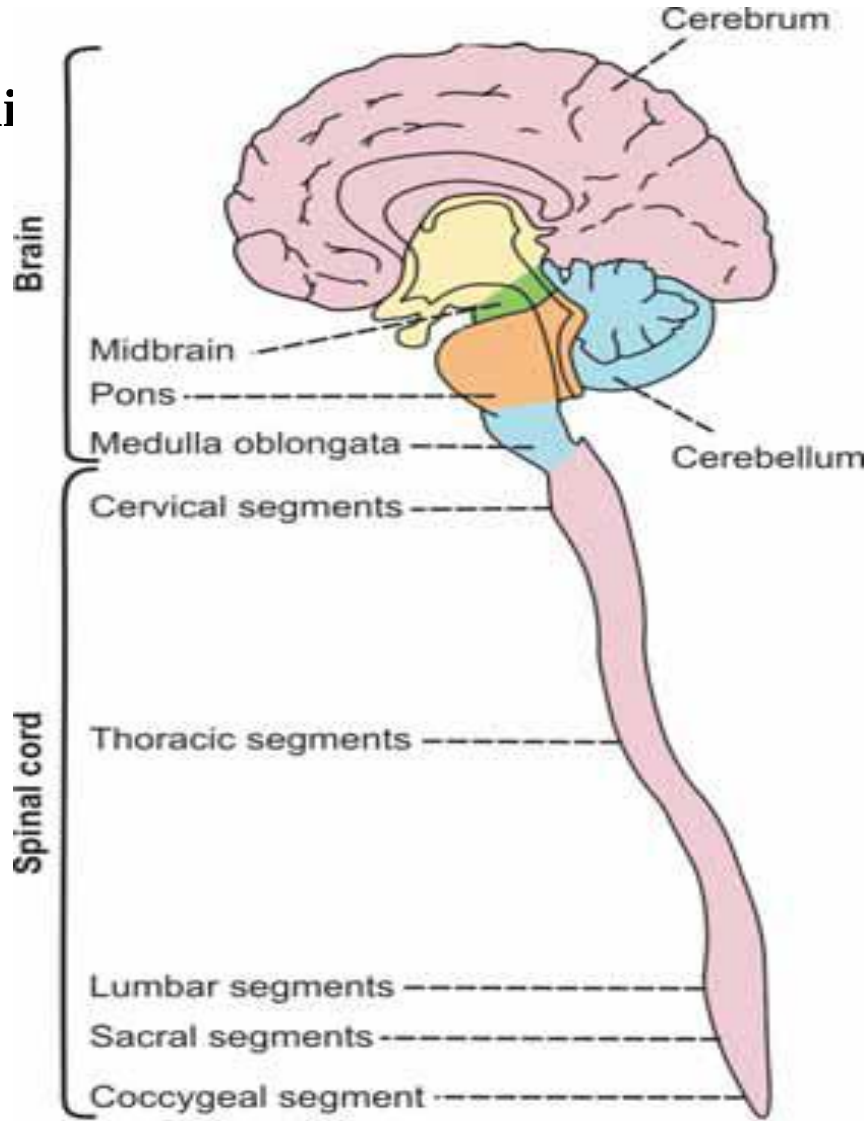
Nervous system controls all the activities of the Body-quicker than the other control system in the body namely, the endocrine system.

Primarily, the nervous system is divided into two parts.

1. Central nervous system (CNS) includes brai and spinal cord. formed by neurons and supporting cells called neuroglia.

The structures

2. Peripheral nervous system.



Nervous system

controls all the activities of the body. It is quicker than the other control system is divided into two parts.

Central nervous system (CNS)

includes brain and spinal cord. It is formed by neurons and the supporting cells called = neuroglia.

2. Peripheral nervous system (PNS)

is formed by the neurons and their processes present in all regions of the body. It consists of cranial nerves arising from brain and spinal nerves arising from the spinal cord. It is again divided into two subdivisions:

1. Somatic nervous system: is concerned with somatic functions. It includes the nerves supplying skeletal muscles. Somatic nervous system controls the movements of the body by acting on the skeletal muscles.

2. Autonomic nervous system : is concerned with regulation of visceral or vegetative functions. So, it is otherwise called vegetative or involuntary nervous system. The autonomic nervous system consists of two divisions, sympathetic division & parasympathetic division.

PERIPHERAL NERVOUS SYSTEM

The peripheral nervous system (PNS) is formed by the neurons and their processes present in all regions of the body. It consists of cranial

nerves arising from brain and spinal nerves arising from the spinal cord. It is again divided

into two subdivisions:

1. Somatic nervous system
2. Autonomic nervous system.

NEURON

Neuron is defined as the structural and functional unit of the nervous system. It is otherwise called nerve cell. Neuron is like any other cell in the body having nucleus and all the organelles in the cytoplasm. However, it is different from other cells by two ways:

1. Neuron has branches or processes called axon and dendrites
2. Neuron does not have centrosome; so it cannot undergo division.

CLASSIFICATION OF NEURON

The neurons are classified by three different methods.

I. Depending upon number of poles

II. Depending upon function

III. Depending upon length of the axon.

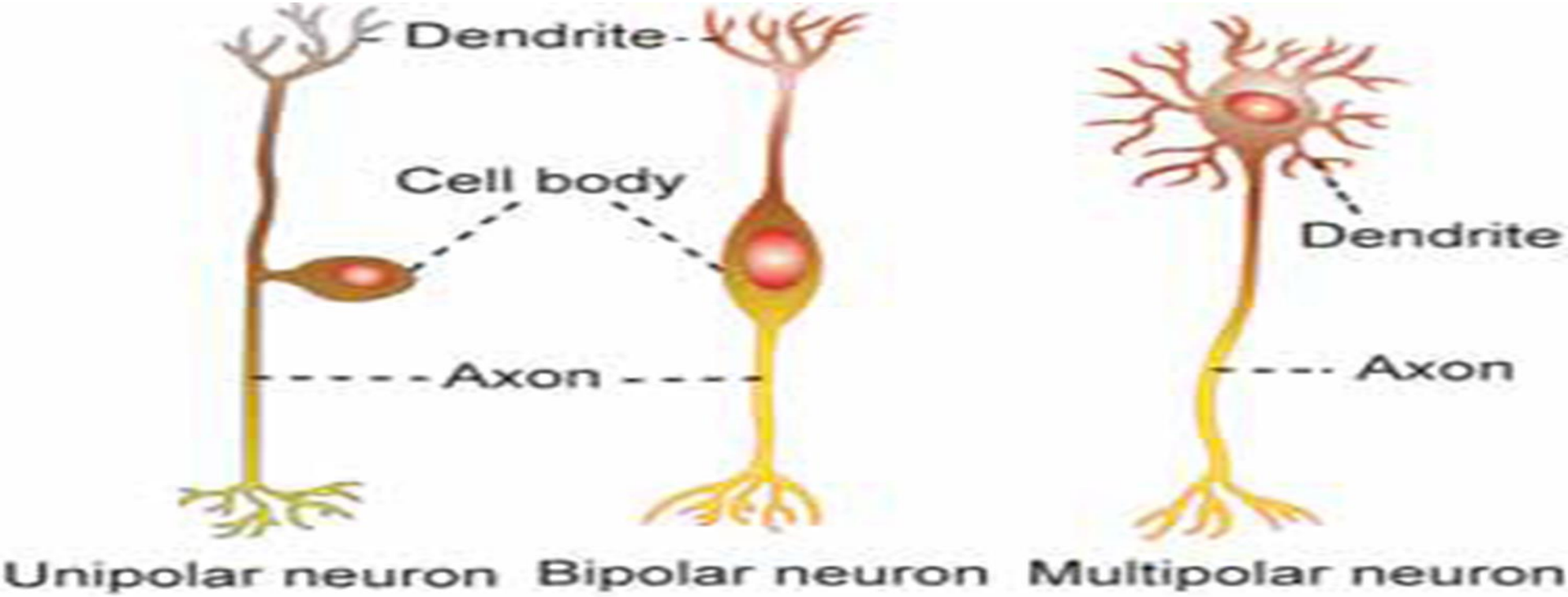
Depending upon Number of Poles

Based on the number of poles from which the nerve fibers arise:

1. Unipolar neurons that have only one pole from which, both the axon and dendrite arise

2. Bipolar neurons which have two poles. Axon arises from one pole and dendrites arise from the other pole.

3. Multipolar neurons which have many poles. One of the poles gives rise to the axon and, all the other poles give rise to dendrites.



Depending upon Function

On the basis of function, the nerve cells are classified into two types:

1. Motor neurons or efferent neurons

which carry the motor impulses from central nervous system to the peripheral effector organs like muscles, glands, blood vessels, etc.

2. Sensory neurons or afferent neurons

which carry the sensory impulses from periphery to the central nervous system.

The Neurons

the basic functional unit of the nervous system.

Function- send impulses to & from CNS and PNS and the effectors(muscles, gland, receptor, nerve endings).

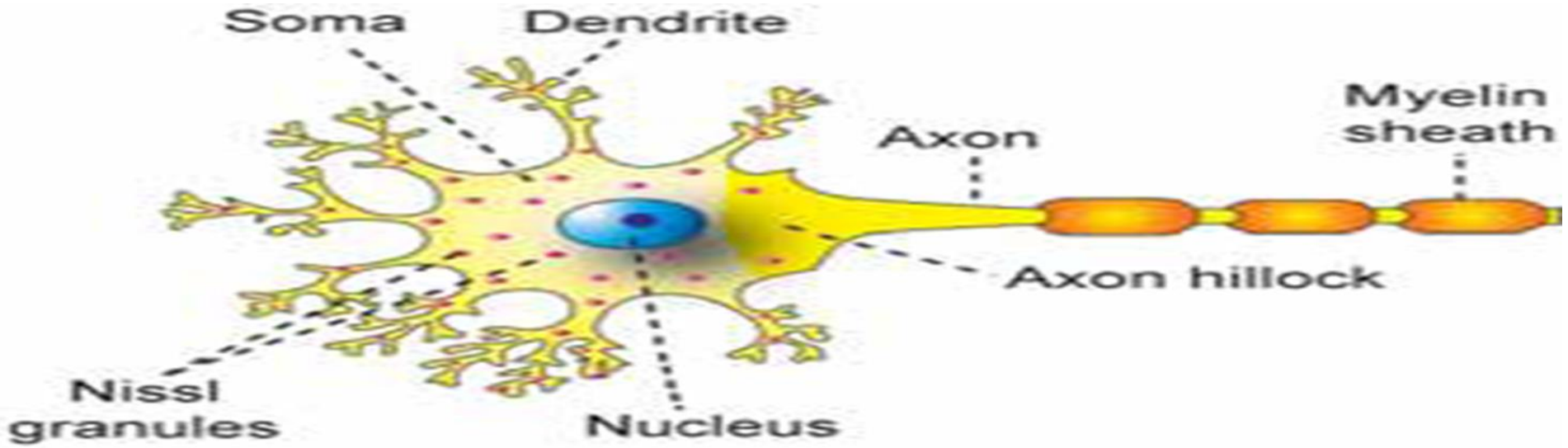
Receive, integrate , and transmit information

Operate through electrical impulses

Communicate with other neurons through chemical signals

The transmission of information along the length of the neuron is electrochemical in nature.

Neurons do not actually touch each other, instead, there is a space between the end of one & the beginning of the next (continuity without contact). A specified chemical, called neurotransmitter- is required to cross the gap between one neuron and the next.



 STRUCTURE OF NEURON

Each neuron is made up of three parts:

1. Nerve cell body 2. Dendrite 3. Axon.

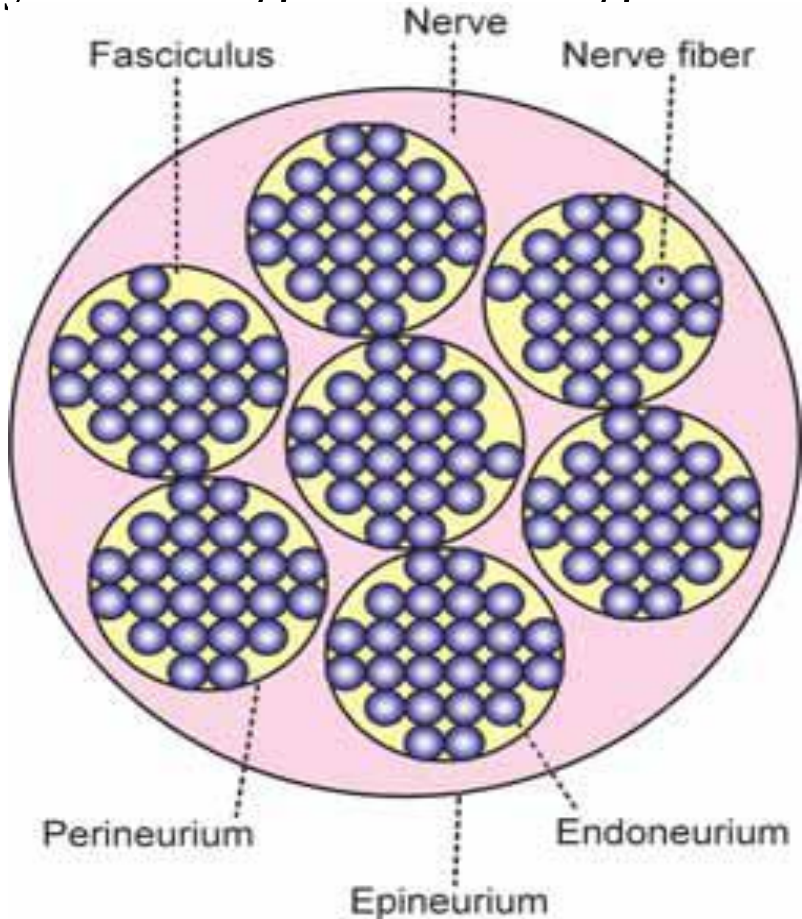
Axon

is longer than dendrite. Each neuron has only one axon, extends for a long distance away from the nerve cell body. The length of the longest axon is about one meter.

Organization of nerve

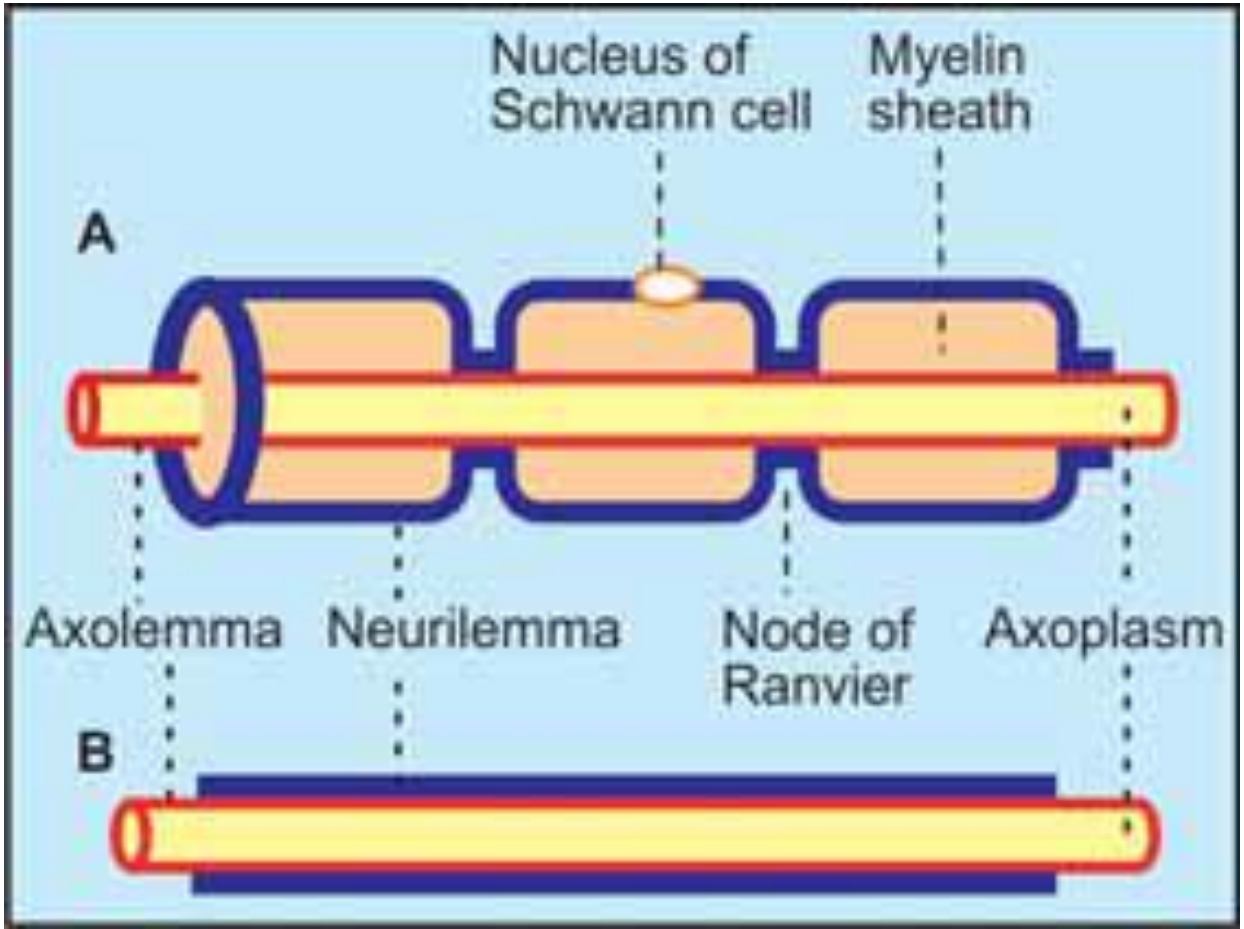
Many axons together form a bundle called fasciculus. Many fasciculi together form a nerve.

whole nerve is covered by tubular sheath, called epineurium. Each fasciculus iscovered by perineurium and each nerve fiber(axon) is covered by endoneurium



The axon has long central core of cytoplasm called axoplasm- is covered by axolemma which is the continuation of the cell membrane of nerve cell body. The axoplasm along with the axolemma is called the axis cylinder of the nerve fiber

The axis cylinder of the nerve fiber is covered by a membrane called neurilemma



Nonmyelinated nerve fiber

The nerve fiber described above is the nonmyelinated nerve fiber which is not covered by myelin sheath.

Myelinated nerve fiber

nerve fibers which are insulated by myelin sheath are called myelinated nerve fibers.

Formation of myelin sheath — Myelinogenesis

formation of myelin sheath around the axon is called myelinogenesis. It is formed by Schwann cells in neurilemma.

Functions of myelin sheath

1. Faster conduction: Myelin sheath is responsible for faster conduction of impulse through the nerve fibers. In the myelinated nerve fibers, the impulses jump from one node to another node by saltatory conduction.

2. Insulating capacity: Myelin sheath has a high insulating capacity. Because of this quality, the myelin sheath restricts the nerve impulse within the single nerve fiber, and prevents the stimulation of neighboring nerve fibers.

CLASSIFICATION OF NERVE FIBERS

Nerve fibers are classified by six methods:

1. Depending upon structure
2. Depending upon distribution
3. Depending upon origin
4. Depending upon function
5. Depending upon secretion of neurotransmitter
6. Depending upon diameter and conduction of impulse (Erlanger-Gasser classification).

1. Depending upon Structure

i. Myelinated nerve fibers that are covered by myelin sheath

ii. Nonmyelinated nerve fibers which are not covered by myelin sheath.

2. Depending upon Distribution

i. Somatic nerve fibers which supply the skeletal muscles of the body

ii. Visceral or autonomic nerve fibers which supply internal organs of the body.

3. Depending upon Origin

i. Cranial nerves arising from brain

ii. Spinal nerves arising from spinal cord.

4. Depending upon Function

i. Sensory or afferent nerve fibers which carry sensory impulses from different parts of the body to the central nervous system

ii. Motor or efferent nerve fibers which carry motor impulses from central nervous system to different parts of the body.

5. Depending upon Secretion of Neurotransmitter

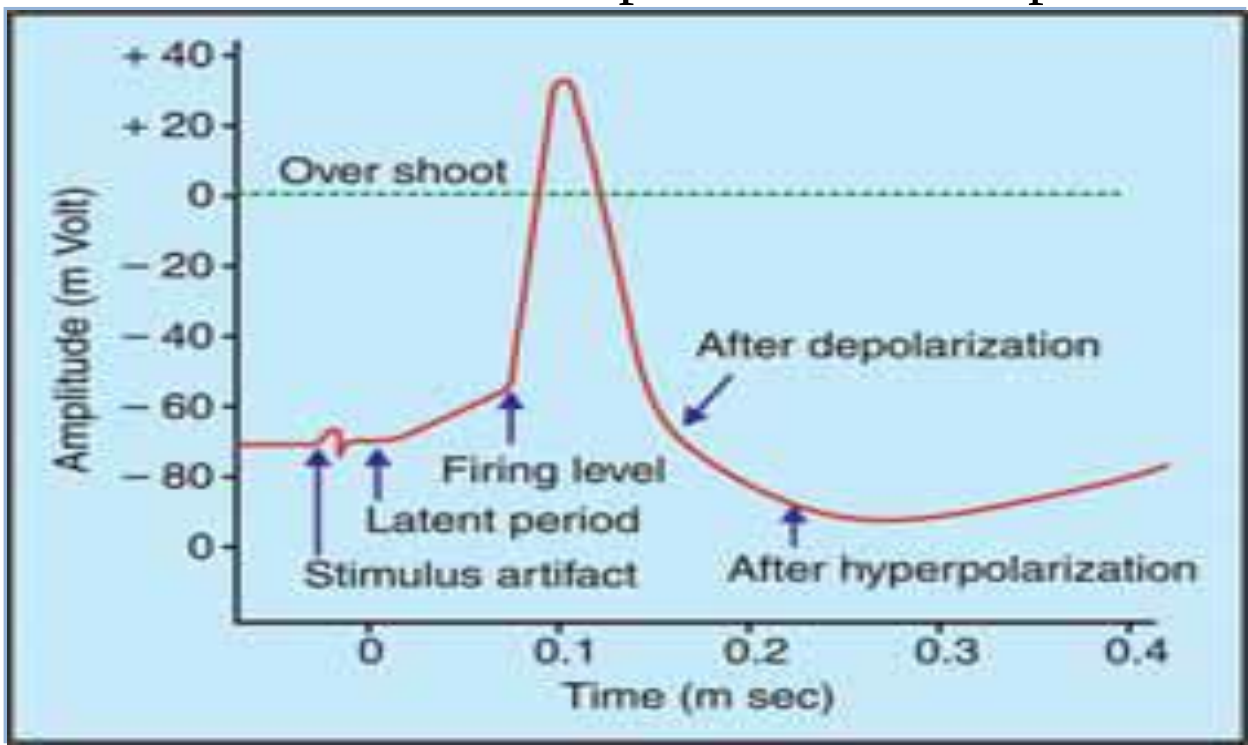
i. Adrenergic nerve fibers that secrete noradrenaline

ii. Cholinergic nerve fibers that secrete acetylcholine.

 PROPERTIES OF NERVE FIBERS

Excitability is as the physiochemical change that occurs in a tissue when a stimulus is applied.

The stimulus is an external agent, which produces excitability in the tissues. When the nerve fiber is stimulated action potential develops.



Mechanism of conduction of action potential

The depolarization occurs first at the site of stimulation in the nerve fiber. It causes depolarization of the neighboring areas. Like this, depolarization travels throughout the nerve fiber.

Depolarization is followed by repolarization.

Conduction through myelinated nerve fiber — Saltatory conduction

Saltatory conduction is the form of conduction of nerve impulse in which, the impulse jumps from one node to another. Conduction of impulsethrough a myelinated nerve fiber is about 50 times faster than through a nonmyelinated fiber.

It is because the action potential jumps from one node to another node of Ranvier instead of travelling through the entire nerve fiber

Mechanism of saltatory conduction

The myelin sheath is not permeable to ions. So, the entry of sodium from extracellular fluid into nerve fiber occurs only in the node of Ranvier, where the myelin sheath is absent. It causes depolarization in the node, and not in the internode.

Thus, the depolarization occurs at successive nodes. So, the action potential jumps from one node to another. Hence, it is called saltatory conduction (saltare = jumping).

DEGENERATION OF NERVE FIBERS

When a nerve fiber is injured, various changes occur in the nerve fiber and nerve cell body- called the degenerative changes. The injury occurs due to the obstruction of blood flow, local injection of toxic substances, crushing of nerve fiber or the transection of the fiber.

Degenerative Changes in the Neuron refers to deterioration or impairment or pathological changes of an injured tissue. When a peripheral nerve fiber is injured, the degenerative changes occur in the nerve cellbody and the nerve fiber same neuron and the adjoining neuron. Accordingly, the degenerative changes are classified into three types:

1. Wallarian degeneration
2. Retrograde degeneration
3. Transneural degeneration.

DEFINITION

Neuroglia or the glia (glia = glue) is the supporting cell of the nervous system. The neuroglial cells are non-excitable and do not transmit nerve impulse (action potential). So, these cells are also called non-neural cells or glial cells.

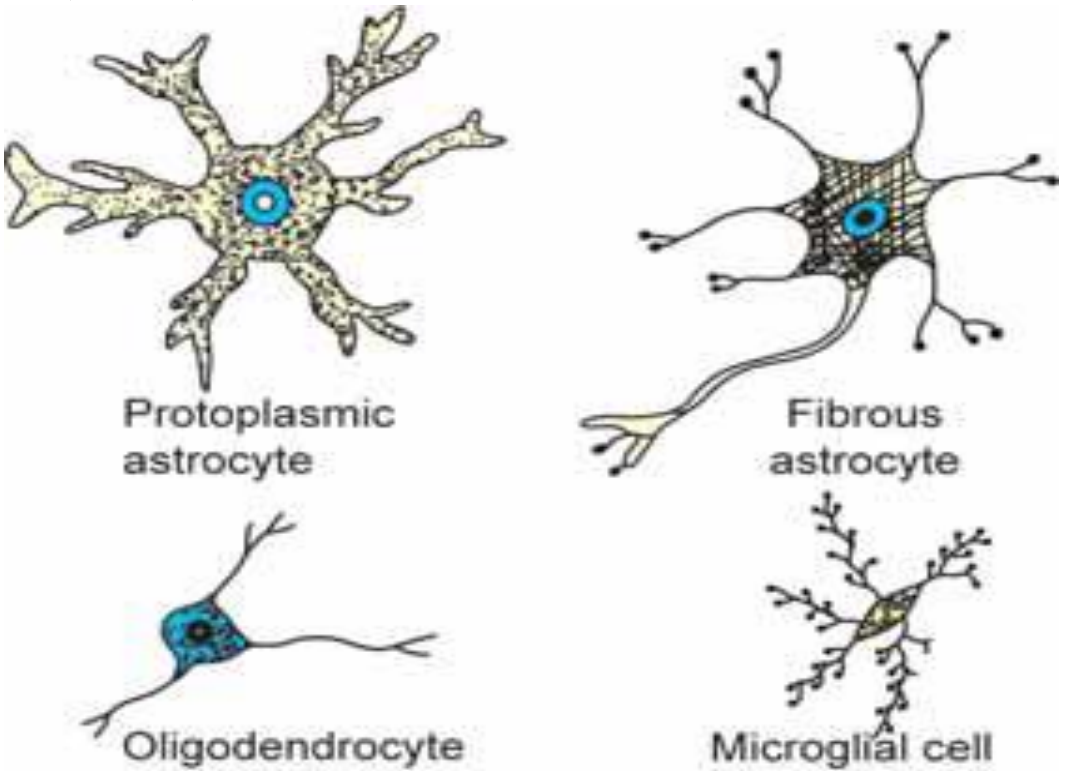
 CLASSIFICATION OF NEUROGLIAL CELLS

The neuroglial cells are distributed in central nervous system (CNS) as well as peripheral nervous system (PNS).

Central Neuroglial Cells

neuroglial cells in CNS are

1. Astrocytes
2. Microglia
3. Oligodendrocytes.



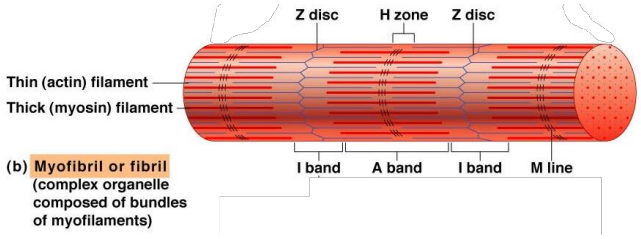
Lecture: Muscle Physiology

I. Anatomy of Skeletal Muscle CELL (Muscle Fiber)

A. General Features
1. multinucleated cells (syncytium: from fusion)
2. sarcolemma - special name for plasma membrane
3. very long compared to other cells (1 - 300 mm)
4. not unusually wide diameter (10 - 100 microns)
5. sarcoplasm - rich in glycogen and myoglobin
6. myoglobin - stores oxygen; similar to hemoglobin
7. special structures: myofibrils and sarcoplasmic reticulum

B. Ultrastructure of Myofibrils
1. muscle cell contains many parallel myofibrils
2. myofibrils have DARK bands (A bands) and LIGHT bands (I bands) that cause "striated" appearance of muscle
3. A band and I band result from the arrangement of overlapping and non-overlapping regions of two types of myofilaments
   a. thick filaments (myosin)
   b. thin filaments (actin)
4. sarcomere - smallest contractile unit of muscle cell
   a. Z-line - connection of actin filaments; dividing line between two adjacent sarcomeres
   b. M-line - connection of myosin filaments
   c. H-zone - non-overlapping region of the myosin filaments around the M-line
   d. A-band - length of myosin filaments
   e. I-band - length of non-overlapping actin filaments

Each muscle cell (fiber) is composed of many myofibrils. Each myofibril contains hundred of accordion-like sarcomeres laid end-to-end. Muscle contraction occurs when the sarcomeres contract by the sliding motion of actin and myosin filaments.



C. Molecular Structure of Actin & Myosin Filaments

1. thick filaments (myosin filaments) 12-16 nm
a. composed of about 200 myosin proteins
i. myosin has a golf club like shape
ii. 2 heads (cross bridges) - can bind to the actin filaments and use ATP
iii. tail - shaft of the thick filament

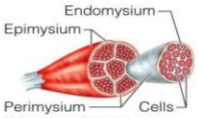
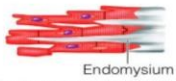
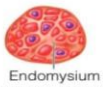
2. thin filaments (actin filaments) 5-7 nm
a. 2 helical chains of F actin (G actin subunits)
I. G actin can bind with myosin heads
ii. tropomyosin - rod-like protein that helps to stiffen F actin structure
iii. troponin - globular protein that can bind Ca^{++} to regulate actin/myosin binding

D. Sarcoplasmic Reticulum and T Tubules

1. sarcoplasmic reticulum - smooth ER that houses Ca^{++}
a. surrounds each myofibril
b. fused to each other at H zones and A/I bands
c. terminal cisternae - around A/I bands

2. T (transverse) Tubules - passageways from extracellular space to the terminal cisternae of SR
a. passage of nerve message directly to SR
b. passage of glucose, oxygen, salts to fiber

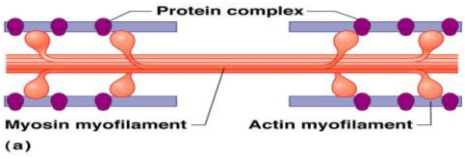
TABLE 6.1 Comparison of Skeletal, Cardiac, and Smooth Muscles *(continued)*

Characteristic	Skeletal	Cardiac	Smooth
Connective tissue components	Epimysium, perimysium, and endomysium	Endomysium attached to the fibrous skeleton of the heart	Endomysium
			
Regulation of contraction	Voluntary; via nervous system controls	Involuntary; the heart has a pacemaker; also nervous system controls; hormones	Involuntary; nervous system controls; hormones, chemicals, stretch
Speed of contraction	Slow to fast	Slow	Very slow
			
Rhythmic contraction	No	Yes	Yes, in some

II. Contraction of Skeletal Muscle Cell

A. Sliding Filament Model (Actin/Myosin Sliding Mechanism)

1. Ca^{++} released from sarcoplasmic reticulum
2. Ca^{++} binds to TnC region of Troponin
3. Troponin changes shape, moving Tropomyosin, exposing binding site on actin filament
4. Attachment - myosin head with ADP + P_i binds actin
5. Power Stroke - myosin head bends, pulling along the actin filament, ADP + P_i are released
6. Detachment - ATP binds to the myosin head, causing detachment from Actin
7. Re-cocking the Head - hydrolysis of ATP → ADP + P releases energy to re-cock the myosin
8. some myosin heads are in contact with actin at all times, allowing "walking motion" to occur
9. 1 cycle = 1 % muscle contraction
10. motion continues until no more ATP is present or Ca^{++} levels drop by re-uptake into SR
11. rigor mortis - muscles stiffen because Myosin heads remain attached to the Actin filaments



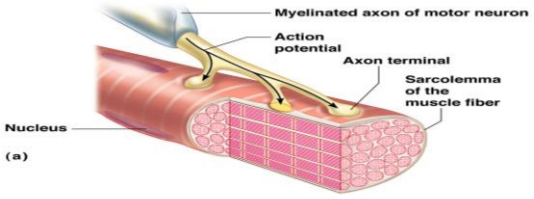
In a relaxed muscle cell, the regulatory proteins forming part of the actin myofilaments prevent myosin binding (see a). When an action potential sweeps along its sarcolemma and a muscle cell is excited, calcium ions (Ca^{2+}) are released from intracellular storage areas (the sacs of the sarcoplasmic reticulum).

III. Regulation of Contraction of a Single Skeletal Muscle Cell

A. Neuromuscular Junction (nmj)

1. neuromuscular junction - nerve/muscle intersection
   a. 1 motor neuron/axon supplies several fibers
   b. 1 centrally located junction per fiber
   c. synaptic vesicles - sacs that contain acetylcholine (ACh-neurotransmitter)
   d. synaptic cleft - space between the axon terminal and the sarcolemma of the muscle cell

e. motor end plate - highly folded part of sarcolemma beneath the synaptic cleft; rich in ACh receptors



B. Signal Transmission and Electrical Excitation of Muscle

1. Nerve Signal Causes Release of ACh from Axon End
   a. action potential along axon causes depolarization of axon terminal
   b. decreased membrane potential causes Voltage-Dependent Ca^{++} Channels on axon terminal to open
   c. Ca^{++} influx into axon terminal causes exocytosis of ACh containing synaptic vesicles
   d. ACh diffuses across the synaptic cleft to bind to ACh receptors of the motor end plate

2. Electrical Excitation of the Sarcolemma
   I. Like most cell membranes, the sarcolemma of muscle cells is polarized: it has more negative charge inside than outside.
   II. ACh triggers an Electrical Excitation of the sarcolemma by opening chemically gated Na^+ Channels, allowing positive charge to rush into the cell. The muscle cell becomes less negative or becomes depolarized.
      a. ACh binds to ACh Receptors which open ACh-Dependent Na+ Channels
      b. these Na^+ Channels allow Na^+ to flow into the muscle cell, causing depolarization
      c. depolarization at the neuromuscular junctions spreads to adjacent sites
      d. Voltage-Dependent Na^+ Channels at the adjacent sites open, allowing more Na^+ in
      e. A wave of depolarization therefore spreads across the entire cell
      f. this cannot be stopped and is called an all-or-none response
      g. entire process occurs in about 1 millisecond (1/1000 second)

      h. A refractory period occurs in which the muscle cell must

repolarize to its resting state.

This happens when the Voltage-Dependent Na^+ Channels close, Voltage-Dependent
K^+ Channels open, and the Na^+-K^+ ATPase pump rebalances the ion concentrations.
Repolarization generally takes very little time (3 milliseconds), while contraction can last
up to 100 milliseconds (1/10 sec). Limits how fast the cell can "re-fire" and contract!

3. Importance of Acetylcholine and Neuromuscular Junction
   a. After binding to ACh Receptors on sarcolemma, ACh is quickly broken down by an enzyme known as Acetylcholinesterase (AChE)
   b. myasthenia gravis - autoimmune disease where immune system attacks ACh Receptors
   c. ACh Antagonists - chemicals that block an ACh receptor
      i. snake venoms - curare and other venoms
4. Coupling of Excitation and Contraction
   a. latent period - time between excitation & contraction
      i. action potential passes down the T Tubules from the sarcolemma surface
      ii. T Tubule depolarization causes the release of Ca^{++} from the sarcoplasmic reticulum
      iii. Ca^{++} increase causes uncoupling of Troponin and sliding of filaments described above
      iv. ATP-Dependent Ca^{++} Pumps pump the Ca^{++} back into the sarcoplasmic reticulum
      v. Low Ca^{++} levels allows Troponin/Tropomyosin blockade of actin and muscle relaxes
   b. Calcium Sequesters - bind Ca^{++} in the cell so it will not form Calcium Phosphate crystals
      i. calmodulin and calsequestrin

REMEMBER: A Skeletal Muscle CELL (Fiber) will contract in an All-or-None fashion when ITS motor neuron stimulates it to fire by releasing ACh!!!!!!!!!!

IV. Contraction of a Skeletal MUSCLE

A. Motor Unit - a single motor neuron and all of the muscle cells stimulated by it

1. # muscle cells per motor neuron = 4 - 400
   - i. muscles of fine control (fingers, eyes and face): fewer muscle cells per neuron
   - ii. muscles of posture and gross movement (gluteus maximus): more muscle cells per neuron
2. axon terminals are distributed on muscle fibers throughout the muscle (not one region)

i. stimulation of one motor unit causes weak contraction throughout the whole muscle

B. Muscle Twitch - the response of a muscle to a single short electrical stimulus

1. strong twitch - many motor units activated; weak twitch - few motor units are activated
2. latent period (3 ms) - time after stimulation for coupling to occur and contraction to start
3. contraction period (10 - 100 ms) - from beginning of contraction to maximum force (tension)
4. relaxation period (10 - 100 ms) - time from maximum force to original relaxed state

C. Graded Muscle Responses (smooth, not All-or-None)

1. Frequency of Stimulation (Wave Summation) - a motor unit may be stimulated over and over again so no relaxation period is possible
   - i. frequency of stimulation cannot be greater than 1 every 3 ms (REFRACTORY PERIOD)
   - ii. motor neurons generally deliver action potentials in volleys with varying frequency
   - iii. tetanus - smooth muscle contraction that occurs when summation is so great that the relaxation period disappears
2. Summation of Multiple Motor Units - as strength of stimulus is increased, more and more motor units are activated in the muscle itself
   - i. threshold stimulus - level of stimulus at which first motor units are activated
   - ii. maximal stimulus - level of stimulus at which all motor units of a

muscle are activated

Muscles of the hand show summation of motor units well. When weak force and delicate motion is needed, few motor units are activated (those with the least # muscle fibers per motor unit). However, when great force is needed, the strength of the stimulus is increased to recruit more motor units (with many muscle fibers per motor unit).

3. Asynchronous Motor Unit Summation - motor units activated in different cycles "average out to produce a smooth muscle contraction

D. Treppe: The Staircase Effect - When a muscle is first used, it will show a gradual increase in force with a maximal stimulus until it is 'warmed up".

E. Muscle Tone - slightly contracted state of muscle that is maintained by reflexes originating in the spinal cord. Maintains posture and readiness for active contraction.

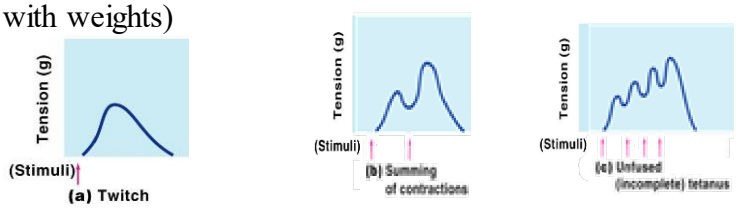
F. Isometric and Isotonic Contractions

a. muscle tension - force generated by a muscle

b. load - force resisting movement of a muscle.
Muscle tension must be greater than load to move it.

c. isometric contraction - muscle doesn't change length (trying to lift a box that is too heavy)

d. isotonic contraction - muscle moves the load (doing bicep curls with weights)



V Force, Velocity, and Duration of Skeletal Muscle Contraction

A. Force of Contraction - determined by several factors

1. number of motor units activated
2. size of muscle (in cross section)
   a. size increased by increasing the SIZE of individual muscle cells (not increasing cell #)
3. Series-Elastic Elements
   a. sheath around the muscle and the connective tissue tendons that attach muscle to bone
   b. "stretching" of non-contractile parts allows time for muscle to produce a tetanic contraction

4. Degree of Muscle Stretch (Actin-Myosin Overlap)
   a. optimal force can be generated when muscle is between 80 - 120% of resting length

B. Velocity and Duration of Contraction
   1. Effect of the Load on a Muscle
      a. smaller the load, faster the contraction
      b. larger load: slower contraction/less duration
   2. Type of Muscle Fiber

      a. Red Slow-Twitch Fibers (small, red)
         i. slow twitch; slow acting myosin ATPases
         ii lots of myoglobin (red) to store oxygen
         iii. many mitochondria, active enzymes
         iv. use fat as primary fuel source
         v. very aerobic, long duration contraction
      b. White Fast-Twitch Fibers (large, pale)
         i. fast twitch; fast acting myosin ATPases
         ii. few mitochondria, primarily anaerobic
         iii. glycogen stores used for anaerobic resp.
         iv. lactic acid produced, fatigues quickly
         V. rapid, intense, short duration contraction
      c. Intermediate Fast-Twitch Fibers (medium, pink)
         i. fast twitch; fast acting myosin ATPases
         ii. aerobic with myoglobin present
         iii. somewhat resistant to fatigue
   3. Muscle Composition by Fiber Type
      a. most muscles have combinations of all 3 types
      b. people differences are genetically determined

VI. Effect of Exercise (and no exercise) on Skeletal Muscle

A. Physiological Adaptations from Exercise
1. aerobic exercise - that requiring steady oxygen

   a. capillaries, myoglobin, mitochondria increase
   b. better endurance and strength

2. resistance exercise - short duration, high load

a. actin, myosin, myofibers all increase
b. hypertrophy - increase in muscle size
b. glycogen stores and connective tissue increase

B Disuse Atrophy

1. lack of use can result in loss of size (atrophy) and strength of a muscle
2. denervation - lack of nervous stimulation can also cause severe atrophy

VII. Muscle Metabolism

A. Pathways for Synthesis of ATP for Contraction

1. ADP - Creatine Phosphate (Immediate Reserve)

Creatine-phosphate + ADP → Creatine + ATP
(Creatine Kinase)

a. used for first 3 - 5 seconds of activity while respiration processes are warming up

2. Anaerobic Respiration (Lactic Acid Fermentation) (Insufficent Oxygen Supply)

glycolyis glucose → pyruvic acid (INSUFFICIENT oxygen)
pyruvic acid → lactic acid

** used for short-term, intense activity (10 - 15 sec)
** used when oxygen demand CANNOT be met by resp/circ
** yields only 2 ATP per glucose
** lactic acid is reconverted to pyruvic acid when oxygen becomes available
** pyruvic acid then broken down all the way to $C0_2$ to release 34 more ATP

3. Aerobic Respiration (Sufficient Oxygen Supply)

glycolyis glucose → pyruvic acid (SUFFICIENT oxygen)
pyruvic acid → $H_20 + C0_2$

** used for more prolonged, steady activity (walking)
** used when oxygen demand CAN be met by resp/circ
** yields 36-38 ATP per glucose (18-19 X anaerobic!!!)
** glycolysis occurs in the sarcoplasm
** oxidative reactions, using pyruvic acid to make more ATP, occurs in the mitochondria

B. Muscle Fatigue, Oxygen Debt, and Heat Production

1 muscle fatigue - inability of a muscle to contract on a physiological basis

a. when there is less ATP than the muscle requires
b. lactic acid decreases pH, affects enzymes
c. salt loss (Na^+, K^+, Ca^{++}); ionic imbalance
d. ATP required to drive Na^+-K^+ ATPase Pump

2. contractures - continuous contracted state of the muscle ("heads" are not released)

3. oxygen debt - oxygen must be "paid back" in order to restore muscle to original rested state:

a. restore reserves of ATP and Creatine Phosphate
b. lactic acid converted back to pyruvic acid
c. restore reserves of glucose and glycogen
d. restore oxygen reserves (stored in myoglobin)
e. athletic conditioning increases the efficiency of oxygen use, thereby reducing oxygen debt

4. heat production - muscle contraction produces heat which can be dangerous (extreme body temperature) or can be useful (generate heat by shivering)

Endocrinology:

It's the science that deals with study of structure, function's, diagnosis and treatment of any disorders in any parts of endocrine system (endocrine glands &their hormones).

Endocrine gland:

Is the ductless gland and its secretions go directly to blood without any ducts in contrast with exocrine glands which have duct to secrete their secretions.

Some organs like pancreas and testis can be considered as mixed gland(exo&endocrine), pancreas secrete insulin and glucagon from islets of Langerhans (endocrine) and can secrete pancreatic juice by duct consider as (exocrine).

Testis also can produce testosterone as an endocrine and produce sperms as an exocrine gland

Functions of the endocrine system:

1. Controls the internal environment of the body by regulation of chemical composition.
2. Helps the body in emergency demands such as; infection, trauma, emotional stress, dehydration, starvation and hemorrhage
3. Plays an important role in growth and development.
4. Regulates the reproduction system including: gamates(sperms& ova), fertilization, nourishment of embryo and fetus, delivery and nourishment of newborn
5. Regulates the organic metabolism and energy balance.

Hormone:

It's a Greek word meaning (stimulate stimulus). It's a chemical substance produced by one or a group of cells and secreted into body fluids and diffused or transported to exert a physiological control effect on other cells of body.

Nature of hormones:

A. General hormones:

Are secreted by specific endocrine glands and transported by blood to cause physiological action at all or almost all body cells. Like growth hormone and thyroid hormones.

B. Specific Hormones:

Hormones affect only specific target tissues, because only these tissues have receptors for the hormone. For example, adrenocorticotropic hormone (ACTH) from the anterior pituitary gland specifically stimulates the adrenal cortex causing it to secrete adrenocortical hormones. Also, ovarian hormones have specific effects on the female sex organs as well as on the secondary sexual characteristics of the female body.

C. Local or Parahormones:

Are chemical messengers or regulators which are not hormones in fact such as:

1. Acetyle Choline (Ach):

Released at parasympathetic nervous system and skeletal nerve endings.

2. Secretin: Released from duodenal wall and transported by blood to pancreas causing watery pancreatic secretion.

3. Cholecystokinin:

Released by intestinal wall and cause contraction of gall bladder and increase enzymatic secretion of pancreas.

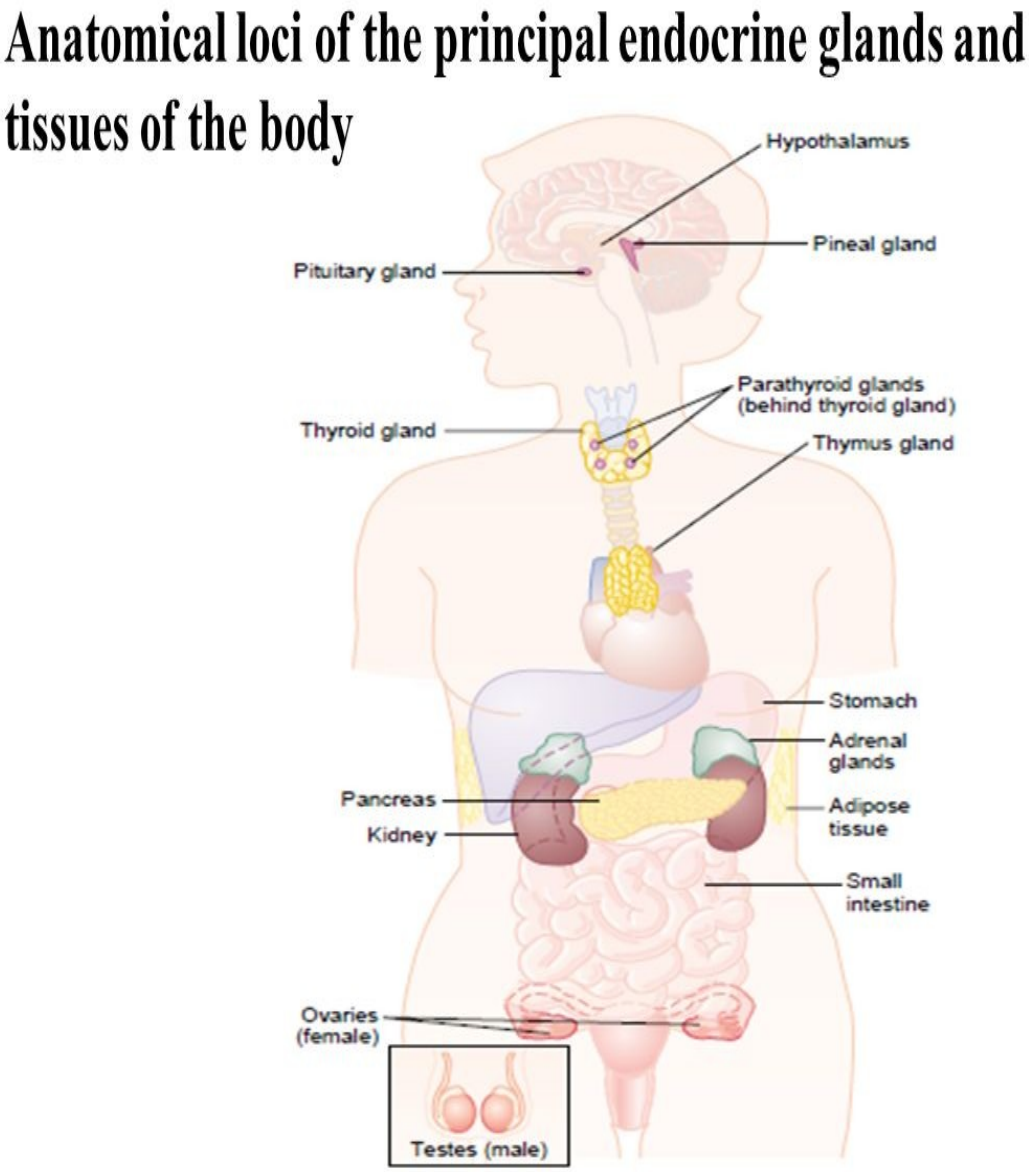
4. Prostaglandin (PGs):

Presents in many tissues and have important local effects in reproduction.

5. Erythropoietin: Released by kidney and stimulate RBCs production by bone marrow.

6. Histamine:

Produced by mast cells and causes vasodilation.



This figure shows the anatomical locations of the major endocrine glands and endocrine tissues of the body, except for the placenta, which is an additional source of the sex hormones.

Chemical Structure and Synthesis of Hormones

There are three general classes of hormones:

1**. Proteins and polypeptides:**

Including hormones secreted by the anterior and posterior pituitary gland, the pancreas (insulin and glucagon), the parathyroid gland (parathyroid hormone), and many others.

2. Steroids:

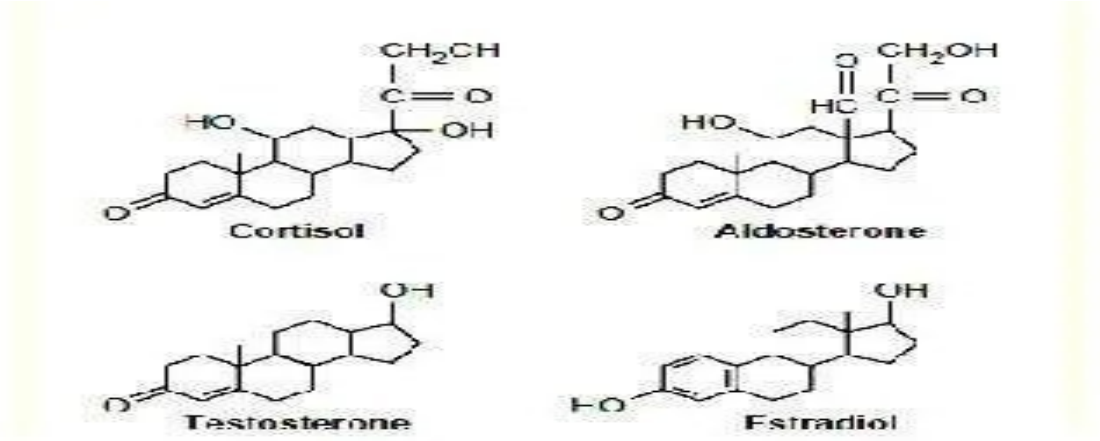
Secreted by the adrenal cortex (cortisol and aldosterone), ovaries (estrogen and progesterone), testes (testosterone), and the placenta (estrogen and progesterone)

. **3. Derivatives of the amino acid tyrosine:**

Secreted by thyroid gland (thyroxine and triiodothyronine) and the adrenal medullae (epinephrine and norepinephrine). There are no known polysaccharides or nucleic acid hormones.

Polypeptide and Protein Hormones are stored in secretory vesicles until needed. Most of the hormones in the body are polypeptides and proteins. These hormones range in size from small peptides with as few as 3 amino acids (thyrotropin-releasing hormone) to proteins with almost 200 amino acids (growth hormone and prolactin). In general, polypeptides with 100 or more amino acids are called proteins, and those with fewer than 100 amino acids are referred to as peptides.

Steroid Hormones are usually synthesized from cholesterol and are not stored The chemical structure of steroid hormones is similar to that of cholesterol, and in most instances they are synthesized from cholesterol itself (the figure show the structure of steroid hormones).



Physiology of Hormonal action:

Target cell is a cell that responds to hormonal action

The first step of a hormone's action is to bind to specific receptors at the target cell

Cells that lack receptors for the hormones do not respond Receptors for some hormones are located on the target cell membrane, whereas other hormone receptors are located in the cytoplasm or the nuclens

When the hormone combines with its receptor, this usually initiates a cascade of reactions in the cell**, with each stage becoming more powerfully activated so that even small concentrations of the hormone can have a large effect.**

Hormonal receptors are large proteins, and each cell that is to be stimulated usually has some 2000 to 100,000 receptors. Also, each receptor is usually highly specific for a single hormone; this determines the type of hormone that will act on a particular tissue. The target tissues that are affected by a hormone are those that contain its specific receptors.

The locations for the different types of hormone receptors are generally the following:-

1. In or on the surface of the cell membrane: The membrane receptors are specific mostly for the protein, peptide, and catecholamine hormones.

2. In the cell cytoplasm: The primary receptors for the different steroid hormones are found mainly in the cytoplasm.

3. In the cell nucleus: The receptors for the thyroid hormones are found in the nucleus and are believed to be located in direct association with one or more of the chromosomes.

The binding between Hormones and receptors can occur by two ways:

A. The interaction between Hormones and receptors on cell membrane:

1. Hormone released by endocrine gland, circulates in blood, reach a target cell, attached to specific receptors and bring a specific message to that cell. The hormone is called (1" messenger).

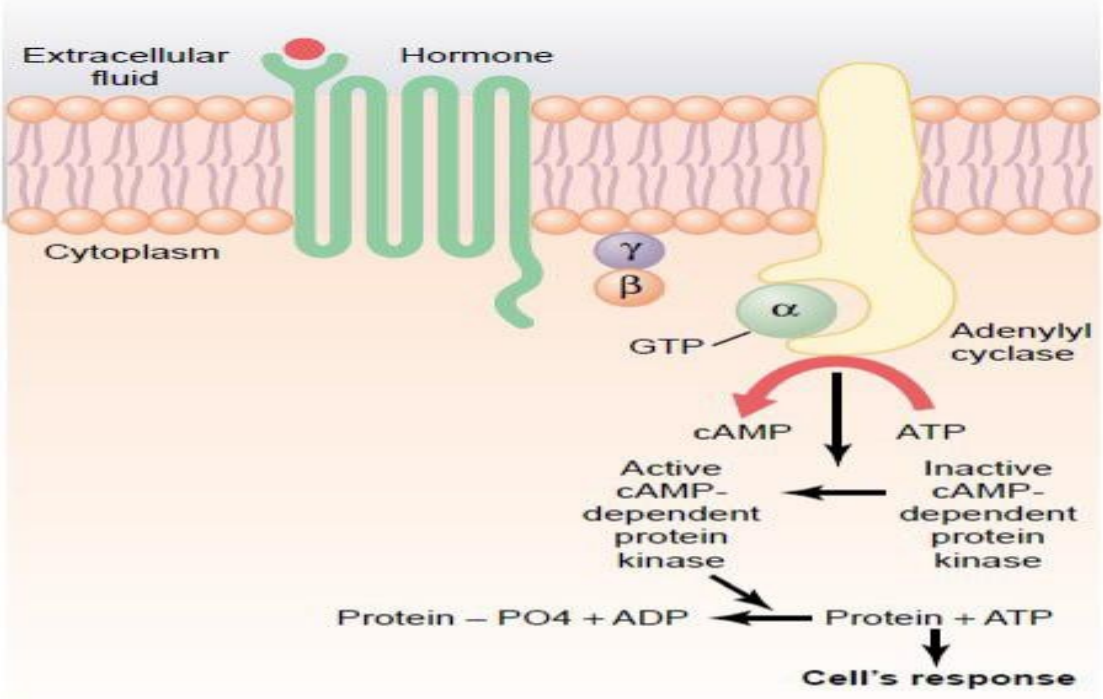
2. This interaction between hormone and specific receptors and forming (Hormone receptor complex) cause activation of adenylyl cyclase enzyme which convert the ATP (Adenosine Tri Phosphate) to cAMP(cyclic Adenosine Mono Phosphate).

3. CAMP acts as the 2 messenger and can alter the cell function according to the message indicated by hormone.

Some hormones that use the adenylyl cyclase-cAMP second messenger system:

Adrenocorticotropic hormone (ACTH)
Angiotensin II (epithelial cells)
Calcitonin
Catecholamines (b receptors)
Corticotropin-releasing hormone (CRH)
Follicle-stimulating hormone (FSH)
Glucagon, Human chorionic gonadotropin (HCG)
Luteinizing hormone (LH), Parathyroid hormone (PTH), Secretin

Somatostatin, Thyroid-stimulating hormone (TSH) and Vasopressin (ADH).

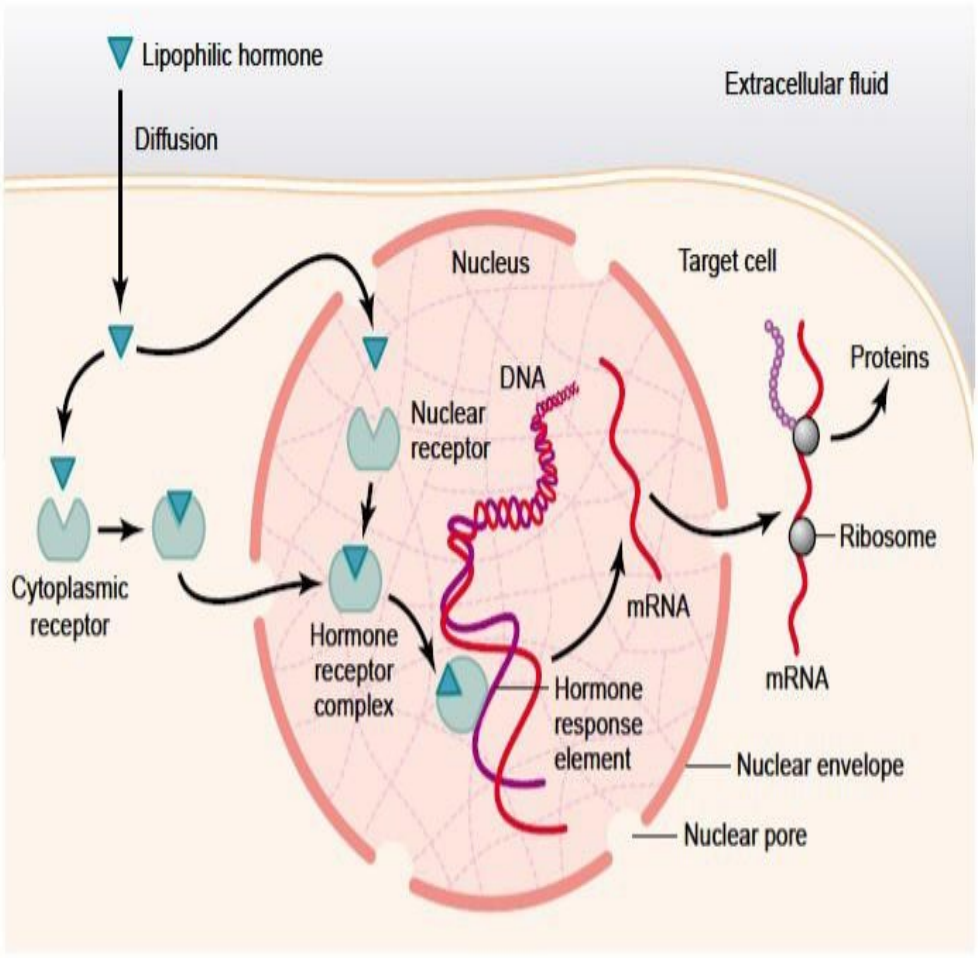


CAMP
is not the only second messenger used by the different hormones. Two other especially important ones are: calcium ions and products of membrane phospholipid breakdown.

B. Interaction between Hormone and intracellular receptors:

Steroid hormones and thyroid hormones can alter cell function by activation of some genes. These hormones can easily pass through cell membrane of target cell because they are lipid soluble. These hormones can alter cell function by this mechanism:

1. Formation of Hormone- Receptor complex inside the cell
2. Movement of H-R complex to the nucleus where it activates a specific gene.
3. Production of mRNA.
4. Production of new protein.



Mechanisms of interaction of lipophilic hormones, such as steroids, with intracellular receptors in target cells.

After the hormone binds to the receptor in the cytoplasm or in the nucleus, the hormone-receptor complex binds to the hormone response element (promoter) on the DNA.

This either activates or inhibits gene transcription, formation of messenger RNA (mRNA), and protein synthesis.

Hormonal interactions:

The action of hormone on target cell is determined by:
1. Concentration of hormone.
2. Numbers of receptors.
3. The manner by which hormones interact with other Hormones.

Types of Hormonal interactions:

A. Permissive Effect:

In this type, the action of one hormone on a target cell required a previous exposure to another Hormone or Hormones. e.g. The exposure of uterus first to estrogen and then to progesterone in order to prepare the uterus to pregnancy.

B. Synergistic Effect:

In this interaction, the effects of two or more hormones complement each other and the target cell will respond effectively to the sum of the Hormones.
e.g. production and secretion of milk by mammary glands require the synergistic effects of prolactine, growth hormone, estrogen and progesterone.

C. Antagonistic Effect:

In this type of interaction, the effect of one hormone on a target cell is opposed by the action of another hormone. eg. calcitonin from thyroid gland lowers blood calcium level while the parathyroid hormone which raises blood calcium level. Insulin lowers blood sugar level while the glucagon raises it.

Feedback Control of Hormone Secretion:

A Negative Feedback Prevents Over activity of Hormone Systems:

In most instances, this control is exerted through negative feedback mechanisms that ensure a proper level of hormone activity at the target tissue. After a stimulus

causes release of the hormone, conditions or products resulting from the action of the hormone tend to suppress its further release. In other words, the hormone (or one of its products) has a negative feedback effect to prevent over secretion of the hormone or over activity at the target tissue.

The controlled variable is often not the secretory rate of the hormone itself but the degree of activity of the target tissue. Therefore, only when the target tissue activity rises to an appropriate level will feedback signals to the endocrine gland become powerful enough to slow further secretion of the hormone

Feedback regulation of hormones can occur at all levels, including gene transcription and translation steps involved in the synthesis of hormones and steps involved in processing hormones or releasing stored hormones. e.g. decrease blood calcium level leading to stimulation of parathyroid hormone that cause increase the blood calcium level, and this increment causing negative feedback signals causing inhibit secretion of parathyroid hormone

B. Positive Feedback:

In a few instances, positive feedback occurs when the biological action of the hormone causes additional secretion of the hormone. One **example of this is the surge of luteinizing hormone (LH) that occurs as a result of the stimulatory effect of estrogen on the anterior pituitary before ovulation.**

The secreted LH then acts on the ovaries to stimulate additional secretion of estrogen, which in turn causes more secretion of LH. Eventually, LH reaches an appropriate concentration, and typical negative feedback control of hormone secretion is then exerted .

Hormonal Transport:

1. Protein hormone such as insulin, glucagon, pituitary hormones, calcitonin parathyroid hormone etc, are usually stored within gland until needed. Up on call, they are then secreted.
2. Steroid hormones such as, aldosterone, cortisol, androgens from adrenal gland cortex, testosterone from testes and estrogen and progesterone from ovaries, all

steroids are not stored but released as produced then circulate in blood as a pure hormones.

Plasma contains specific carrier proteins for steroids hormones and Thyroxin such as:

a. Thyroxin-Binding Globulin (TBG).
b. Corticosteroid Binding Globulin (CBG) (Transcortin).
c. Sex Hormone Biding Globulin (SHBG).
d. Neurophysin binds with oxytocin and ADH in posterior pituitary gland

The binding of hormone to proteins has many importances:

1. For transport hormones.
2. Prevent diffusion of hormones to the tissues.
3. Prolong hormone effect.
4. Prevent toxic effects and side effects of high doses of hormones.
5. Make it in active until it become free

Interaction of Endocrinology and Nervous system:

The two great control systems work together within the body, the nervous system work as an afferent branch bring impulses to hypothalamus, then endocrine system release hormones to complete the reflex.

Endocrine system serve as a wireless communication system and the nervous system serve as a wire system play together to keep the homeostasis.

e.g. **The ovulation in rabbit** is an example for neuro-endocrine interaction-

1. In mating the physical stimulation of cervix sends impulse to travel through spinal cord

2. Impulse reaches to hypothalamus and stimulates it to release (GnRH) or (GnRF) goes to anterior pituitary gland.

3. GnRH or GRF stimulates the anterior pituitary gland to release Luteinizing Hormone (LH).

4. LH travels through circulating system to ovaries and stimulates mature follicle to induce rupture and ovulation.

Pituitary Gland (Hypophysis):

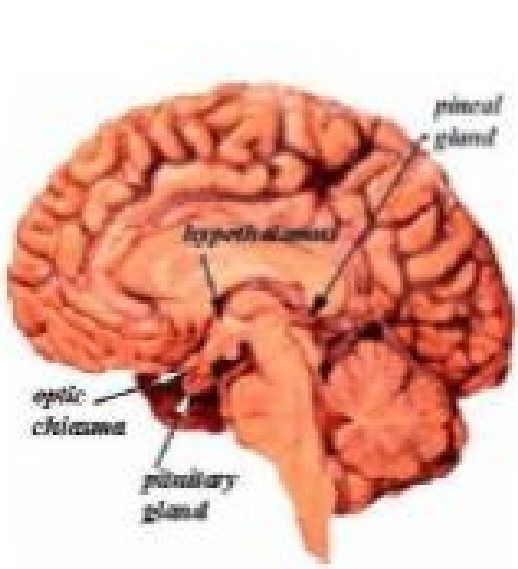
It's the master gland of body, it's in fact two glands are closely associated with hypothalamus

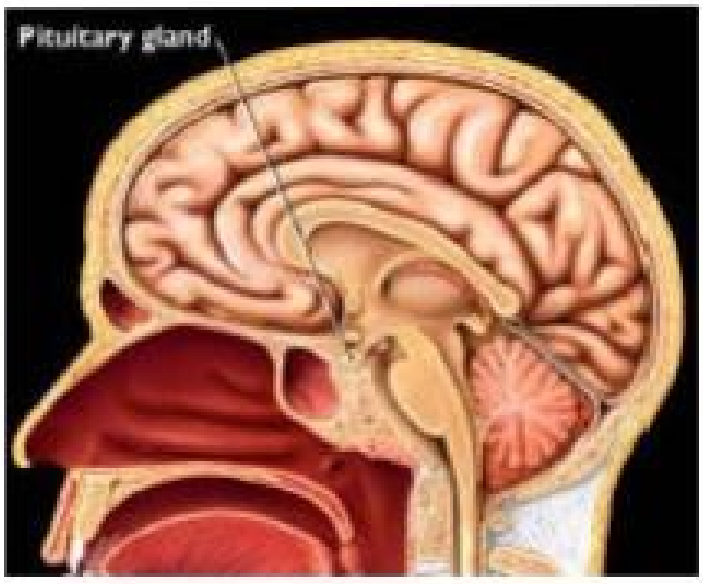
A. Adenohypophysis or Anterior lobe of pituitary gland:

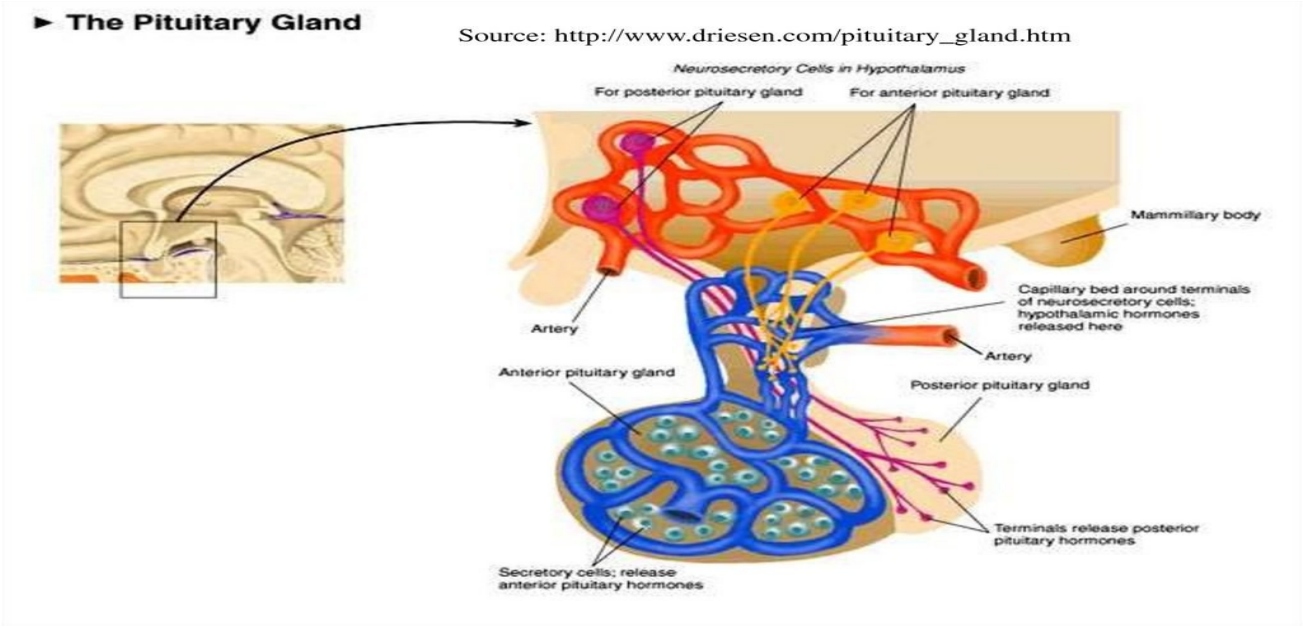
This part is associated with hypothalamus by portal system carry blood from hypothalamus to capillaries of Adenohypophysis.

B. **Neurohypophysis or Posterior lobe of pituitary gland:**

This is part directly connected to the hypothalamus by hypothalamic-hypophyseal tract (nervous tract). Hormones released from neurohypophysis are synthesized in certain hypothalamic neurons and move down the axon of nerve tracts and stored in terminal of axon in neurohypophysis. Therefore, the neurohypophysis is a storage location for hormones produced by hypothalamus.







Hypothalamic Releasing and Inhibitory Hormones That Control Secretion of the Anterior Pituitary Gland:

1. Thyrotropin-Releasing Hormone (TRH): Stimulates secretion of TSH from anterior pituitary gland

2. Gonadotropin-Releasing Hormone (GnRH): Stimulates secretion of FSH and LH by anterior pituitary gland.

3. Corticotropin-Releasing Hormone (CRH): Stimulates secretion of ACTH by anterior pituitary gland

4. Growth Hormone-Releasing Hormone (GHRH): Stimulates secretion of growth hormone by anterior pituitary gland. (somatotropin).

5. Growth Hormone Inhibitory Hormone (GHIH): Inhibits secretion of growth hormone by anterior pituitary gland (somatostatin).

6. Prolactin-Releasing Hormone (PRH): Stimulate secretion of prolactin by Adenohypophysis.

7. Prolactin-Inhibiting Hormone (PIH): Inhibits secretion of prolactin by Adenohypophysis.

Hormones of the Anterior Pituitary Gland and Their Physiological Functions

1. Growth hormone (GH or somatotropin):

a. stimulates body growth until reach to adult size and maintain that size;
b. stimulates lipolysis; **c.** protein metabolism: GH stimulates transcription of DNA and then formation of mRNA to protein synthesis. **d**. increases insulin secretion from beta cells of pancreas that lead to increase glucose uptake and then increment carbohydrate metabolism.

2. Adrenocorticotropic Hormone (ACTH; corticotropin): Stimulates production of glucocorticoids and androgens by the adrenal cortex; maintains size of zona fasciculate and zona reticularis of cortex.

3. Thyroid-stimulating Hormone (TSH; Thyrotropin): Stimulates production of thyroid hormones (T3, T4 and Calcitonin) by thyroid follicular cells; maintains size of follicular cells.

4. Gonadotropines:

a. Follicle-Stimulating Hormone (FSH): Stimulates development of ovarian follicles, regulates spermatogenesis in the testis.
b. **Luteinizing Hormone (LH):** in females: Causes ovulation and formation of the corpus luteum in the ovary, stimulates production of estrogen and progesterone by the ovary; in males: it's called Interstitial Cells Stimulating Hormone (ICSH) stimulates testosterone production by the testis (Leydig cells).

5. **Prolactin (PRL):** Stimulates milk production and secretion from mammary glands.

Hormones of Neurohypophysis (posterior lobe):

1. **Oxytocin**: produced by Para Ventricular Nucleus (PVN) in hypothalamus, its actions:
a. contraction of smooth muscles of the uterus.
b. contraction of the myothelial cells in mammary glands and cause milk ejection
c. help transport of sperms in uterus during copulation.

Control: suckling and stimulation of cervix and vagina leading to stimulate releasing of oxytocin

2. **Anti Diuretic Hormone (ADH) or Vassopressin:** produced by Supra Optic Nucleus (SON) in hypothalamus, its functions
a. prevents excess loss of water in urine by increasing water and sodium reabsorption in distal tubules and collecting ducts.
b. has a small effect of constriction of blood vessels and will increase blood pressure

Mechanism of action: concentrated blood leads to increase the osmotic pressure and will lead to stimulation of osmoreceptors (in hypothalamus) all that leads to increase ADH and water reabsorption from kidney tubules.

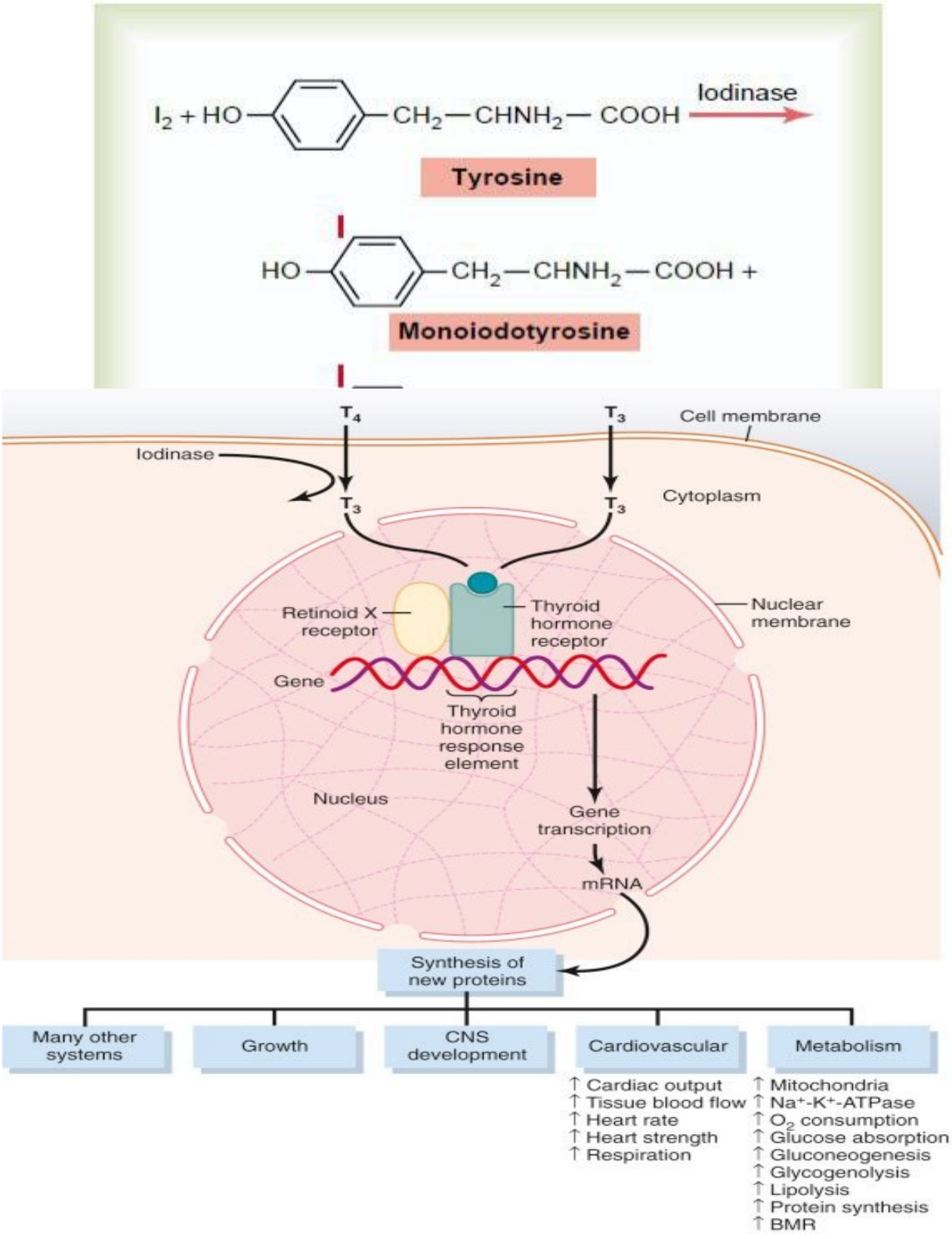
Thyroid Gland:

Located below larynx and surround the trachea, thyroid hormones are synthesized from iodine and amino acid tyrosine, thyroid hormones are:
1. Thyroxine (Tetraiodo thyronine or T4)
2. Triiodothyronine or T3, T3 is more active than T4.

Both hormones are bound with proteins to be transported transport in blood and their functions are:

a. Both T3&T4 regulate metabolism, they increase the rate of 02 consumption and thus the rate of carbohydrate metabolism and protein break down and fat metabolism are increased and finally increase heat production and rise body temperature.

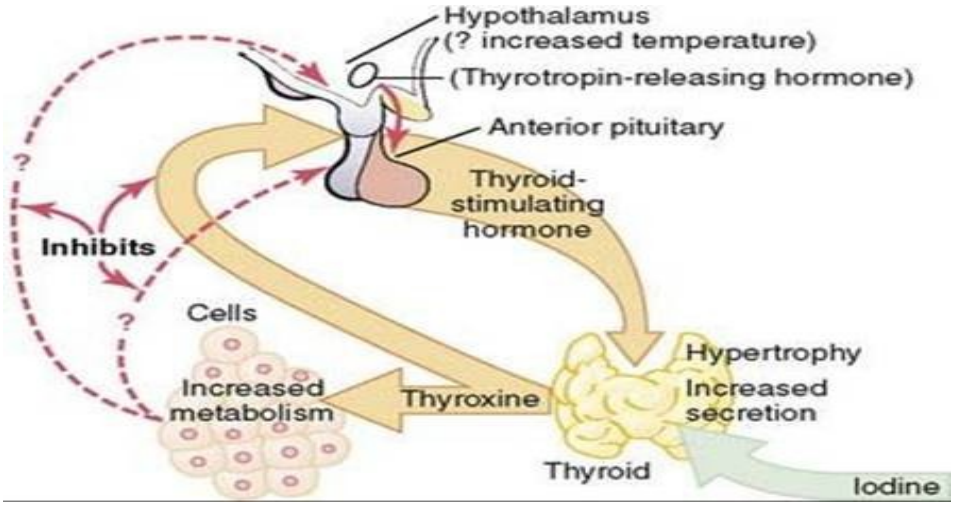
b. Both hormones work with growth hormone to regulate growth especially in nervous system.



Regulation of T3&T4 production: that's by many ways:

a. Role of hypothalamus:

T3&T4 TRH (from hypothalamus) TSH (from anterior pituitary gland) and that will act on thyroid gland†T3&T4 and this increment leads to inhibit releasing
of TRH by negative feedback mechanism



b. Pregnancy-metabolic rate that will need T3&T4.
c. Cold climate-1T3&T4 to maintain body temperature.

3. Calcitonin: secreted from c-cells of thyroid gland which regulate ca++ level in blood by stimulation of calcium uptake by bones (calcitonin-blood calcium level).

Parathyroid Gland:
Parathyroid gland are located in the posterior part of thyroid gland, their hormone is parathyroid hormone (PTH) which regulates the concentration of calcium and certain other minerals in blood.

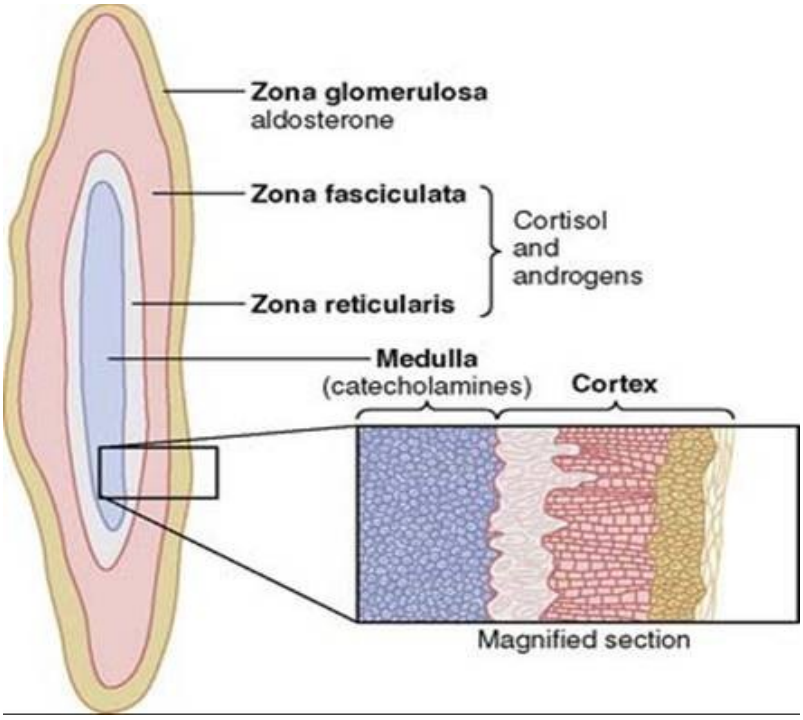
PTH and calcitonin have antagonistic effects; PTH action is along with vitamin D to maintain calcium concentration in blood as well as the role of calcitonin:
blood calcium-PTH (with action of vit D)-
1.calcium releasing from bones.
2.calcium absorption from intestine.
3. calcium excretion from kidneys

All of that leads to rise calcium level in blood and return to normal blood calcium-
PTH&Calcitonin will-
1.store of calcium in bones.
2 .calcium absorption.
3.Tcalcium excretion.

All of that leads to calcium level in blood and return to normal
Note: PTH leading to increase phosphate excretion by kidney.

Adrenal Gland:

The two adrenal glands, each of which weigh about 4 grams, lies at the superior poles of the two kidneys; each gland is composed of two distinct parts, the adrenal **medulla and the adrenal cortex.**



The adrenal medulla, the central 20 per cent of the gland, is functionally related to the sympathetic nervous system; it secretes the hormones epinephrine (adrenaline) and norepinephrine (nor-adrenaline) in response to sympathetic stimulation.

The adrenal medulla consists of masses of neurons that is part of sympathetic branch of A.N.S. In addition to release their neurotransmitters at synapse, it releases them into blood and act as endocrine gland, the adrenal gland releases:
1. Adrenaline (epinephrine). 2. Nor-adrenaline (nor-epinephrine).

The releasing of them triggered by nervous stimulation in response to physical or mental stress. Some effects of them:
a. Increase rate and strength of heart rate will lead to increase blood pressure
b. Rise the blood sugar.
c. Increase metabolic rate.
d. Broncho-dilation
e. Pupils dilation (mydriasis).

<u>The Adrenal cortex consists of three layers</u>:

a. Zona glomerulosa: thin layer located underneath the capsule forming about 15% of adrenal cortex, this layer can secrete significant amount of aldosterone. The secretion of aldosterone is controlled mainly by the extracellular fluid concentrations of angiotensin II and potassium, both of which stimulate aldosterone secretion.

b. Zona Fasciculata: the middle and widest layer, constitutes about 75 per cent of the adrenal cortex and secretes the glucocorticoids cortisol and corticosterone, as well as small amounts of adrenal androgens and estrogens. The secretion of these cells is controlled in large part by the hypothalamic-pituitary axis via adrenocorticotropic hormone (ACTH)

c. Zona Reticularis: the deepest layer of the cortex, secretes the adrenal androgens dehydroepiandrosterone (DHEA) and androstenedione, as well as small amounts of estrogens and some glucocorticoids. ACTH also regulates secretion of these cells, although other factors such as cortical androgen-stimulating hormone, released from the pituitary, may also be involved.

The mechanisms for controlling adrenal androgen production, however, are not nearly as well understood as those for glucocorticoids and mineralocorticoids.

Aldosterone and cortisol secretion are regulated by independent mechanisms. Factors such as angiotensin II that specifically increase the output of aldosterone and cause hypertrophy of the zona glomerulosa have no effect on the other two zones. Similarly, factors such as ACTH that increase secretion of cortisol and adrenal androgens and cause hypertrophy of the zona fasciculata and zona reticularis have little or no effect on the zona glomerulosa.

Some Functions of the Mineralocorticoids-Aldosterone:

a. Aldosterone increases renal tubular reabsorption of sodium and secretion of potassium.
b. excess aldosterone increases extracellular fluid volume and arterial pressure but has only a small effect on plasma sodium concentration.

Although aldosterone has a potent effect in decreasing the rate of sodium ion excretion by the kidneys, the concentration of sodium in the extracellular fluid often rises. (aldosterone increase reabsorption of Na and water from renal tubules).

Some disorders in adrenal gland:

A. Addison disease:

Hyposecretion of adrenal cortex. Caused b:
1. Destruction of adrenal cortex by infection.
2 Destruction by auto immune diseases.
3. Inherited mutation in ACTH receptors in adrenal cells

B. Cushing syndrome:

Excess levels of glucocorticoids. Caused by:

1. Increase production of ACTH.
2. Increase production of adrenal hormones themselves (e.g. by tumor).
3. As a result of glucocorticoids therapy of some disorders such as Rheumatoid Arthritis or preventing rejection of an organ transplant.

In turn, these hormones cause almost the same effects as direct stimulation of the sympathetic nerves in all parts of the body.

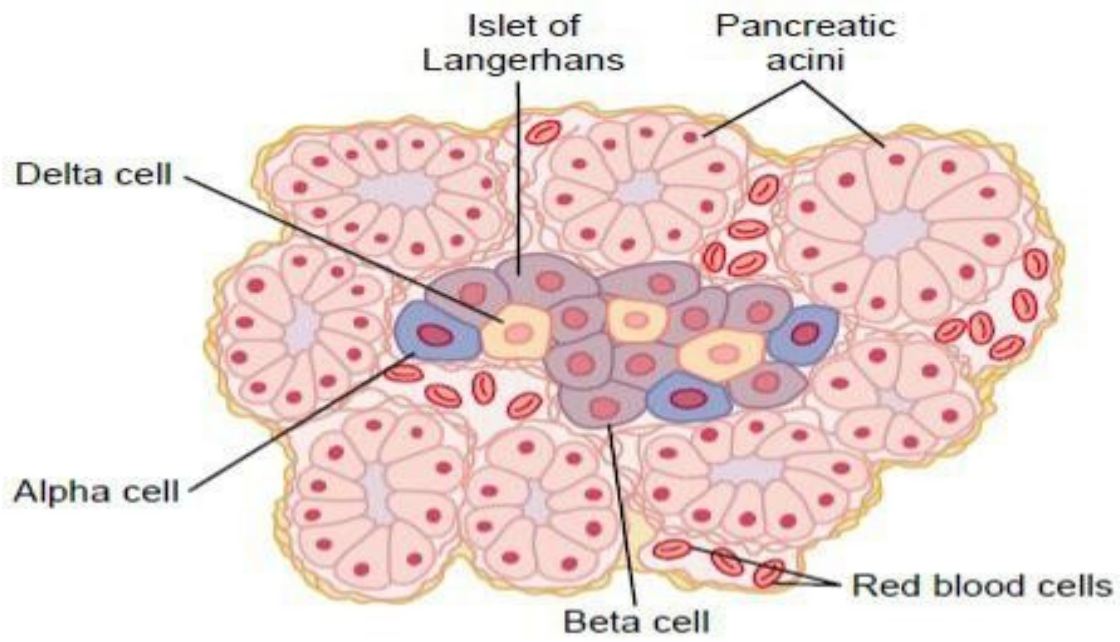
The adrenal cortex secretes an entirely different group of hormones, called corticosteroids. These hormones are all synthesized from the steroid cholesterol, and they all have similar chemical formulas. However, slight differences in their molecular structures give them several different but very important functions.

Pancreas:

The pancreas is composed of two major types of tissues: (1) the acini, which secrete digestive juices into the duodenum, and (2) the islets of Langerhans, which secrete insulin and glucagon directly into the blood.

The human pancreas has 1 to 2 million islets of Langerhans, each only about 0.3 millimeters in diameter. The islets contain three major types of cells, alpha, bera, and delta cells, which are distinguished from one another by their morphological and staining characteristics.

The alpha cells, about 25 per cent of the total, secrete glucagon. The beta cells, constituting about 60 per cent of all the cells of the islets, lie mainly in the middle of each islet and secrete insulin and amylin, a hormone that is often secreted in parallel with insulin, although its function is unclear. The delta cells, about 10 per cent of the total, secrete somatostatin.



Glucagon, a hormone secreted by the alpha cells of the islets of Langerhans when the blood glucose concentration falls, has several functions that are diametrically opposed to those of insulin. Most important of these functions is to increase the blood glucose concentration, an effect that is exactly the opposite that of insulin, which promotes the degradation of glycogen into glucose-1-phosphate.

Insulin is synthesized in the beta cells by the usual cell machinery for protein synthesis, beginning with translation of the insulin RNA by ribosomes attached to the endoplasmic reticulum to form an *insulin*.

The mechanism by which insulin causes glucose uptake and storage in the liver (decrease blood glucose level) includes several almost steps:

1. Insulin inactivates liver phosphorylase, the principal enzyme that causes liver glycogen to split into glucose. This prevents breakdown of the glycogen that has been stored in the liver cells.

2. Insulin causes enhanced uptake of glucose from the blood by the liver cells. It does this by increasing the activity of the enzyme glucokinase, which is one of the enzymes that cause the initial phosphorylation of glucose after it diffuses into the liver cells.

3. Insulin also increases the activities of the enzymes that promote glycogen synthesis, including especially glycogen synthase, which is responsible for

polymerization of the monosaccharide units to form the glycogen molecules. The net effect of all these actions is to increase the amount of glycogen in the liver.

Somatostatin secreted from delta cells of islets of Langerhans, somatostatin has multiple inhibitory effects as follows:

1. Somatostatin acts locally within the islets of Langerhans themselves to depress the secretion of both insulin and glucagon

2. Somatostatin decreases the motility of the stomach, duodenum, and Gallbladder.

3. Somatostatin decreases both secretion and absorption in the gastrointestinal tract.

Diabetes Mellitus

Diabetes mellitus is a syndrome of impaired carbohydrate, fat, and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin. There are two general types of diabetes mellitus:

1. **Type I diabetes, also called insulin-dependent diabetes mellitus (IDDM). and is caused by lack of insulin secretion.**
2. **Type II diabetes, also called non-insulin-dependent diabetes mellitus (NIDDM), and is caused by decreased sensitivity of target tissues to the metabolic effect of insulin.**

This reduced sensitivity to insulin is often called insulin resistance. In both types of diabetes mellitus, metabolism of all the main foodstuffs is altered. The basic effect of insulin lack or insulin resistance on glucose metabolism is to prevent the efficient uptake and utilization of glucose by most cells of the body, except those of the brain.

As a result, blood glucose concentration increases, cell utilization of glucose falls increasingly lower, and utilization of fats and proteins increases.

Some hormones of Gut:

1. Gastrin:

Secreted by cells in stomach and duodenum and stimulate the exocrine cells of the stomach to secrete gastric juice (HCl-Hydrochloride & pepsin).

2. Somatostatin:

Secreted by cells in gastric glands and acts on:

a. Stomach: inhibits releasing of gastrin and HCI

b. Duodenum: inhibits releasing of secretin and cholycystokinin

c. Pancreas: inhibits releasing of glucagon.

(Somatostatin also secreted by hypothalamus and pancreas).

3. Secretin:

Secreted by specific cells in duodenum when they exposed to acidic contents of the emptying stomach and it stimulates the exocrine portion of pancreas to secrete bicarbonate into pancreatic juice (nutrilization).

4. Cholycystolainin (CCK):

Secreted by cells in duodenum and jejunum when they are exposed to food, and its action is that:

1. On gall bladder contraction and force its contents of bile into the intestine.
2. On pancreas: stimulation of releasing of pancreatic digestive enzymes into pancreatic juice.

CCK also act on vagal nerve and acts on medulla oblongata and gives satiety signals (that's enough food for now).

Hormones of Kidney:

1. Erythropoietin:
Acts on bone marrow to increase R.B.Cs production and it is stimulated by bleeding and moving to high altitudes.

2. Calcitriol:
The active form of Vit D and it's promoted by action of PTH, and its actions on:
a. Intestines to increase absorption of calcium ions to blood
b. Bones to mobilize calcium ions from bones to blood

3. Rennin (enzyme):
Acts on angiotensinogen and converts it into angiotensin-I to angiotensin-II by angiotensin converting enzyme (ACE). The action of the angiotensin-II:

1. Constricts the walls of arteriols.
2. Stimulates the proximal tubules in kidney to Na reabsorption
3. Stimulates adrenal cortex to release aldosterone
4. Increases strength of heart beat.
5. Stimulates pituitary gland to release ADH. (all that above lead to raise blood pressure).

Hormones of the Heart:

Heart releases two peptides:

1. **A-Type Natriuretic Peptide (ANP):**
   Secreted from stretched atria.

2 .B-Type Natriuretic Peptide (BNP):
Released from stretched ventricles.

Both of them lower blood pressure by:
1. Relaxing arteriols.
2. Inhibiting releasing of rennin and aldosteron.
3. Inhibiting reabsorption of Na by kidney.

Prostaglandins (PGs):

Biologically, prostaglandins are active lipids that are derived from arachidonic acid in nearly every mammalian cells and secreted into surrounding fluids in a minute quantities and are potent in their action.

PGs also called local or tissue or para hormones because their site of action is the immediate area in which they produced.

PGs were so named because they were first found in seminal fluid which produced by prostate gland.

PGs released in response to chemical and mechanical stimuli. PGs are classified into several groups designated by letters (A through) or (PGA-PGI), PGs are believed to be regulators or modulators of cell metabolism:

PGE-T CAMP (second messenger) activity.

PGF-1 cGMP (second messenger)-[activity.

The importance of PGs in both normal physiology and pathology like:

1. Normal physiology: in relation to smooth muscles, blood flow, reproduction platelets function, fat metabolism respiration, nerve impulses transmission and immune response

2. Pathology: as in inflammation, neoplasia, fever and intensifying pain Some examples for variable actions of PGs:

PGE&PGF are antagonistic to each other in controlling cellular function; for example PGF-cGMP-constriction of blood vessels, bronchial constriction Uterine

contraction, leutolysis while PGE-cAMP vasodilation, Permeability of blood vessels, inhibits platelets aggregation in clotting, acts as sedative and temperature of body.