physiology : is the science that deal with the study of the function of the healthy living organisms and the changes which occurs during activity .The goal of physiology is to explain the physical and chemical factors that are responsible for the origin, development, and progression of life.

Cells as the Living Units of the Body:

The basic living unit of the body is the cell. Each organ is an aggregate of many different cells held together by intercellular supporting structures. Each type of cell is specially adapted to perform one or a few particular functions. there are about 75 trillion additional cells of other types that perform different functions. Although the many cells of the body often differ markedly from one another.

The Extracellular Fluid—The "Internal Environment"

About 60 per cent of the adult human body is fluid, mainly a water solution of ions and other substances. Although most of this fluid is inside the cells and is called intracellular fluid, about one third is in the spaces outside the cells and is called extracellular fluid. This extracellular fluid is in constant motion throughout the body. It is transported rapidly in the circulating blood and then mixed between the blood and the tissue fluids by diffusion through the capillary walls.

In the extracellular fluid are the ions and nutrients needed by the cells to maintain cell life. Thus, all cells live in essentially the same environment the extracellular fluid. For this reason, the extracellular fluid is also called the internal environment of the body.

Differences Between Extracellular and Intracellular Fluids.

The extracellular fluid contains large amounts of Na+, Cl-, and Co3- plus nutrients for the cells, such as oxygen, glucose, fatty acids, and amino acids. It also contains Co2 that is being transported from the cells to the lungs to be excreted, plus other cellular waste products that are being transported to the kidneys for excretion.

The intracellular fluid differs significantly from the extracellular fluid; specifically, it contains large amounts of K+, Mg+, and Po4-3 instead of the Na+ and Cl- found in the extracellular fluid. Special mechanisms for transporting ions through the cell membranes maintain these differences .

Homeostatic" Mechanisms of the Major Functional Systems :

The term homeostasis is used by physiologists to mean maintenance of nearly constant conditions in the internal environment.

Essentially all organs and tissues of the body perform functions that help maintain these constant conditions. For instance, * the lungs provide oxygen to the extracellular fluid to replenish the oxygen used by the cells, *the kidneys maintain constant ion concentrations, and* the gastrointestinal system provides nutrients.

A- Extracellular Fluid Transport System:

Extracellular fluid is transported through all parts of the body in two stages:

1- The first stage is movement of blood around the circulatory system.
2- 2-The second is movement of fluid between the blood capillaries and the cells.

B-Origin of Nutrients in the Extracellular Fluid

1- **The Respiratory System**: during circulation , each time the blood passes through the body, it also flows through the lungs. The blood picks up O2 in the alveoli, thus acquiring the O2 needed by the cells.

2- **The gastrointestinal tract**.:. A large portion of the blood pumped by the heart passes through the walls of gastrointestinal organs. Here, different dissolved nutrients, including carbohydrates, fatty acids, and amino acids, are absorbed from the ingested food into the extracellular fluid of the blood.

3- **Liver and Other Organs That Perform Primarily Metabolic Functions** :Not all substances absorbed from the gastrointestinal tract can be used in their absorbed form by the cells. The liver changes the chemical compositions of many of these substances to more usable forms, and other tissues of the body—fat cells, gastrointestinal mucosa, kidneys, and endocrine glands—help modify the absorbed substances or store them until they are needed.

4-Musculoskeletal System:This system provides motility for a-obtaining the food requiring for nutrition ,also protection against adverse surroundings

5-Kidneys.: Passage of the blood through the kidneys removes most substances from the plasma that are not needed by the cells. These substances include different end products of cellular metabolism, such as urea and uric acid; they also include excesses of ions and water from the food that might have accumulated in the extracellular fluid.

C- Regulation of Body Functions:

- **Nervous System**: The nervous system is composed of three major parts: a- the sensory input portion b- the central nervous system (or integrative portion), c- the motor output portion
- **Hormonal System of Regulation** : Located in the body are eight major endocrine glands that secrete chemical substances called hormones. Hormones are transported in the extracellular fluid to all parts of the body to help regulate cellular function. For instance

Thyroid hormone increases the rates of most chemical reactions in all cells, thus helping to set the tempo of bodily activity.

Insulin controls glucose metabolism.

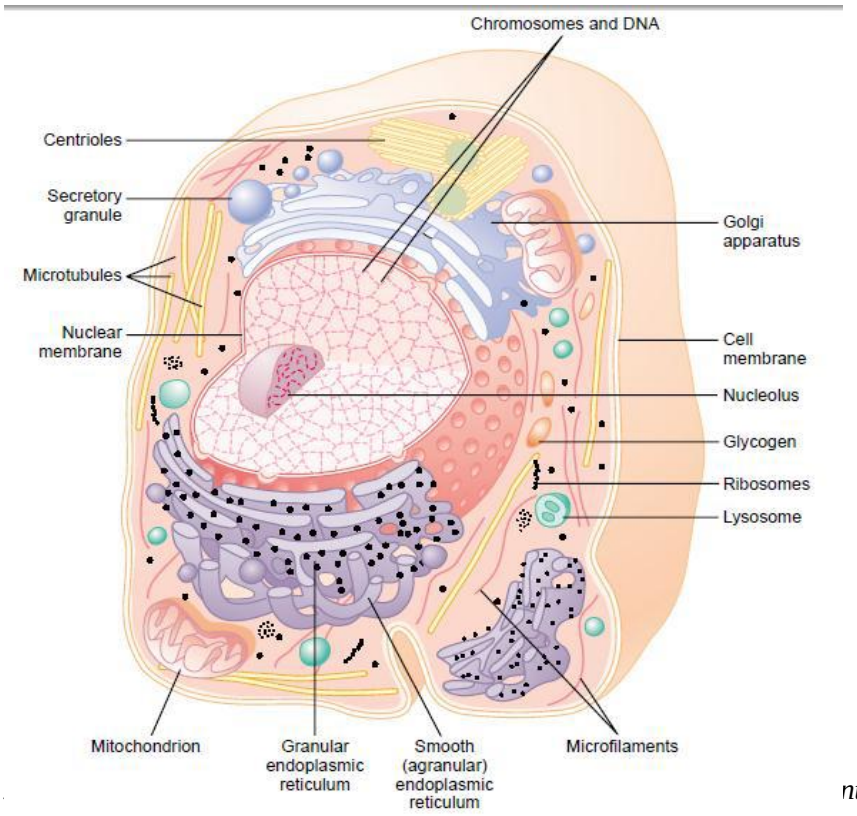
adrenocortical hormones control sodium ion, potassium ion, and protein metabolism.

parathyroid hormone controls bone calcium and phosphate. Thus, the hormones are a system of regulation that complements the nervous system. The nervous system regulates mainly muscular and secretory activities of the body, whereas the hormonal system regulates many metabolic functions

- **Reproduction**

Sometimes reproduction is not considered a homeostatic function. It does, however, help maintain homeostasis by generating new beings to take the place of those that are dying.

Organization and general function cells:



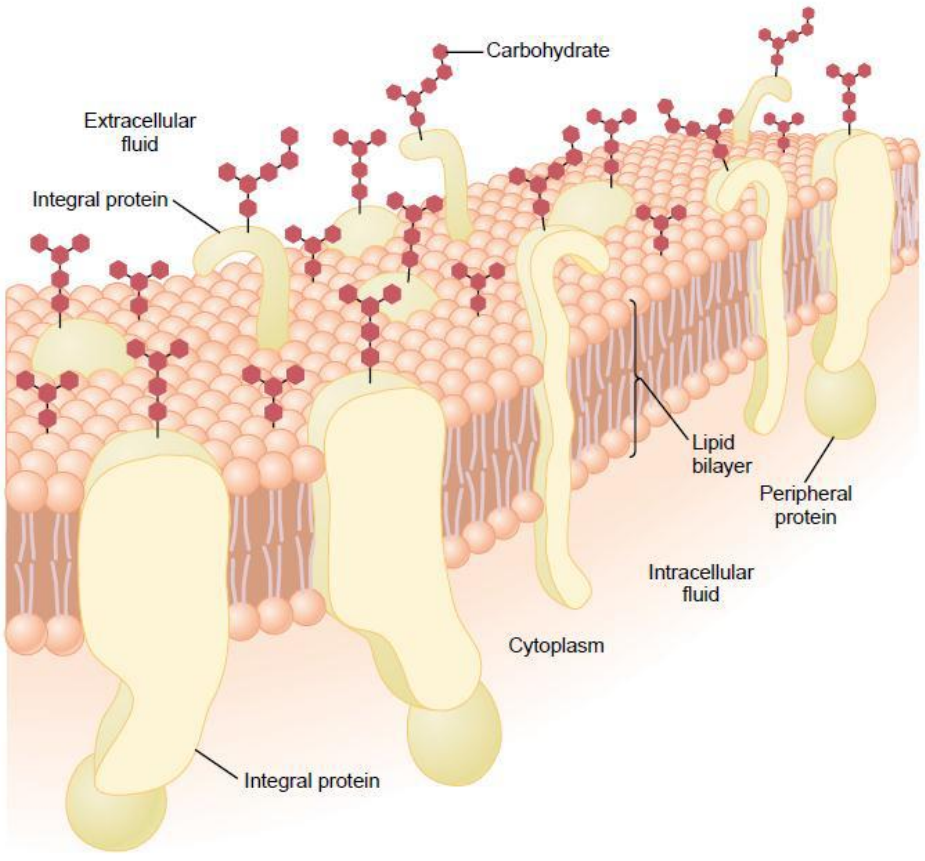
CELL MEMBRANE

The plasma membrane (often called the cell membrane) defines the boundaries of a cell . similar membranes form the boundaries of the organelles within cells . All membranes are composed of the same structural components.The plasma membrane consists of:

phospholipids bilayer, which is a thin, double-layered film of lipids—each layer only one molecule thick—that is continuous over the entire cell surface. One end of each phospholipid molecule is soluble in water; that is, it is hydrophilic. The other end is soluble only in fats; that is, it is hydrophobic. The phosphate end of the phospholipid is hydrophilic, and the fatty acid portion is hydrophobic. The polar (charged) phosphate end of the molecules are oriented toward the inner & outer surface , while non-polar (fatty acid) ends point toward each other in the interior of the membrane .

The cholesterol molecules in the membrane are also lipid in nature . These molecules, in a sense, are dissolved in the bilayer of the membrane. They mainly help determine the degree of permeability (or impermeability) of the bilayer to water-soluble constituents of body fluids. Cholesterol controls much of the fluidity of the membrane as well.

Cell Membrane Proteins : globular masses floating in the lipid bilayer. These are membrane proteins, most of which are glycoproteins. Two types of proteins occur: integral proteins that protrude all the way through the membrane, and peripheral proteins that are attached only to one surface of the membrane and do



not penetrate all the way through. . when the protein extends throughout the thickness of the membrane it is called trans membrane protein channel.

Functions of Cell Membrane Proteins :

1- Structural proteins contribute to the structure of cell membrane .
2- Some cell membrane proteins are " cell adhesion molecule" that anchor cells to their neighbors or to the basal lamina .
3- Some proteins function as a " pumps" for active transport of substances.
4-Carrier proteins transport substances down their electrochemical gradient.
5- "Ion channels" permit passage of ions in to or out of cell when activated .
6- "Aquaporin" are membrane proteins present in most cells , which act as water channels permitting high rate of water flow through the membrane .
7-The peripheral proteins function almost entirely as "enzymes" or as controllers of transport of substances through the cell membrane pores.

Carbohydrates.: Carbohydrates have little structural function in the cell except as parts of glycoprotein molecules, but they play a major role in nutrition of the cell. Sugar combine with proteins to form glycoproteins or with lipids to form glycolipids . Some of Carbohydrates serve as recognition sites that allow cells to recognize other cells in cell- to- cell interactions.

The primary function of cell membrane :

1- To regulate the internal environment of the cell & thus maintain homeostasis by controlling the passage of substances in to and out of the cell .
2- Cell membrane also play a part in transmitting information.

Cytoplasm and Its Organelles:

The cytoplasm is filled with both minute and large dispersed particles and organelles .The clear fluid portion of the cytoplasm in which the particles are dispersed is called cytosol; this contains mainly dissolved proteins electrolytes, and glucose.

1- The endoplasmic reticulum (ER) : is an extensive network of interconnected membrane – bound vesicles that transports proteins and possibly other substances synthesized by the cell . The surface of smooth ER is thought to be the site of lipid synthesis and the rough ER (with its ribosomes) the site of protein synthesis .

2- Ribosomes : small bodies that lack membranes , are found on the surface of the rough ER and in the cytoplasm . They serve as sites for protein synthesis .

3- The Golgi apparatus : consists of a stack of membrane- bound vesicles . its processes proteins package by the cell .

4- Mitochondria : consist of an outer smooth membrane & an inner folded membrane (which surrounded the matrix) . mitochondria contain the enzymes that carry out oxidative energy – producing reactions .

5- The nucleus : is the control center of the cell . it is surrounded by a nuclear envelope and contains chromosomes & one or more nucleoli .

6- Cell inclusions : are not true organelles , but rather consist of ingested substances such as fat or glycogen.

7- Lysosomes : formed from Golgi apparatus , its contain digestive enzymes (hydrolases) that are released when a cell engulfs particles , is injured or dies ; thus , its help in intracellular digestion of food, bacteria, damaged cell structures etc.

8- Peroxisomes : formed by self- replication or budding from smooth ER, they are similar to lysosomes , but smaller in size . they contain enzymes(oxidases) that oxidize various organic substances producing H2O2 ;thus , helps in the detoxification of injurious substances.

Transport of Substances Through the Cell Membrane:

I. Diffusion :

The diffusion is the net movement of similar molecules from their area of higher concentration to their area of lower concentration.

- Movement occur in all directions .
- Movement occur along the gradient.

2. Facilitated diffusion:

In facilitated diffusion ,the molecule combine with a carrier substance (a protein molecule) that is embedded in the membrane This type of diffusion is like other types of diffusion except for the carrier's ability to help the molecule move across the membrane .(its move from higher to lower concentration) . due to molecule too large to pass through the pores and or not sufficiently soluble in the membrane lipids to diffuse through them.

3. Osmosis:

move of water from its own area of higher concentration to its own area of lower concentration at a greater rate than it move in the opposite direction . This net movement of water across a selectively permeable membrane is Osmosis . Osmosis occur particularly if the membrane is permeable only to water molecules.

Osmotic pressure : is the force under which water moves from an area of low solute concentration to an area of high solute concentration

Tonicity : the term tonicity is used to describe the osmolality of a solution relative to plasma . Tonicity is a measure of the ability of the solution to change the volume of cell by altering their water content .

Isotonic : Solution that have the same osmolality as that of plasma are said to be isotonic to that of plasma , e.g. 0.9 % sodium chloride , 5% dextrose in water etc.

Hypertonic : a solution is hypertonic when it causes a net movement of water out of the cell ; that is , when the volume of the cell decreases & the volume of the solution increases .

Hypotonic : a solution is hypotonic when it causes a net movement of water in to the cell ; that is , when the volume of the cell increases & the volume of the solution decreases

4. Filtration :

In some situations in the body substances are pushed through membranes by pressure , such as the pressure the pressure of flowing blood . this phenomenon , called filtration. This pressure is called hydrostatic pressure . Filtration occurs as blood flows through the capillaries.

5. Active transport :

The transport of a substances against a gradient using an enzyme , a carrier , & ATP . Active transport causes molecules to move against concentration gradients from areas of lower to areas of higher concentration.

The substances to be actively transported :

1- Attaches to a carrier molecule that causes the substance to move across the cell membrane .

2- An enzyme that is usually part of the carrier molecule release energy from ATP . The energy is required because the substances is being moved against the concentration gradient.

The carrier molecule is a protein or glycoprotein & it has on its surface a specific carrier site for the substance it transports .

Actively transported substances include :-

1- Ions such as Na+ , K+, Ca++, Fe++ , H+& I- .

2- Some sugar , A.A , & other organic substances are moved across membranes with the energy made available by the active transport of Na+ in the same direction .

6. Endocytosis (Pinocytosis & Phagocytosis) :

Pinocytosis : also called cell drinking , the process by which the cell take in small particles including water droplets .

Phagocytosis : also called cell eating , the process by which cells take in large particles .

Protein molecules , water , & ions can be taken in by pinocytosis.

Debris from dead cells & microorganisms are taken in by phagocytosis.

Protein synthesis:

Protein are large molecules that contain carbon ,hydrogen ,oxygen and nitrogen .some protein also contain sulfur .a normal ,lean adult body is 12-18‰ protein .much more complex in structure than carbohydrate or lipid ,protein have many roles in the body and are largely responsible for the structure of body tissue .other protein work as motor to drive muscle contraction .antibodies are proteins that defines against invading microbes .some hormone that regulate homeostasis also are protein.

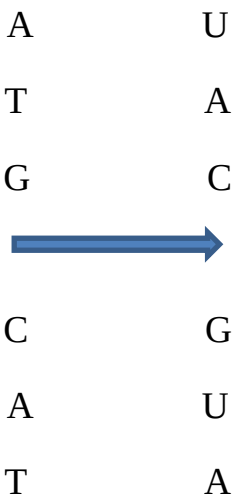
Function of protein:

Type of protein	**function**
Structural	Form structural frame work of various parts of the body **Example**: collagen in bone and other connective tissue and keratin in skin ,hair and finger nail .
Regulatory	Function as hormone that regulate various physiological processes ,control growth and development ,as neurotransmitters ,mediate responses of nervous system**.** **Example:** the hormone insulin ,which regulates blood glucose level ,and a neurotransmitter known as substance p ,which mediates sensation of pain in the nervous system
Contractile	Allow shorting of muscle cells ,which produces movement **Example**: myosin and actin
Immunological	aid responses that protect body against foreign substance and pathogens **Example**: antibodies and interleukins
Transport	Carry vital substance throughout body **Example**: hemoglobin ,which transport most oxygen and some carbon dioxide in the blood
Catalytic	Act as enzyme that regulate biochemical reaction s **Example** :salivary amylase and ATPase

Protein synthesis:

Describe the sequence of event s in protein synthesis .although cells synthesis many chemical to maintain homeostasis much of cellular machinery is devoted to synthesizing large number of proteins.

In the process called gene expression ,a genes DNA is used as a template for synthesis of a specific protein .First ,in a process aptly named transcription ,the information encoded in a specific reign of DNA is transcribed (copied) to produce a specific molecule of RNA . in a second process ,referred to as translation ,the RNA attach to a ribosome ,where the information contain in RNA is translated into a corresponding sequence of amino acids to form a new protein molecules DNA and RNA store genetic information as sets of three nucleotides .a sequence of three such as nucleotides in DNA is called a base triplet .each DNA base triplet is transcribed as a complementary sequence of three nucleotide ,called a codon ,a given codon specifics a particular amino acid .the genetic code is the set of rules that relate the base triplet sequence of DNA to the corresponding codons of RNA and the amino acids they specify.



Transcription

is the first step of gene expression, in which a particular segment of DNA is copied into RNA (especially mRNA) by the enzyme RNA polymerase. Both DNA and RNA are nucleic acids, which use base pairs of nucleotides as a complementary language. During transcription, a DNA sequence is read by an RNA polymerase, which produces a complementary, antiparallel RNA strand called a primary transcript.

Transcription proceds in the following general steps:

1. RNA polymerase, together with one or more general transcription factors, binds to promoter DNA.
2. RNA polymerase creates a transcription bubble, which separates the two strands of the DNA helix. This is done by breaking the hydrogen bonds between complementary DNA nucleotides.
3. RNA polymerase adds RNA nucleotides (which are complementary to the nucleotides of one DNA strand).
4. RNA sugar-phosphate backbone forms with assistance from RNA polymerase to form an RNA strand.
5. Hydrogen bonds of the RNA–DNA helix break, freeing the newly synthesized RNA strand.

The stretch of DNA transcribed into an RNA molecule is called a transcription unit and encodes at least one gene. If the gene encodes a protein, the transcription produces messenger RNA (mRNA) the mRNA, in turn, serves as a template for the protein's synthesis through translation. Alternatively, the transcribed gene may encode for either ribosomal RNA (rRNA), transfer RNA (tRNA). Overall, RNA helps synthesize, regulate, and process proteins; it therefore plays a fundamental role in performing functions within a cell.

Major steps of Transcription :

1-initiation

Transcription begins with the binding of RNA polymerase, together with one or more general transcription factor, to a specific DNA sequence referred to as a "promoter" to form an RNA polymerase-promoter "closed complex". In the "closed complex" the promoter DNA is still fully double-stranded..

2-Elongation

One strand of the DNA, the template strand (or noncoding strand), is used as a template for RNA synthesis. As transcription proceeds, RNA polymerase traverses the template strand and uses base pairing complementarity with the DNA template to create an RNA copy. Although RNA polymerase traverses the template strand from 3' → 5', the coding (non-template) strand and newly

formed RNA can also be used as reference points, so transcription can be described as occurring 5' → 3'. This produces an RNA molecule from 5' → 3', an exact copy of the coding strand (except that thymines are replaced with uracil's, and the nucleotides are composed of a ribose (5-carbon) sugar where DNA has deoxyribose (one fewer oxygen atom) in its sugar-phosphate backbone).

mRNA transcription can involve multiple RNA polymerases on a single DNA template and multiple rounds of transcription (amplification of particular mRNA), so many mRNA molecules can be rapidly produced from a single copy of a gene

3-Termination

RNA polymerase also recognizes signals for chain termination, which includes the release of the nascent RNA and the enzyme from the template.

Translation:

In the process of translation , the nucleotide sequence in an mRNA molecule specifies the amino acid sequence of protein .ribosomes in the cytoplasm carry out translation .the small subunit of a ribosome has a binding site for mRNA .the large subunit has two binding site for tRNA molecules a p sit and A site .the first tRNA molecule bearing its specific amino acid attaches to mRNA at the p site .the A site hold the next tRNA molecule bearing its amino acid .translation occurs in the following way:

1-An mRNA molecule binds to the small ribosomal subunit at the mRNA binding site .special tRNA called initiator tRNA bind to the start codon (AUG) on mRNA ,where translation begins .the tRNA anticodon (UAC) attach to the mRNA codon (AUG) by pairing between the complementary bases .besides being the start codon .AUG is also the codon for the amino acid methionine .thus methionine is always the first amino acid in a growing polypeptide

2-next, the large ribosomal subunit attached to the small ribosomal subunit mRNA complex, creating a function ribosome .the initiator tRNA with its amino acid (methionine),fits into the P site of ribosome.

3- the anticodon of another tRNA with its attached amino acid pairs with the second mRNA codon at the sit of the ribosome.

4-a component of the large ribosomal subunit catalyzes the formation of a peptide bound between methionine which separates from its tRNA at the p site ,and the amino acid carried by the tRNA at the A site

5-after peptide bond formation ,the tRNA at the p site detaches from the ribosome and the ribosome shifts the mRNA strand by one codon .the tRNA in the A site bearing the two peptide protein shifts into the p sit ,allowing another tRNA with its amino acid to bind to a newly exposed codon at the A site .step3-5 occur repeatedly and the protein lengthens progressively

6-protein synthesis end when the ribosome reach a stop codon at A site which causes the completed protein to detach from the final tRNA .when the tRNA vacates the A site ,the ribosome split into its large and small subunit protein synthesis progresses at a rate of about 15 peptide bond per second .as the ribosome move along the mRNA and before it completes synthesis of the whole protein ,another ribosome may attach behind it and begin translation of the same mRNA strand ,several ribosomal attached to the same mRNA constitute a polyribosome. The simultaneous movement of several ribosome along the same mRNA molecule permits the translation of one mRNA into several identical protein at the same time

PHYSIOLOGY OF MUSCLE

The muscles are excitable cells; they are machines to convert the chemical energy to mechanical energy.

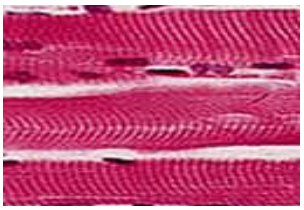
The muscle can be excited electrically, mechanically, chemically → action potential (A.p.).

It differs from the nervous system by the fact that it has a contractile mechanism which is activated by A.p.

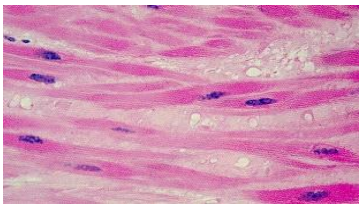
Types of muscle:

1- **Skeletal muscles:** These are voluntary muscles attach to bones.
2- **Smooth muscles**: Involuntary muscle. It is Muscle of the viscera (e.g., in walls of blood vessels, intestine, & other 'hollow' structures and organs in the body).
3- **Cardiac muscles:** Muscle of the heart. Involuntary.

40% of the body is skeletal muscles and 10% are smooth and cardiac muscles.



Skeletal muscles



Smooth muscles

Cardiac muscles

Characteristics of muscle:

- excitability - responds to stimuli (e.g., nervous impulses)
- contractility - able to shorten in length
- extensibility - stretches when pulled
- elasticity - tends to return to original shape & length after contraction or extension

Functions of muscle:

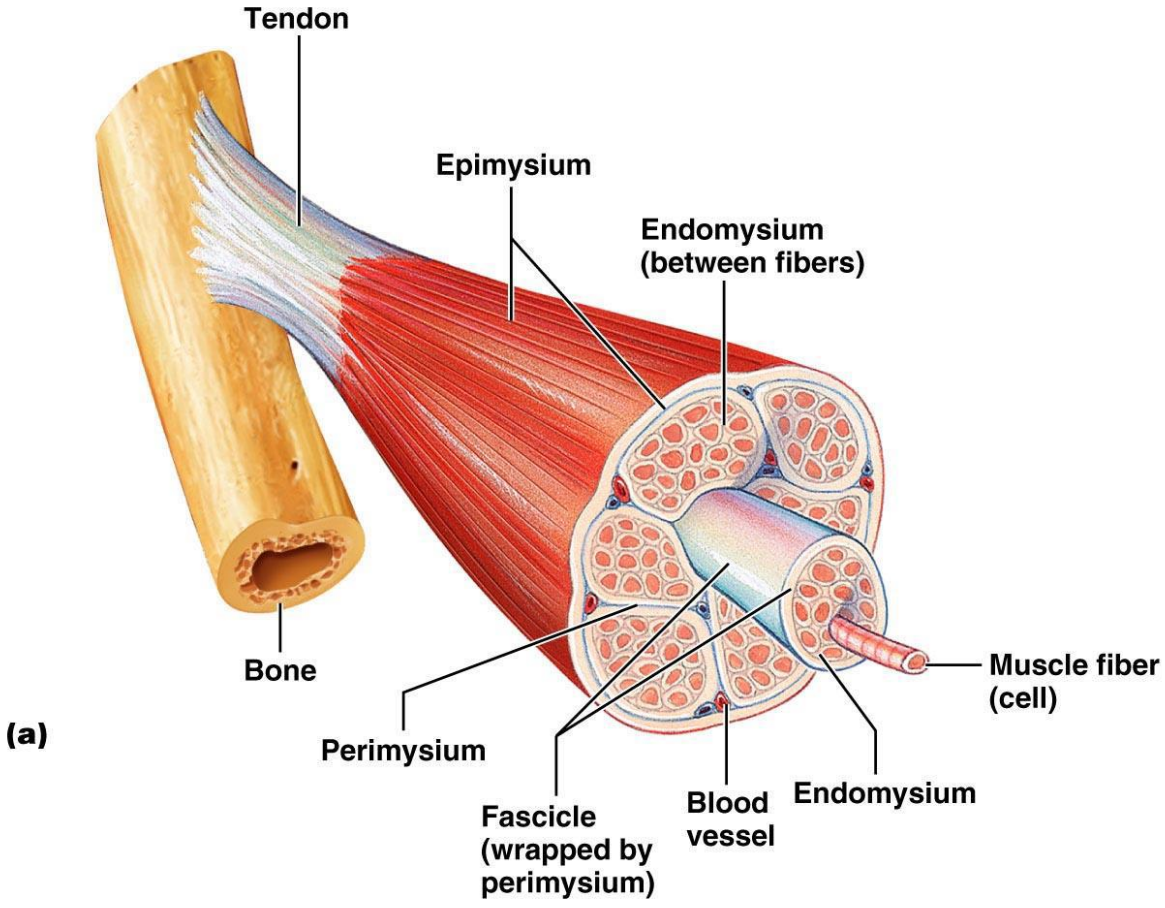
1-motion. **2**-maintenance of posture. **3**-heat production

The skeletal muscle

Morphology of Skeletal Muscle Fiber

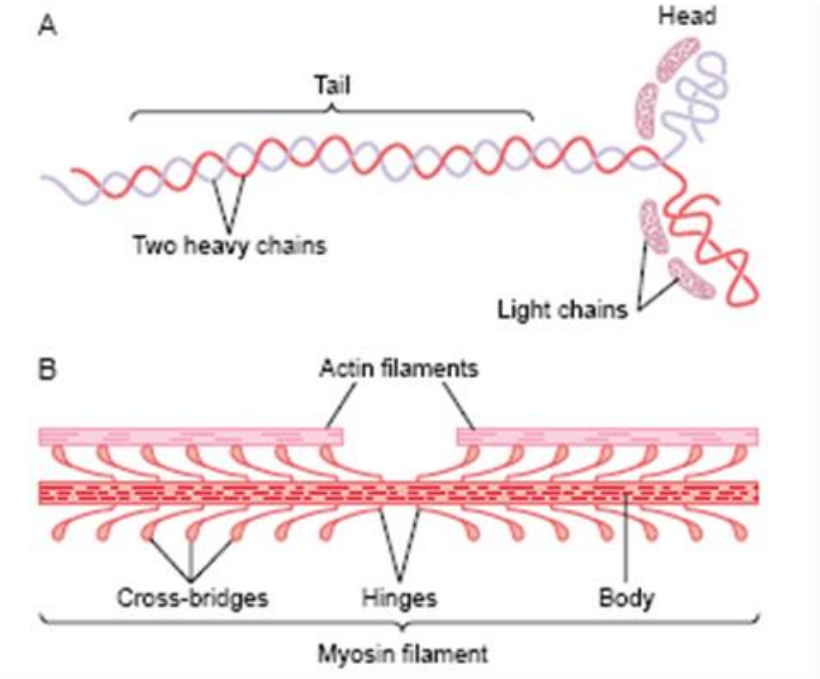
About 40 % of the body is skeletal muscle, and another 10 % is smooth and cardiac muscle .

Skeletal muscle is a striated, voluntary (neurogenic) muscle needs nerve supply to work. All skeletal muscles are composed of many fibers. Muscle fiber is a single cell, multinucleated cylindrical shape surrounded by cell membrane called sarcolemma and each fiber extends the entire length of the muscle and is usually innervated by only one nerve ending, located near the middle of the fiber. Each of these muscle fibers is made up of successively smaller subunits called (myofibrils). Each myofibrils composed of contractile protein.



contractile protein

The thick filament : composed of several hundreds of myosin molecules, each molecule consists of 6 polypeptide chains (4 light and 2 heavy chains). 2 heavy chain wrap spirally form the tail and on the end of the tail folded bilaterally will form the arm and the head. The head of myosin molecule form the cross-bridges which bind with actin. The head of myosin molecule contains actin binding sites and 2 ATPase activity sites (to produce the energy necessary for contraction).



The thin filament :thin filaments composed of three proteins, actin, tropomyosin and troponin.

Actin contain active sits on its surface in which the cross –bridges of myosin attached

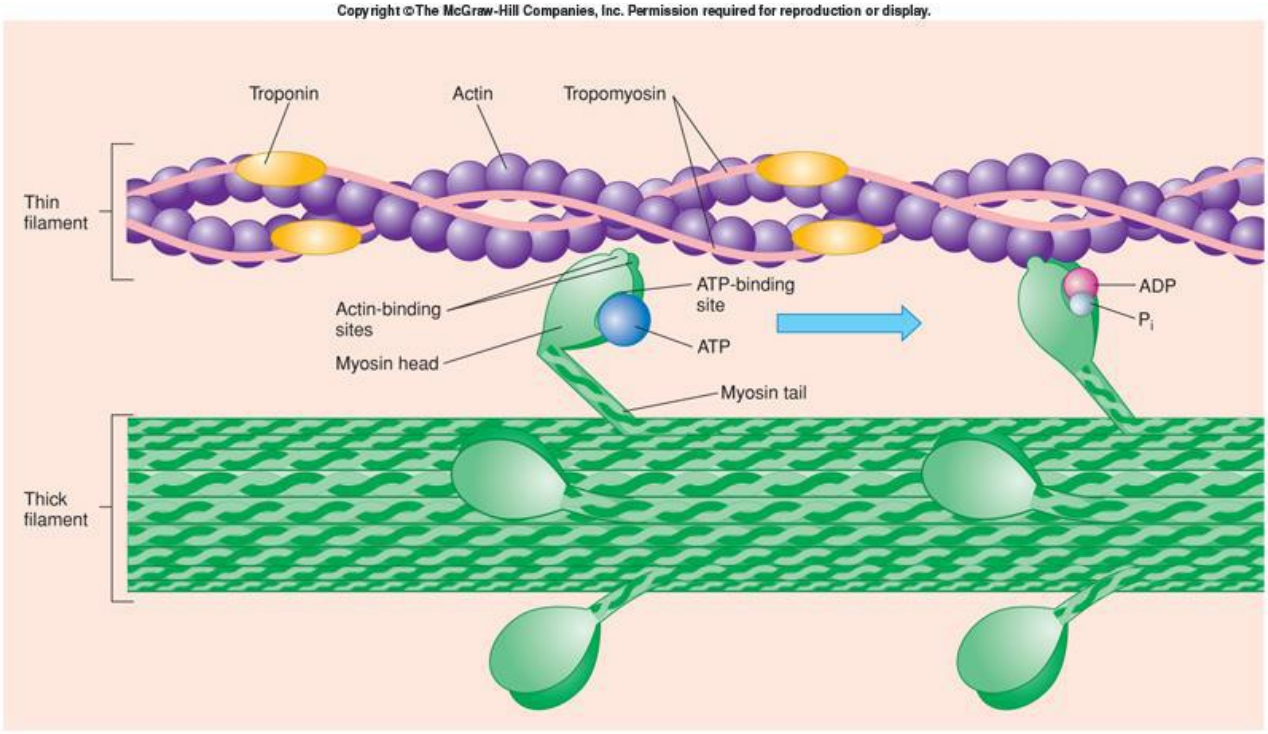
Tropomyosin: lie on the top of the active site of actin strands

Troponin: are 3 loosely bound protein subunits

-Troponin I :has strong affinity to actin .The troponin(I) binds to actin so inhibit interaction between actin and myosin

-Troponin C :has strong affinity to Ca ion, which is necessary to initiate contraction

-Troponin T :has affinity for tropomyosin form troponin tropomyosin complex



The myosin and actin filaments partially inter digitate and thus cause the myofibrils to have alternate light and dark bands, as The **light** bands contain only actin filaments and are called **I bands** . The **dark** bands contain myosin filaments, as well as the ends of the actin filaments where they overlap the myosin, and are called **A bands**, therefore the entire muscle fiber has light and dark bands giving the skeletal and cardiac muscle the striated appearance

The ends of the actin filaments are attached to the Z disc. From this disc, these filaments extend in both directions .actin held in place by Z disc

Z -disc: is a filamentous protein passes across the myofibril and from one myofibrils to anther attaching myofibrils to one anther. The ends of the actin filaments attached to Z-disc

Sarcomere: is the portion of myofibrils that lie between two successive Z –disc. It is a smallest functional unit of amyofibril necessary to produce contraction .

Sarcolemma :cell membrane of muscle fiber

Sarcoplasm :is the cytoplasm of the muscle fiber contain mitochondria, myofibrils and sarcoplasmic reticulum

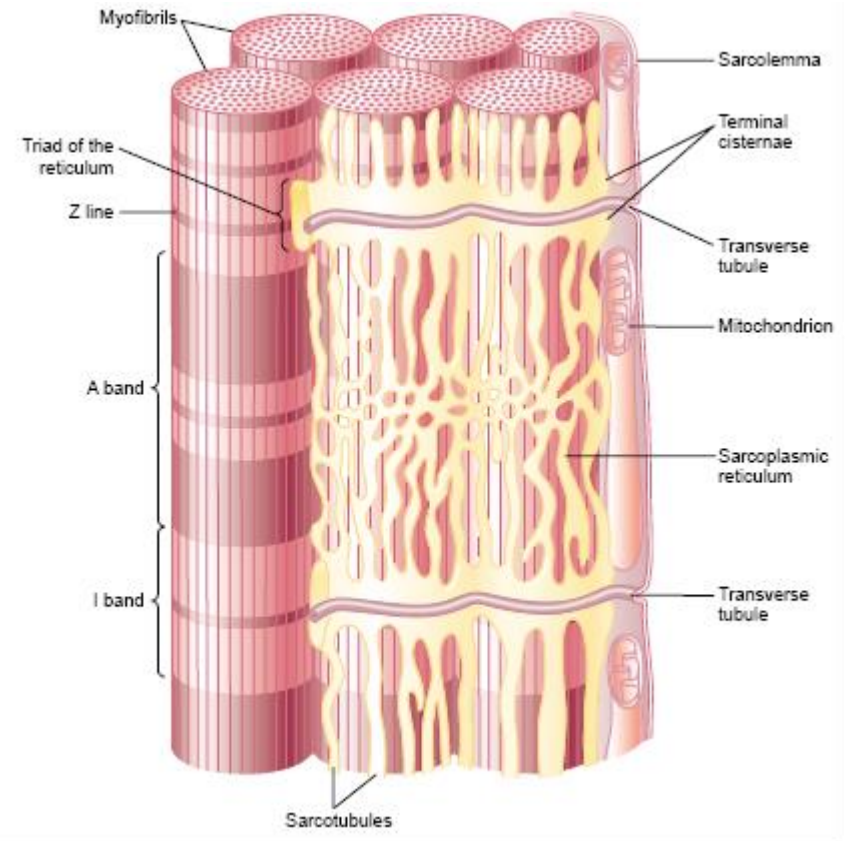
The sarcotubular system: It is composed of:

a)The transverse tubules(T-tubules): originate as invaginations from cell membrane, penetrating the muscle fiber from one side to the opposite side, thus communicating with the ECF. T-tubules help for rapid transmission of action potential from the membrane deep into the muscle.

b) The sarcoplasmic reticulum which composed of:

١-Longitudinal tubules.

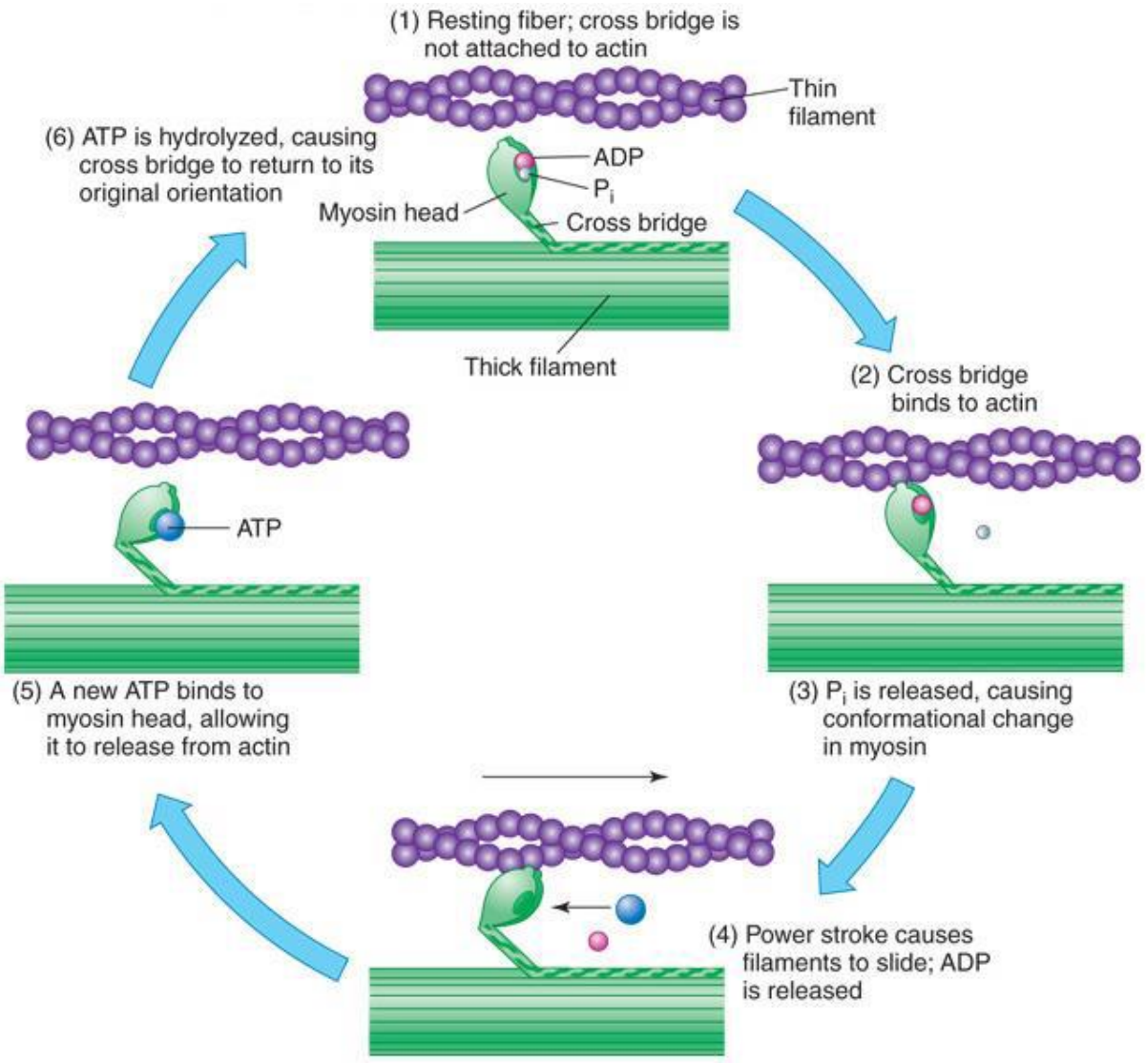
٢-Terminal cisterns: large chambers adjacent to T-tubules giving the appearance of **triad**(1 T-tubule and 2 cisternae). It stores calcium ions with abundant Ca channels and Ca pumps.



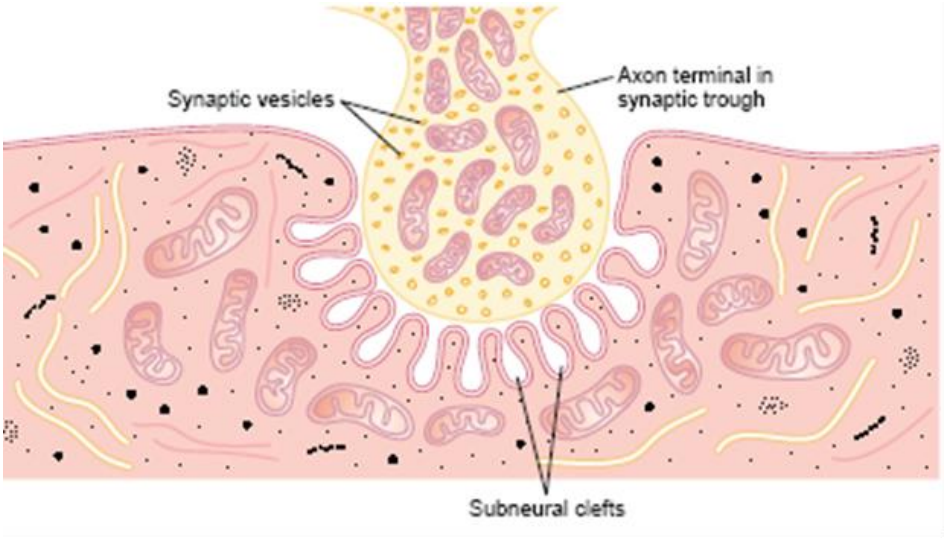
Molecular mechanism of muscle contraction

In the relaxed muscle the troponin-I is tightly bound to actin; tropomyosin covers the active sites of actin thus, troponin-tropomyosin complex represent the **relaxing proteins** which inhibit interaction between actin and myosin

When the Ca ion bind with troponin C this uncover the active sites of the actin. Then the activated head of myosin cross-bridges attaches to an active sites of actin, here the head automatically tilts towards the arm (called power stroke) so dragging the actin filaments along with it immediately after tilting the head released from the active site then return to its normal perpendicular direction and then it combined with new active site of actin, then the head tilts again, and the actin filament moves another step. Thus, the heads of the cross-bridges step by step walk along the actin filament, pulling the ends of two successive actin filaments toward the center of the myosin this is called "**walk-along" theory**



neuromuscular junction: As the motor nerve reaches the muscle fiber, it loses its myelin and divides into a number of terminals. The axon terminal contains many small vesicles of the neurotransmitter acetylcholine. The nerve ending invaginates into a thickened, folded depression in the muscle membrane called the **motor end plate** .Usually there is one junction for each muscle fiber, this invagination is called synaptic gutter and the space between the axon terminal and the muscle fiber is called synaptic cleft(contain acetylcholine esterase that destroy acetylcholine (Ach).



Excitation- contraction coupling

١-when action potential travel along a motor nerve to its ending ,voltage gated calcium channels open and allow calcium ions to diffuse to the interior of the nerve terminal.

٢- The calcium ions exert an attractive influence on the acetylcholine vesicles, drawing them to the neural membrane adjacent to the dense bars. The vesicles then fuse with the neural membrane and empty their acetylcholine into the synaptic space by the process of exocytosis

٣-The acetylcholine open the acetylcholine- gated channels, which allows sodium ion to flow into muscle fiber, this initiate end plate potential (The sudden entrance of sodium ions into the muscle fiber causes the electrical potential inside the fiber to increase in the positive direction as much as 50 to 75 millivolts), which is necessary to initiate an A.P

٤-The action potential travels along the muscle fiber membrane causing the sarcoplasmic reticulum to release calcium ion into myofibrils

٥-The Ca ions uncover the active sites of actin and initiates attractive force between the actin and myosin cross-bridges causing the actin filaments to slid inward among the myosin filaments .This is the contractile process which is occur by **sliding filament mechanism**. The energy for this mechanism is supplied by the ATP cleavage by ATPase enzyme present in the myosin head.

٦-After a fraction of a second the Ca ion are pumped back into the sarcoplasmic reticulum where they remain stored until another muscle A.P arrives again .this removal of Ca ion from myofibrils causes muscle contraction to cease.

Note :When active re-pumping of calcium is inhibited, relaxation cannot occur and muscle stays in contraction.

Why sodium ions flow through the acetylcholine gated channels than any other ions؟

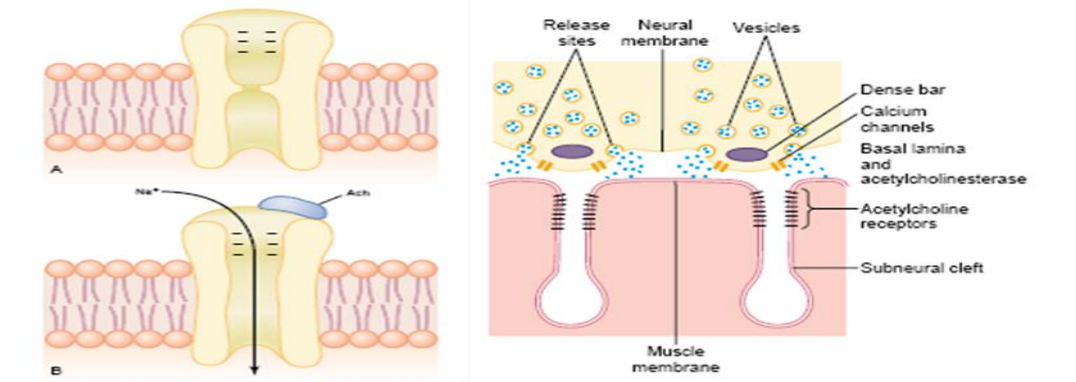
١-high concentration of sodium ions in the extracellular fluid

2-the very negative potential on the inside of the muscle membrane, –80 to –90 millivolts, pulls the positively charged sodium ions .

The acetylcholine then it is removed rapidly by two means:

(١)Most of the acetylcholine is destroyed by the enzyme acetylcholine esterase

(2) A small amount of acetylcholine diffuses out of the synaptic space or reuptake by process of pinocytosis.



Simple muscle twitch:

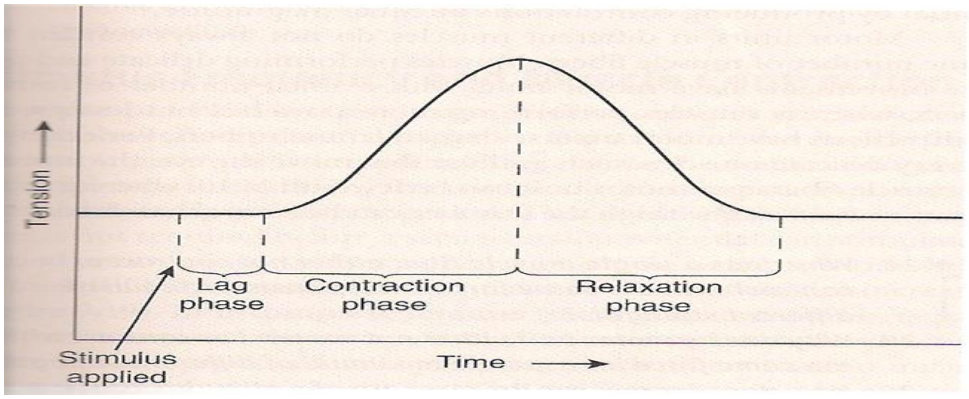
The contraction of a muscle in response to a stimulus , its occur in 3 parts

latent period :The time between application of stimulus to the motor nerve and the beginning of contraction

contraction period : the time during which contraction occurs, muscle shortens & does its work

relaxation period: time during which relaxation occurs ,muscle elongates & returns to original position

refractory period: the refractory period is short which means that skeletal muscle can under go summation and tetanization via repeated stimulation (e.g. Lifting heavy weight)

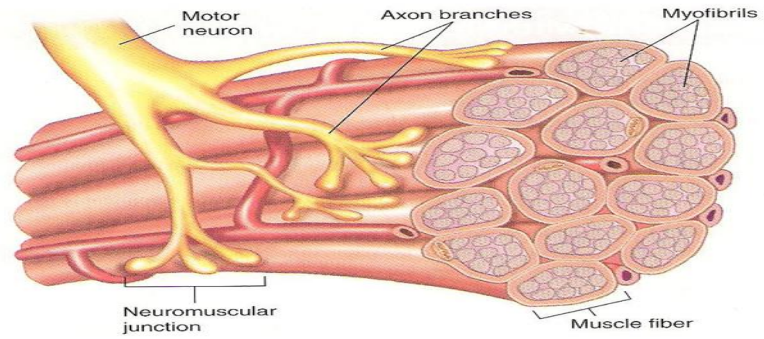


Motor unit

All the muscle fibers which is innervated by a single motor nerve are called motor unit.

Muscle that react rapidly for precise function may have only 2-3 muscle fibers in motor unit e.g laryngeal muscle.

While muscle that don't need precise function may have 100 muscle fiber in motor unit.



Types of muscle contraction :

Two types, isometric and isotonic

Isometric: tension of muscle increase but do not change in length e.g when person push against the wall

Isotonic contraction: there is change in length but the tension not changed e.g lifts an object

Most contractions are a mixture of the two(e.g: running)

Energy expenditure during contraction:

Energy is needed for

١-Sliding of actin on myosin filaments

2-Repumping of calcium ions from sarcoplasm into sarcoplasmic reticulum to .start muscle relaxation

3-Maintenance of resting membrane potential by Na-K pump-

Source of energy for muscle contractions

1-The immediate source of energy is **ATP**.The concentration of ATP in the muscle fiber is sufficient to maintain full contraction for only 1 to 2 seconds

2-**glycolysis** of glycogen (previously stored in the muscle cells). The glycolytic reactions can occur even in the absence of oxygen

3-oxidative metabolism. (This means combining oxygen with the glucose and fatty acids) to liberate ATP**.**

Muscle Fatigue: Prolonged and strong contraction of a muscle leads to the state of muscle fatigue. Muscle fatigue is directly proportion to the rate of depletion of muscle glycogen and ATP.

Skeletal Muscle Tone: Even when muscles are at rest they are in state of continuous small degree of contraction called muscle tone which is probably due to reflex impulses from the spinal cord. Muscle tone decreases during sleep and absent in death

Physiology of Smooth Muscle

Morphology: smooth muscle is unstriated, involuntary muscle and differ from skeletal and cardiac muscle fiber being much smaller; the sarcoplasmic reticulum is poorly developed. The contractile proteins are actin, myosin, and tropomyosin but no troponin.

There are two main types of smooth muscle, the visceral(unitary) and the multiunit .

I-Multi-Unit Smooth Muscle.

1-non-syncytial i.e this type of smooth muscle is composed of separate smooth muscle fibers .Each fiber operates independently of the others often is innervated by a single nerve ending

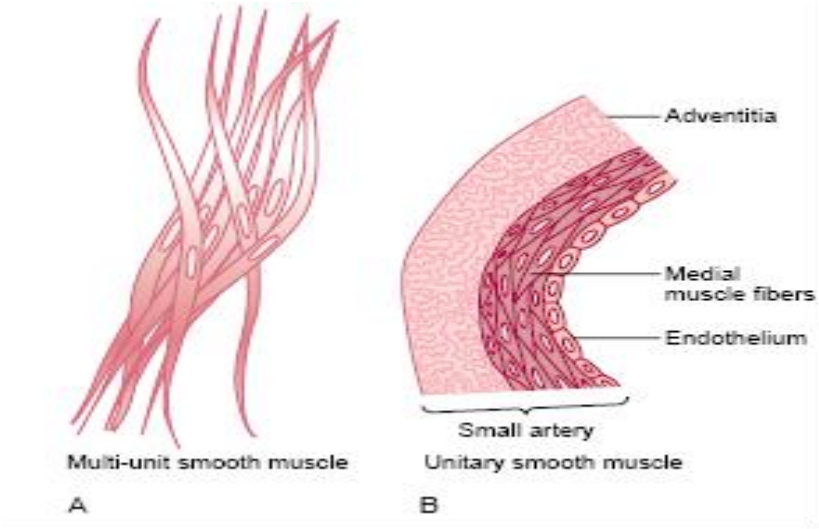
2-Neurogenic: controlled by external nerve supply.

3-Contraction not spread widely therefore needed for fine localized contractions (eg: ciliary muscle and iris of the eye)

٤-Very sensitive to acetylcholine and noradrenaline

II-Single-unit Smooth Muscle. Also called "unitary" or syncytial or visceral smooth muscle it means a mass of hundreds to thousands of smooth muscle fibers that contract together as a single unit (either the whole muscle contracts or the whole muscle relaxes). The fibers usually are arranged in bundles, and their cell membranes are adherent to one another at multiple points called **gap junction** through which ions and A.P can flow freely from one muscle cell to the next

e.x gut muscle, bile ducts, ureters, uterus, and many blood vessels.



Neuromuscular Junctions of Smooth Muscle

I-Neuromuscular junctions of the highly structured type found on skeletal muscle fibers do not occur in smooth muscle. Instead, the autonomic nerve fibers that innervate smooth muscle branch diffusely on top of a sheet of muscle fibers, these fibers do not make direct contact with the cell membranes but instead they form diffuse junctions that secrete their transmitter substance into the matrix coating of the smooth muscle ;then the transmitter substance diffuse to the cell.

II-The axons that innervate smooth muscle fibers divides into many branch, each branch containing series of swollen region called varicosities contain vesicles that contain neurotransmitter substance.

III-the vesicles of the autonomic nerve fiber endings contain acetylcholine in some fibers and norepinephrine in others but they are never secreted by the same nerve fibers. Acetylcholine is excitatory in some organs and inhibitory in others, the same is true for noradrenaline. this is depend on the type of receptor(excitatory or inhibitory receptors). When Ach excite muscle fiber, noradrenaline will inhibit it and vice versa.

Most blood vessels respond to norepinephrine and epinephrine (from sympathetic stimulation) by producing vasoconstriction (this response is mediated through alpha 1-adrenergic receptors). Blood vessels in skeletal muscle and cardiac muscle respond to these catecholamines producing vasodilation because the smooth muscle possess beta-adrenergic receptors

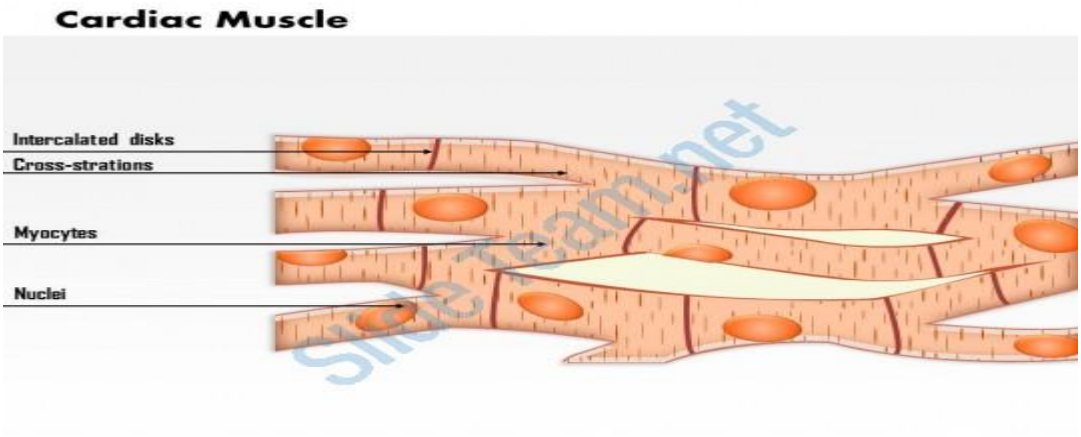
In the multi-unit type of smooth muscle, the varicosities are separated from the muscle cell membrane by as little as 20 to 30 nanometers—the same width as the synaptic cleft that occurs in the skeletal muscle junction. These are called contact junctions

Cardiac Muscle

Morphology and physiological characteristics:

The heart actually two separate pumps: a right heart Receive blood from the peripheral organ and pumps blood to the lungs, and a left heart receive blood from lung and pumps blood to the peripheral organs. The heart is composed of three major types of cardiac muscle: atrial muscle, ventricular muscle, and specialized excitatory and conductive muscle fibers.

Cardiac muscle is striated, branching, involuntary have single nucleus, and have typical myofibrils that contain actin and myosin filaments (troponin and tropomyosin also present) and their organization give the striated appearance of cardiac muscle fiber ;these filaments lie side by side and slide along one another during contraction in the same manner as occurs in skeletal muscle. Cardiac muscle has a smooth sarcoplasmic reticulum(SR) but less abundant and less organized than in skeletal muscle. Cardiac muscle are connected by intercalated discs (they are actually cell membranes that separate individual cardiac muscle cells from one another). The intercalated disc contains desmosomes(provide strong mechanical union between cardiac muscle fiber) and gap junction (protein- tunnels, allow direct transmission of the depolarizing from cell to cell provide electrical union between cardiac muscle fiber); thus cardiac muscle act as a **single unit(syncytium),** in which the cardiac cells are so interconnected that when one of these cells becomes excited, the action potential spreads to all of them, Normally, potentials are not conducted from the atrial syncytium into the ventricular syncytium directly. Instead, they are conducted only by a specialized conductive system called the A-V bundle .Cardiac muscle fiber is myogenic (can work without nerve supply). cardiac muscle cell has rich mitochondria and blood supply, thus cardiac muscle resist fatigue. (fig 20)



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parameters	Skeletal muscles	Smooth muscles	Cardiac muscles
Morphology	Striated cylindrical	Un striated spindle	Striated Branching
	Voluntary	In voluntary	In voluntary
Position	Skelton	Viscera	In heart
Nucleus	Multinucleated	Single nucleus	Single nucleus
Nerve supply	Motor nerve	Autonomic	Autonomic
Autorhythmicity	Not present	Present	Present
Tetaniztion	Possible	Partially possible	Not possible
S R	Well developed	Not well define	Not well define
Intercalated disc	Not present	Present in some fiber	present
Pace maker	No pace maker	In some fiber	present
Source of Ca	sarcoplasm	ECF	ECF and sarcoplasm
Neuromuscular junction	Synaptic cleft	Contact junction Diffusion junction	
rmp	-90	-50 - -60	-85

Physiology of nerve

Muscle and nerve are the excitable tissues that we are going to talk about; they are excitable because they have electrical phenomenon i.e. they are polarized.

The nervous system in general is divided into:

The central nervous system (CNS) which means the brain and the spinal cord.

The peripheral nervous system (PNS) which include the somatic and the autonomic nervous system.

The neurons are excitable cells specialized for reception, integration and transmission of nerve impulses.

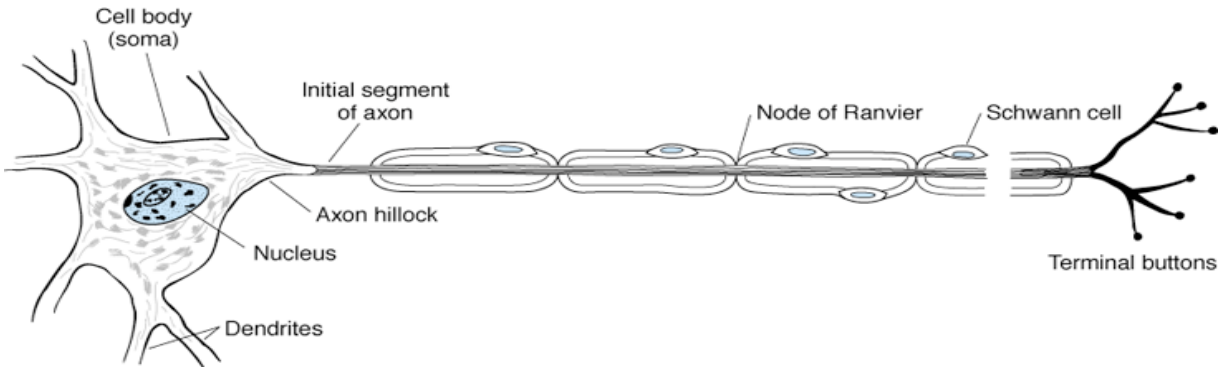
The neurons in general are composed of 3 major parts:

1- The soma: which is the main body of the neuron, contains specialized cytoplasm, single nucleus and other granules.

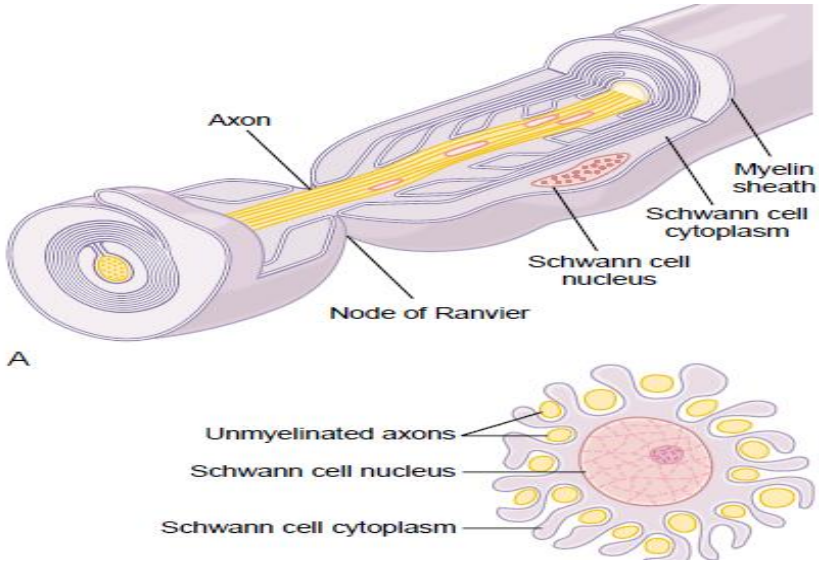
2- Dendrites :which are great number of branching projections from the soma that conduct towards the cell body.

The soma and the dendrites form a large area which is specialized for reception, and the processes of other neurons terminate at this area to form what is called synapses by which the neurons communicate with each other.

3- axon, which extends from the soma membrane to the periphery, it conducts away from the cell body. It starts from a thick area called the axon hillock, after that the part of the axon is called the initial segment (thinner), then the axon remains the same diameter until its termination (axon knob),where the chemical substance (neurotransmitter) is released in response to nerve impulse.



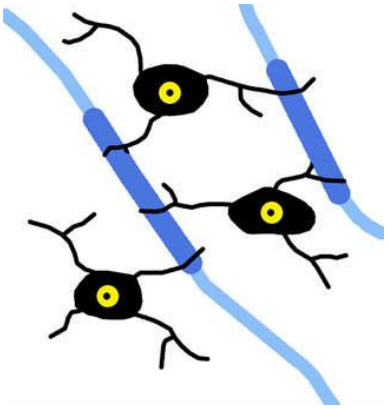
Each axon in the peripheral nervous system after a short distance from its origin is covered by a series of schwann cells which are the supporting cells of the peripheral nervous system; they form the myline sheath of the nerve. The myline is a lipoprotein complex formed of many layers, and it is not continuous, it is interrupted by a small exposed area of 1 microne in length which is called "Node of Ranvier" that forms the myline sheath between 2 adjacent nodes.



Not all the nerve fibers are mylinated, some are not mylinated but surrounded by Schwann cells without the deposition of myline (axons more than 1 micrometer in diameter is mylinated, but less than 0.5 micrometer in diameter are not mylinated).

In the CNS the neurons, contain glial cells (neuroglia), there are 10- 50 times as many glial cells as neurons.

Also in the CNS there is microglia, oligodendrocytes and astrocyte. The astrocytes support the CNS and transport substances between the neurons and the blood vessels and contribute in making blood brain barrier(BBB). Oligodendrocytes produce the myline sheath. Microglia, provide support and phagocyte bacteria.

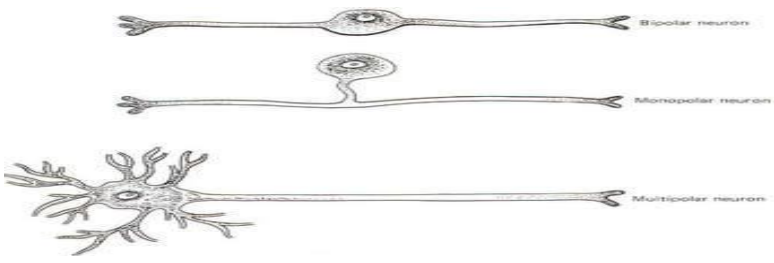


Oligodendrocytes

TYPES OF NEURONS:

Structurally divided into;

1- Bipolar neurons: the cell body has only 2 processes, one is the axon and the other is the dendrite e.g in nose, eye, and ears.
2- unipolar neurons: has a single process extending from the cell body then after a short distance it will divide into 2 branches.
3- 3- multipolar has many processes arising from the cell body, only one is the axon ,the rest are the dendrites



Functional organization of the neuron:

1 - The receptor zone or dendritic zone: it represents the site for the reception of nerve signals, and much local potential are going to be formed in this area.

2- The initial segment zone: it is the site and origin of the conducting impulses; it is the site where the nerve impulses are generated.

3- The axonal zone: or called the transmitting zone where the nerve impulses are transmitted.

4- The nerve ending zone: the site where the nerve impulses causes the release of the neurotransmitter to affect other neuron or muscle fiber.

Neural communication:

The neurons communicate with each other by 2 types of communication:

1- The electronic potential (generator potential): Local, non-propagated potentials called, synaptic, generator, or electrotonic potentials

2- The action potential (nerve impulse).

Both types are physiochemical disturbances due to change in conduction across the cell membrane. The first type is a local non-propagated potential used for communication between neurons which are very close to each other e.g. the brain and the eye, where large number of information are sent or received by adjacent cells.

The second type is a propagated disturbance used to send information for long distances without any loss of energy.

The ionic basis of the resting membrane potential:

The resting membrane potential of a large nerve fiber when not transmitting nerve signal is about -90 mv i.e. the potential inside the fiber is 90 mv ,more negative than the outside (actually it is -70 mv in small nerve fibers, but -90 mv in large nerves).

So the origin of the resting membrane potential is due to the contribution of the following factors:

1- The contribution of the K ion diffusion potential.

2 - The contribution of the Na ion diffusion potential through the nerve membrane.

3- The contribution of the Na_ K ion pump.

Regarding the leakage of K and Na ions through the nerve membrane It is because of the concentration gradient across the cell membrane, Na ions try to pass inside the cell down their concentration gradient .K ions try to pass outside the cell down the concentration gradient, but the channels in the cell membrane are more permeable to K ions than to Na ions about 100 times**.**

The Na-K ion pump:

It pumps Na ions to the outside of the cell and K ions to the inside, this is an electrogenic pump (also it requires energy), because more positive charges are pumped to the outside than inside (3 Na ions to the outside for each 2 K ions to the inside) i.e. Na ions accumulate outside the cell while K accumulates inside the cell, leaving a net deficit of positive ions inside leading to a negative potential across the membrane. It also causes large concentration gradient for Na and K ions across the resting membrane potential, these gradients are:

Na ions (outside) 142 meq/L

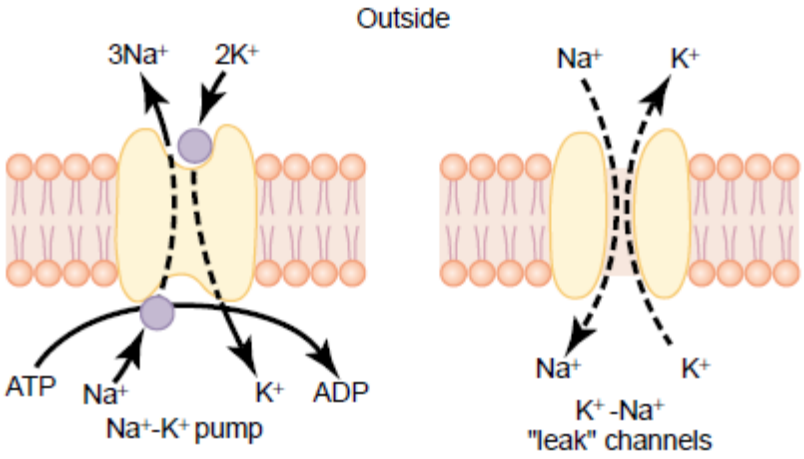
Na ions (inside) 14 meq /L

So the ratio of this ion from inside to outside is 0.1

K ions (outside) 4 meq/l

K ions (inside) 140 meq/ l

so the ratio of this ion from inside to outside is 35.0



In addition to the Na –K pump and ion fluxes there are proteins with negative charges inside the cell; all of these give the membrane a negative charge inside. The net result polarization is negative inside and positive outside.

Nerve action potential:

Nerve signals (are coded information) transmitted by action potentials which are rapid changes in the membrane potential in response to stimulus that spread rapidly along the nerve fiber membrane. The stimulus could be electrical, chemical and thermal.

So if we apply a stimulus and record the changes in the membrane potential we will notice the following

Sudden change from the normal resting negative membrane potential (-70 mv) to a positive potential, then return back to the negative potential. The action potential moves along the nerve fiber until it comes to the fiber end.

The successive stages in action potential are as follows:

1-The resting stage: this is the resting membrane potential ,before the action potential begins i.e. the membrane is polarized, due to the presence of negative potential (-90 mv).

2- The latent period (latency): is also an isoptential state, the membrane here is still polarized. It is the interval starting from the beginning of stimulation to the beginning of potential changes. This period corresponds to the time taken by the stimulus to pass along the nerve fiber to the recording

3- The depolarization stage: the membrane suddenly becomes very permeable to Na ions, because of opening of Na ion channels, allowing large amounts of Na ions to diffuse to the interior of the axon. The potential increases rapidly in the positive direction (it rises about 15 mv) called depolarization.

4- The repolarization stage:

the Na ion channels begin to close and the K ion channels open(i.e. K ion channels delayed after that of Na), then rapid diffusion of K ions to the exterior which reestablish the normal negative resting membrane potential which is called repolarization.

The repolarization is rapid until 70%, after that it becomes slower until reaching the resting membrane potential.

Energy source and production in the nerve fiber:

The major part of the energy requirement of nerve—about 70%—is the portion used to maintain polarization of the membrane by the action of Na^{+}-K^{+} ATPase. During maximal activity, the metabolic rate of the nerve doubles the normal.

nervous system

The nervous system is anatomically divided into two parts, the **Central Nervous System** (the brain and the spinal cord) and the **Peripheral Nervous System** (ganglia, 12 pairs of cranial nerves and 31 of pair's spinal nerves).

The Central Nervous System:
The Brain

We can divide the brain into six parts in terms of physiological functions:
1. Cerebrum; **2.** Epithalamus, Thalamus and Hypothalamus; **3.** Midbrain; **4.** Cerebellum; **5.** Pons **6.** Medulla oblongata.

1. Cerebrum - This is the most developed area of brain in the human species and is considered to be the center of the highest functions. The major functions include: awareness of sensory perception; voluntary control of movement (regulation of skeletal muscle movement); language; personality traits; sophisticated mental activities such as thinking, memory, decision making, predictive ability, creativity and self-consciousness. We will examine 4 lobes of the cerebrum.

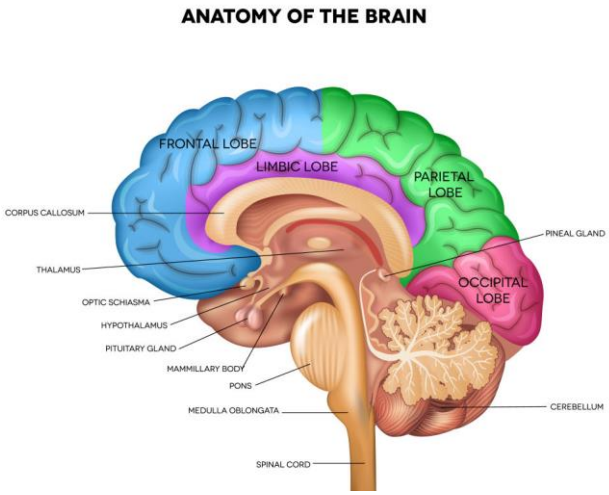
The Frontal Lobe - Concerned with higher intellectual functions and is involved in the many behavioral aspects of humans. . The motor cortex controls the movement of the rest of the body ,initiation, activation, and performance of the actual movement.

The Parietal Lobe - This lobe is primarily concerned with the interpretation and integration of sensory inputs. The Somatosensory cortex is associated with reception and perception of touch, vibration, and position sense of the body.

The Temporal Lobe - The temporal lobe contains the auditory cortex - for the reception and interpretation of sound information, and the olfactory cortex - for the sense of smell. It also houses the language cortex to recognition and interpretation of language.

The Occipital Lobe - This lobe contains the primary visual cortex for visual information interpretation.

The Limbic system The limbic system is the "emotional brain", participating in the creation of emotional states such as fear, anger, pleasure, affection, arousal, etc. and processing vivid memories associated with those states



2. Epithalamus, Thalamus and Hypothalamus

The **epithalamus** contains the **pineal gland**, a hormone secreting endocrine structure. Under the influence of the hypothalamus, the pineal gland secretes the hormone *melatonin*, which prepares the body for the night-time stage of the sleep/wake cycle..

The **Hypothalamus** controls and regulates many important functions of the body, including:

1) Control of the Autonomic Nervous System - adjusts, coordinates, and integrates the A.N.S. centers in the brain that regulate heart rate, blood pressure, bronchiole diameter, sweat glands, etc. It does this via the Parasympathetic and Sympathetic divisions of the A.N.S.

2) Control of Emotional Responses - in association with the limbic system, it forms part of the emotional brain. Regions involved in fear, pleasure, rage and sex drive are located in the hypothalamus.

3) Regulation of Body Temperature - the body's thermostat and *set point* is located in the hypothalamus. There are also 2 centers in the hypothalamus that respond to changes in the set point.

Heat-losing center: activation of this center causes sweating and cutaneous vasodilation.

Heat-promoting center: activation of this center causes shivering and cutaneous vasoconstriction.

4) Regulation of Hunger and Thirst Sensations - hypothalamus contains the feeding and thirst centers.
Feeding center: this center is always active and stimulates hunger which is 'fed' by eating.
Satiety center: stimulated when satisfied, this inhibits the always hungry feeding center.
Thirst center: osmoreceptors detect changes in osmotic pressure of blood, ECF, stimulate thirst.

5) Control of the Endocrine System - controls the release of pituitary hormones. Controls the anterior pituitary gland, when the hypothalamus releases hormones, it can stimulate or inhibit the release of other hormones form the pituitary (6 hormones). Also, it makes the 2 hormones (oxytocin and antidiuretic hormone (ADH)) that are stored in the posterior pituitary and released when signaled. All of these hormones regulate many other organs in the body.

3. Midbrain Portions receive visual input auditory input from the medulla oblongata and are involved in cranial reflexes, e.g., when you turn your head if you thought you heard your name called out.

4. Cerebellum - Means 'little brain'. The **Cerebellum** has two primary functions:
1) Controls postural reflexes of muscles in body - i.e., it coordinates rapid, automatic adjustments to maintain equilibrium, e.g. regaining your balance when you start to fall.

2) Produces skilled movements - involved in implementing routines for fine tuned movements. Controlled at the conscious and subconscious level, refines learned routines (e.g. driving, skating, playing an instrument) until the action becomes routine..

5. Pons - Plays a role in the regulation of the respiratory system. Contains two 'pontine' respiratory centers: **1)** the pneumotaxic center and **2)** the apneustic center. The pons is not responsible for the rhythm of breathing (the medulla oblongata is) but controls the changes in depth of breathing.The pons also prevents over inflation of the lungs.

6. Medulla Oblongata
The medulla oblongata is the last division of the brain. It becomes continuous with the spinal cord. It houses some very important visceral or vital centers,
1) the cardiac center - adjusts the force and rate of the heartbeat

2) the vasomotor center - regulates the diameter of blood vessels and therefore systemic blood pressure (constriction increases and dilation decrease blood pressure

3) the respiratory center - for control of the basic rhythm and rate of breathing. Additional centers regulate sneezing, coughing, hiccupping, swallowing and vomiting.

Spinal Cord

The basic structure of the spinal cord is that it is the downward continuation of medulla oblongata starting at the foramen magnum. It descends to about the level of the second lumbar vertebra, tapering to a structure called the conus medullaris.

The cord projects 31 pairs of spinal nerves on either side (8 cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal) that are connected to the peripheral nerves. A cross section of the spinal cord exhibits the butterfly-shaped gray matter in the middle, surrounded by white matter. As in the cerebrum, the gray matter is composed of nerve cell bodies. The white matter consists of various ascending and descending tracts of myelinated axon fibers with specific functions.

The spinal cord serves as a passageway for the ascending (going up) and descending (going down) fiber tracts that connect the peripheral and spinal nerves with the brain. Each of the 31 spinal segments is associated with a pair of dorsal root ganglia. These contain sensory nerve cell bodies. The axons from these sensory neurons enter the posterior aspect of the spinal cord via the dorsal root. The axons from somatic and visceral motor neurons leave the anterior aspect of the spinal cord via the ventral roots. Distal to each dorsal root ganglion the sensory and motor fibers combine to form a spinal nerve - these nerves are classified as mixed nerves because they contain both afferent (sensory) and efferent (motor) fibers.

The Cranial and Spinal Meninges

The delicate neural tissue of the brain and spinal cord is not only protected by the bones of the skull and vertebral column but also by layers of specialized membranes, called cranial and spinal meninges. Listed below are the 3 layers (from outer most to inner most) and the spaces they create. Bone; Epidural space; Dura mater, Arachnoid layer, Pia mater and Nervous tissue.

Cerebrospinal Fluid

Cerebrospinal fluid (**CSF**) flows within the ventricles of the brain, the central canal of the spinal cord and out to the subarachnoid spaces surrounding the brain and spinal cord. It serves as a medium for the transfer of substances between the blood and the nervous tissues as well as a liquid buffer, absorbing mechanical

shocks to the brain or the cord. Most of CSF is provided by the **choroid plexuses** that reside in lateral, third and fourth ventricles. In adults, the total volume of this fluid has been calculated to be from 125 to 150 ml . It is continuously formed, circulated and absorbed. Approximately 450 ml (nearly 2 cups) of CSF are produced every day

The CSF circulates throughout the base of the brain, down around the spinal cord as well as upward over the cerebral hemispheres. The CSF is then absorbed primarily through arachnoid villi into the superior sagittal sinus and re-joins the blood circulation.
The obstruction of the normal CSF flow or overproduction of CSF from a choroid plexus papilloma (a benign tumor of the choroid plexus) can lead to a condition known as **hydrocephalus** - an excessive accumulation of CSF in the ventricles or in the subarachnoid space. In newborns it results in an enlarged cranium, as the young skull bones are not yet fused and the infant cranial cavity can expand. In adults, however, it is typically accompanied by serious increase in intracranial pressure (ICP).

The Peripheral Nervous System
The central nervous system is connected to the peripheral nervous system by nerves. The PNS can be viewed as an extension of the CNS, connected to it by sensory and motor neurons and ganglion. The PNS can be divided into two parts, the Somatic Nervous System (SNS) and the Autonomic Nervous System (ANS). The SNS is responsible for movement of the body and its effector tissue is skeletal muscle. The ANS is responsible for automated responses that occur in the body (e.g., heart rate, blood pressure) and the effector tissues are cardiac muscle, smooth muscle and glands.
The Somatic Nervous System
The somatic nervous system is for the control of the skeletal muscle of the body, so essentially this means it controls body movement. For the most part this is voluntary, that is, it is under conscious control, you ‘think’ about it first. In fact, the main region of the central nervous system that sends signals out to the SNS is located in the frontal lobe. As we know from earlier, this is located in the cerebrum, which is the seat of the conscious mind.

The SNS in Summary:
Neurons: 1 motor neuron.
Effector Tissue: Skeletal Muscle.
Neurotransmitter: ACh.
Receptors: Nicotinic.
Action: Excites tissue causing contraction.
Control: Voluntary (except reflexes).

The Autonomic Nervous System (ANS):

The ANS coordinates cardiovascular, respiratory, digestive, urinary and reproductive functions.

This system helps to control arterial pressure, gastrointestinal motility, gastrointestinal secretions, urinary bladder, sweating, body temperature, and many other activities. Some of theses activity regulated partially and some others entirely regulated by ANS.

Basic anatomy of ANS :

• Preganglionic neuron

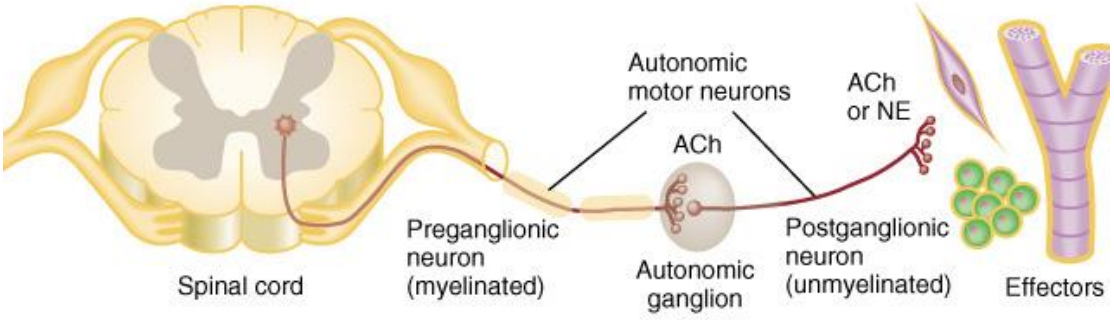
– Cell body in brain or spinal cord.

– Axon is myelinated that extends to autonomic ganglion.

• *Postganglionic neuron*

– Cell body lies outside the CNS in an autonomic ganglion

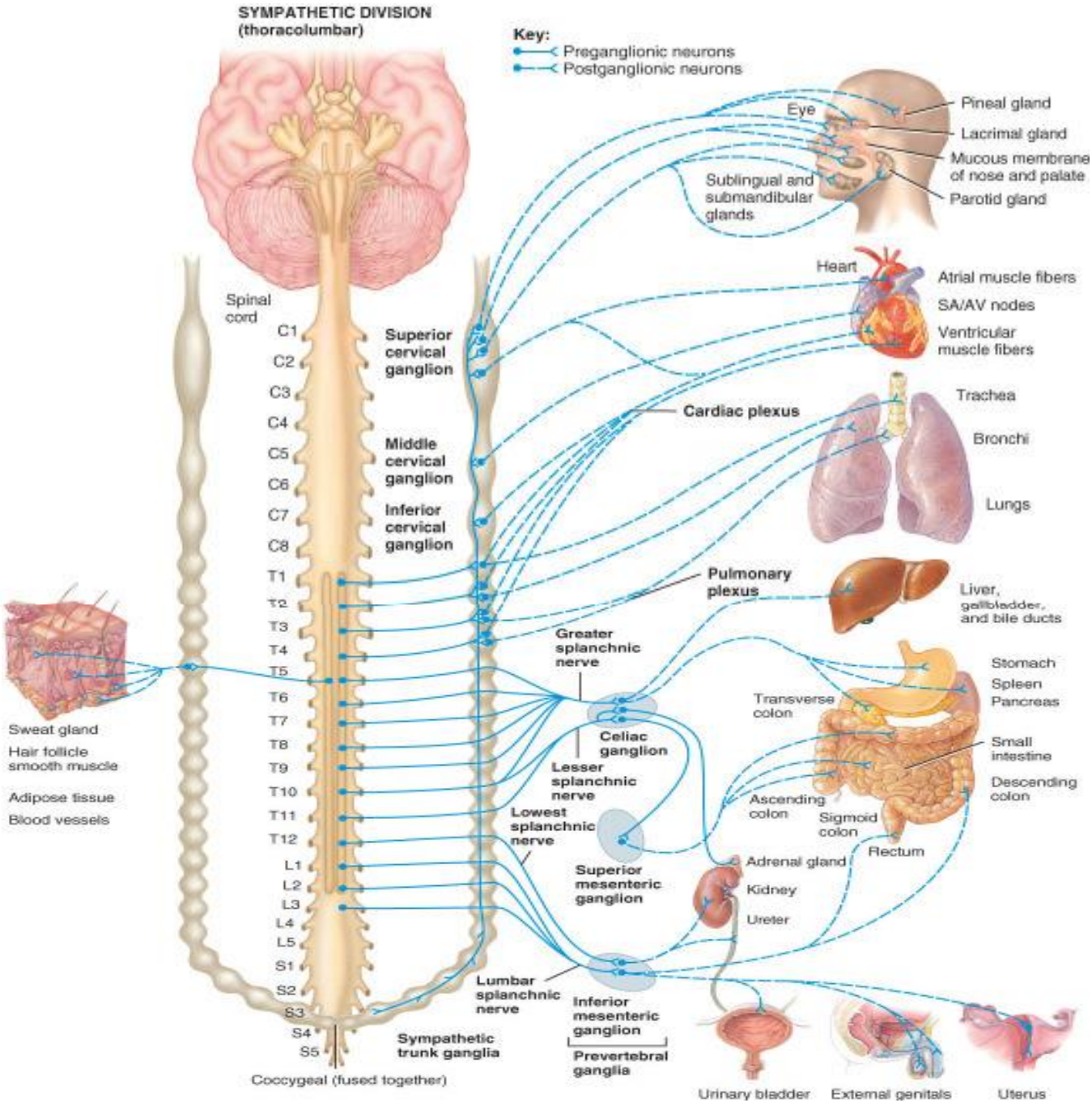
– Axon is unmyelinated that terminates in a visceral effector.



The ANS is composed of 2 anatomically and functionally distinct divisions, the sympathetic system and the parasympathetic system. Both systems are tonically active. In other words, they provide some degree of nervous input to a given tissue at all times. Therefore, the frequency of discharge of neurons in both systems can either increase or decrease. As a result, tissue activity may be either enhanced or inhibited. This characteristic of the ANS improves its ability to more precisely regulate a tissue's function. Without tonic activity, nervous input to a tissue could only increase.

Many tissues are innervated by both systems. Because the sympathetic system and the parasympathetic system typically have opposing effects on a given tissue, increasing the activity of one system while simultaneously decreasing the activity of the other results in very rapid and precise control of a tissue's function. Several distinguishing features of these 2 divisions of the ANS are summarized in Table 1.

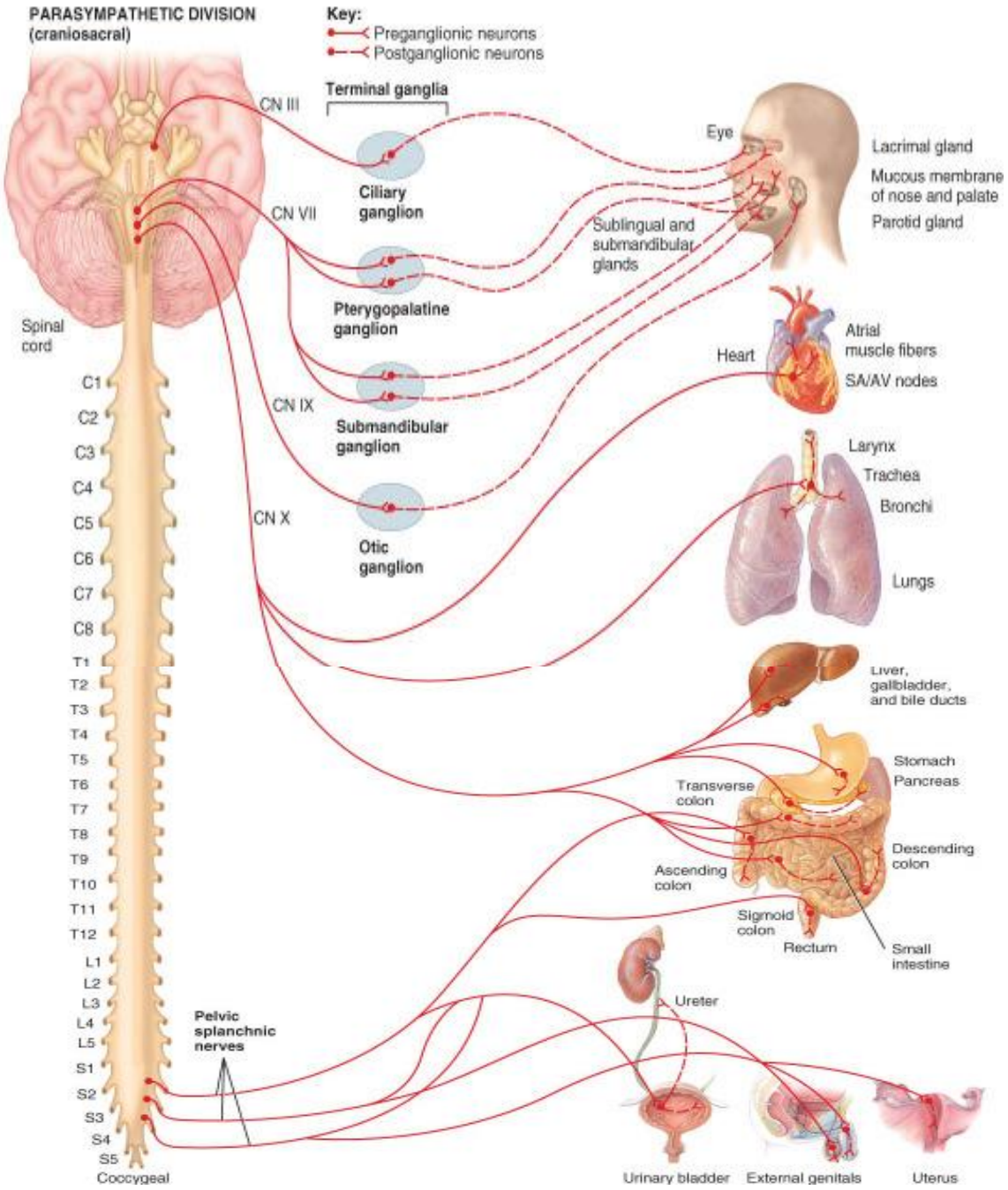
	Parasympathetic	Sympathetic
Originates in	Sacral region of spinal cord, medulla, midbrain	Thoracic and lumbar regions of spinal cord
Neuron Pathways	Longer pathways, slower system	Very short neurons, faster system
Cardiovascular System (heart rate)	Decreases heart rate	Increases contraction, heart rate
Pulmonary System (lungs)	Bronchial tubes constrict	Bronchial tubes dilate
Musculoskeletal System	Muscles relax	Muscles contract
Pupils	Constrict	Dilate
Gastrointestinal System	Increases stomach movement and secretions	Decreases stomach movement and secretions
Salivary Glands	Saliva production increases	Saliva production decreases
Adrenal Gland	No involvement	Releases adrenaline
Glycogen to Glucose Conversion	No involvement	Increases; converts glycogen to glucose for muscle energy
Urinary Response	Increase in urinary output	Decrease in urinary output



The sympathetic nervous system.

Sympathetic Ganglia

- These ganglia include the sympathetic trunk or vertebral chain ganglia that lie in a vertical row on either side of the vertebral column.
- Other sympathetic ganglia are the collateral ganglia that lie anterior to the spinal column and close to large abdominal arteries.



The parasympathetic nervous system.

Parasympathetic Ganglia

- Parasympathetic ganglia are the terminal ganglia that are located very close to or actually within the wall of a visceral organ.

Sympathetic Division

The preganglionic neurons of the sympathetic system arise from the thoracic and lumbar regions of the spinal cord (segments T1 through L2). Most of these preganglionic axons are short and synapse with postganglionic neurons within ganglia found in the sympathetic ganglion chains. These ganglion chains, which run parallel immediately along either side of the spinal cord, each consist of 22 ganglia. The preganglionic neuron may exit the spinal cord and synapse with a postganglionic neuron in a ganglion at the same spinal cord level from which it arises. The preganglionic neuron may also travel more rostrally or caudally (upward or downward) in the ganglion chain to synapse with postganglionic neurons in ganglia at other levels. In fact, a single preganglionic neuron may synapse with several postganglionic neurons in many different ganglia. Overall, the ratio of preganglionic fibers to postganglionic fibers is about 1:20. The long postganglionic neurons originating in the ganglion chain then travel outward and terminate on the effector tissues

Other preganglionic neurons exit the spinal cord and pass through the ganglion chain without synapsing with a postganglionic neuron. Instead, the axons of these neurons travel more peripherally and synapse with postganglionic neurons in one of the sympathetic collateral ganglia. These ganglia are located about halfway between the CNS and the effector tissue.

Parasympathetic Division

The preganglionic neurons of the parasympathetic system arise from several nuclei of the brainstem and from the sacral region of the spinal cord (segments S2-S4). The axons of the preganglionic neurons are quite long compared to those of the sympathetic system and synapse with postganglionic neurons within terminal ganglia which are close to or embedded within the effector tissues. The axons of the postganglionic neurons, which are very short, then provide input to the cells of that effector tissue.

Neurotransmitters of the Autonomic Nervous System:

The 2 most common neurotransmitters released by neurons of the ANS are acetylcholine and norepinephrine. Neurotransmitters are synthesized in the axon varicosities and stored in vesicles for subsequent release. Nerve fibers that release acetylcholine are referred to as cholinergic fibers. These include all preganglionic fibers of the ANS, both sympathetic and parasympathetic systems; all postganglionic fibers of the parasympathetic system; and sympathetic postganglionic fibers innervating sweat glands. Nerve fibers that release norepinephrine are referred to as adrenergic fibers. Most sympathetic postganglionic fibers release norepinephrine.

Receptors for Autonomic Neurotransmitters

As discussed in the previous section, all of the effects of the ANS in tissues and organs throughout the body, including smooth muscle contraction or relaxation, alteration of myocardial activity, and increased or decreased glandular secretion, are carried out by only 3 substances, acetylcholine, norepinephrine, and epinephrine. Furthermore, each of these substances may stimulate activity in some tissues and inhibit activity in others.

These conditions usually increased sympathetic discharge rate and this in turn will lead to:

1. Dilation of pupil.
2. Increased heart rate.
3. Increased blood pressure.
4. Increased blood glucose.
5. Increased blood fatty acids.
6. Increased blood flow to the vital organ and this lead to better perfusion.
7. Decreased blood flow to the skin and viscera and divert blood to skeletal muscles.
8. Decreased the threshold of reticular formation (part of the central nervous system responsible for sleep) making the individual alert and more awake.

Generally, the sympathetic nervous system is known as "Catabolic System" where energy, glucose, and fatty acids are broken down for energy to face the emergency.

The Endocrine System

The endocrine system is a chemical control system. It functions in conjunction with the nervous system to control the internal environment (homeostasis).

I. Endocrine Glands

Glands without ducts

1. Secrete HORMONES ("to set in motion") into the intercellular spaces and they pass directly into the blood and is then distributed to all parts of the body via the circulatory system.

2. Hormones - chemical secretions of the endocrine glands.
   a. chemical types -
      1). proteins and polypeptides
      2). Amines
      3). steroid

3. Hormones - act to maintain homeostasis by altering cellular activity.
4. Hormones can affect

   a. organ or groups of organs directly
   b. other endocrine glands called

Nervous System vs. Endocrine System

	Nervous System	Endocrine System
Effects	rapid & short-lasting	slower & longer lasting
Controls	muscles & glands	activities of cells: a. metabolism b. reproduction c. stress responses d. fluid-electrolyte balance e. acid-base balance f. energy balance

I. Pituitary Gland - (Hypophysis) [Master Gland]

A. Location

1. in Sella Turcica of sphenoid bone
2. attached to Hypothalamus by a stalk called Infundibulum

B. Structure

1. Anterior lobe – [glandular part] - Adenohypophysis
2. Posterior lobe – [neural part] – Neurohypophysis

C. Anterior Pituitary - (Adenohypophysis)

1. Hormone secretions controlled by secretions from the hypothalamus produced by nerve cells and control the release of hormones by Endocrine glands; these hormones are called releasing factor

Growth Hormone (GH) - Somatotrophic Hormone (STH)

1. Increases Growth and Maintenance of Organs by:

    a. stimulating protein anabolism
    b. promotes fat catabolism (use of fat rather than sugars for energy)

2. Abnormal Secretions of STH

    a. Gigantism -- hypersecretion during childhood (before epiphyseal plates close)
    b. Acromegaly -- hypersecretion during adulthood
    c. Dwarfism -- hyposecretion during childhood
    d. Cachexia (Simmond's Disease) - hyposecretion during adulthood causes premature aging and atrophy of organs

Prolactin - (Lactogenic Hormone)

1. promotes breast development during pregnancy
2. stimulates mammary glands to produce milk after delivery

Thyriod Stimulating Hormone (TSH) - (Thyrotropin)

1. promotes growth of the Thyroid Gland
2. stimulates the secretion of the Thyroid Hormone

Adrenocorticotropin -- (ACTH)

1. promotes growth of the Adrenal Cortex
2. stimulates the secretion of Cortical Hormones
3. stimulates Fat Catabolism & Glycogenesis

Gonadotropins - FSH and LH

1. Follicle Stimulating Hormone (FSH)
    a. female - stimulates the Ovarian Follicles to Develop and produce ova
        - stimulates the Ovarian Follicles to secrete Estrogens
    b. male - stimulates the production of sperm
        - stimulates the secretion of Testosterone

2. Luteinizing Hormone (LH)
    a. female - associated with FSH in development of the Ovarian

Follicles
- stimulates development of the Corpus Luteum following ovulation
- stimulates Corpus Luteum to secrete Progesterone

b. male - stimulates the Interstitial Cells to secrete Testosterone (also called Interstitial Cell Stimulating Hormone [ICSH])

D. **Posterior Pituitary Lobe (Neurohypophysis)**

1. **Antidiuretic Hormone (ADH) (vasopressin**) - produced in the hypothalamus and collected and secreted by the posterior lobe

a. increases the permeability of the kidney tubules to water
b. promotes the reabsorption of the water from the urinary filtrate resulting in a smaller volume of urine
c. Diabetes insipidus - condition resulting in larger volumes of urine produced - may be treated with vasopressin

2. **Oxytocin**

a. stimulates powerful contractions of the pregnant uterus at the time of delivery
b. causes milk ejection from the lactating breast

II. THYROID GLAND

A. Location - lower aspect of larynx and upper trachea
- two lateral lobe connected by an isthmus on anterior surface of superior trachea

B. Histology & Physiology

1. Thyroid Follicles - functional units
a. follicle cells secrete Thyroxine (Thyroid Hormone)
Thyroxine is a combination of Tyrosine & Iodine to make two compounds: Tetraiodothyronine - T_4
Triiodothyronine - T_3

Thyroxine is transported in the blood as Thyroid-binding Globulin (TBG)

2. thyroxine Action -

a. Calorigenic Effects - increases Catabolism and produces extra body heat
1 mg of thyroxine = an increased heat production of 1000 calories

b. Growth & Development - produce growth and development of tissues and organs
- Nervous Tissue particularly affected

- hyposecretion results in Mental Retardation

3. Metabolic Effects -

a. diuretic
b. protein and carbohydrate catabolism (stimulates cellular uptake)
c. increases activity of nervous system
d. increases heart rate
e. causes muscular weakness

4. Parafolliclar Cells - secrete Thyrocalcitonin (TCT)

a. decreases excretion of Calcium & Phosphate ions
b. increases Osteoblast activity - Ca^{+2} & PO^{-3} deposition in bone

5. Disorders of the Thyroid

a. Hyperthyroidism (Grave's disease)

- increases nervousness and irritability
- elevated BMR
- exophthalmos - results in edema behind the eyes

b. Hypothyroidism

Cretinism - occurs if the hyposecretion is during fetal or early developmental life.
- results in reduced metabolism
- results in reduced growth
- results in mental retardation

Myxedema - occurs if the hyposecretion is during adult life
- results in reduced metabolism
- results in reduced mental & physical activity
- results in increased blood pressure
- results in accumulation of subcutaneous fluids

III. **Parathyroids**

A. Location - 4 or 5 small round bodies on the posterior surface of the lateral lobe of the thyroid gland

B. Function - secretes the Parathyroid hormone that controls Blood Calcium homeostasis

1. increases Ca^{+2} and Mg^{+2} absorption from the Intestines, Kidneys and Bones [raises blood calcium levels]

2. increases PO^{-3} excretion [lowers blood phosphate levels]

C. Disorders of parathyroid activity

1. Hypocalcemia - causes by hyposecretion of PTH
-results in Tetany [muscle spasms and convulsions]

2. Hypercalcemia - causes by hypersecretion of PTH
-results in a fibrous bone disease

IIII. **Adrenal Glands**

A. Location - consists as two triangular glands and each sit like a cap on the kidneys

B. Adrenal Cortex - secretes the Adrenal Cortical Hormones

1. Glucocorticoids produced by cells of the Zona Fasciculata

a. corticosterone
b. cortisol (hydrocortisone)
c. cortisone
- elevates blood sugar levels by acceleration of glycogenolysis and glucogenolysis - [causes conversion of proteins into carbohydrates - resulting in "Tissue Wasting"]
- promotes protein catabolism
- promotes fat catabolism
- promotes vasoconstriction to maintains normal blood pressure
- promotes stress resistance through Anti-Inflammatory actions

2. Mineralocorticoids - produced by the cells of the Zona Glomerrulosa

a. aldosterone
- causes Sodium retention and Potassium excretion
- causes water retention and blood pressure increases

3. Gonadocorticoids - produced by cells of the Zona Reticularis

a. these are the sex hormones that are produced by the adrenal cortex in small amounts in both males and females

4. Abnormal Adrenal Cortical Function:

a. Addison's Disease - caused by Hyposecretion of Cortical hormones
- results in increased blood potassium levels
- results decreased sodium retention and dehydration
- results decreased blood glucose levels
- results decreased blood pressure
- results decreased stress resistance
- results increased risk of kidney failure

b. Cushing's syndrome - causes by Hypersecretion of Cortical Hormones
- results in shifts of the body fat to the face and shoulders
- results in general body weakness
- results in altered carbohydrate & electrolyte metabolism

c. Adrenogenital Syndrome - caused by Hypersecretion of Gonadotropins
- results in premature sexual development in both males and females
- results in masculinization of females

C. Adrenal Medulla Hormones - Epinephrine & Norepinephrine

Effects: - Sympathomimetic
- Increased blood pressure due to increased heart rate & constriction of blood vessels
- Increased respiratory rate and dilation of bronchioles
- Increased blood sugar and cellular metabolism
- Decreased digestive tract activity

VII. **Pancreas** - (Islets of Langerhans cells)

A. Hormones

1. Insulin - secreted by the Beta Cells
- promotes lower blood glucose levels by:
- promoting glycogenesis, protein synthesis, and lipogenesis
- promoting cellular uptake

2. Glucagon - secreted by the Alpha Cells
- promotes higher blood glucose by:
- promoting glycogenolysis

Physiology of Blood

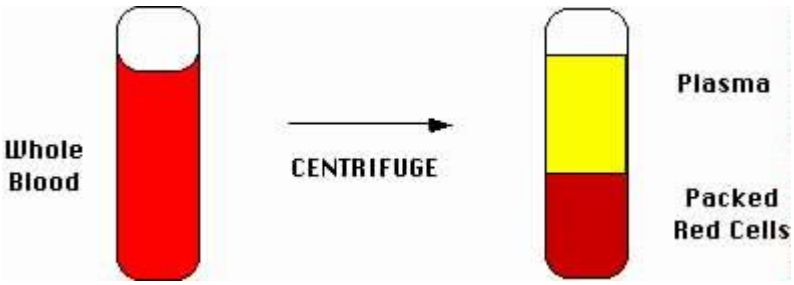
Components, Characteristics, Functions of Blood

Major Components of Blood

1. Formed elements - the actual cellular components of blood (special connective tissue)
    a .erythrocytes - red blood cells
    b. leukocytes - white blood cells
    c. platelets - cell fragments for clotting
2. Blood plasma - complex non-cellular fluid surrounding formed elements; protein & electrolytes.

Separation of Components in a Centrifuge

	VOLUME	LAYER
clear/yellowish PLASMA	55%	top
thin/whitish buffy coat with leukocytes & platelets	<1%	middle
reddish mass - erythrocytes	45%	bottom



Characteristics of Blood

1. bright red (oxygenated)
2. dark red/purplish (unoxygenated)
3. much more dense than pure water
4. pH range from 7.35 to 7.45 (slightly alkaline)
5. slightly warmer than body temperature 38 °
6. typical volume in adult male 5-6 liters
7. typical volume in adult female 4-5 liters
8. typically 8% of body weight

Major Functions of Blood

1. Distribution & Transport
    a. oxygen from lungs to body cells
    b. carbon dioxide from body cells to lungs
    c. nutrients from GIT to body cells
    d. nitrogenous wastes from body cells to kidneys
    e. hormones from glands to body cells

2. Regulation (maintenance of homeostasis)

a. maintenance of normal body pH by blood proteins (albumin) & bicarbonate

b. maintenance of circulatory/interstitial fluid of electrolytes .

c. maintenance of temperature .

3. Protection

a. platelets and proteins "seal" vessel damage

b. protection from foreign material & infections by leukocytes, antibodies& complement proteins.

Plasma (the liquid part of blood)

General Characteristics

1. plasma makes up 55% of normal blood by volume
2. water is 90% of the plasma by volume
3. many different solutes in the plasma
   a. albumin - pH buffer & osmotic pressure
   b. globulins - binding proteins & antibodies
   c. clotting proteins - prothrombin & fibrinogen
   d. other proteins - enzymes, hormones, others
   e. nutrients - glucose, fatty acids, amino acids, cholesterol, vitamins
   f. electrolytes - Na^{+}, K^{+}, Ca^{++}, Mg^{++}, Cl^{-}, phosphate, sulfate, bicarbonate, others

BONE MARROW

In the adult, red blood cells, many white blood cells, and platelets are formed in the bone marrow. In the fetus, blood cells are also formed in the liver and spleen, and in adults such extra medullary hematopoiesis may occur in diseases in which the bone marrow becomes destroyed or fibrosed. In children, blood cells are actively produced in the marrow cavities of all the bones. By age 20, the marrow in the cavities of the long bones(upper humerus and femur). Active cellular marrow is called red marrow; inactive marrow that is infiltrated with fat is called yellow marrow.

The bone marrow contains stem cells that differentiate into one or another type of committed stem cells (progenitor cells). These in turn form the various differentiated types of blood cells. (, lymphocytes, erythrocytes, eosinophils, and basophils, whereas neutrophils and monocytes.

Erythrocytes (red blood cells; RBCs)

Structure

1. 7.5 micron diameter; 2.0 micron thick
2. biconcave disk shape.
3. mature cells are anucleate (no nucleus)
4 no mitochondria.
6. ratio erythrocytes: leukocytes = 800:1
7. red blood cell count: as cells per cubic millimeter
   i. normal male count - 5. to 5.8 million
   ii. normal female count - 4.3 to 5.2 million

Functions (oxygen & carbon dioxide transport)

Hemoglobin

The red, oxygen-carrying pigment in the red blood cells of vertebrates is hemoglobin, a protein with a molecular weight of 64,450. Hemoglobin is a globular molecule made up of 4 subunits .Each subunit contains a heme moiety conjugated to a polypeptide. Heme is an iron-containing porphyrin derivative . The polypeptides are referred to collectively as the globin portion of the hemoglobin molecule.

There are many types of hemoglobin**.**

1. **(Hemoglobin A)** the normal adult human hemoglobin have 2 alpha and 2 beta polypeptide

2.(Hemoglobin F) The blood of the human fetus normally contains fetal hemoglobin. Fetal hemoglobin is normally replaced by adult hemoglobin soon after birth.it have 2 alpha and 2 gama

3-(myoglobin):respiratory pigment found in muscles have one heme molecule and one polypeptide

4- **(neuroglobin)**, an oxygen-binding globin, is found in the brain. It appears to help supply O_2 to neurons

Reactions of Hemoglobin

1.**oxygenation**:Hemoglobin binds O_2 to form oxyhemoglobin, O_2 attaching to the Fe^{2+} in the heme. The affinity of hemoglobin for O_2 is affected by pH, temperature, and the concentration in the red cells of 2,3-diphosphoglycerate (2,3-DPG). Increasing 2,3-DPG and temperature leade to decreasing the affinity of hemoglobin for O_2

2. **Carbon monoxide** reacts with hemoglobin to form carbon monoxyhemoglobin (carboxyhemoglobin). The affinity of hemoglobin for O_2 is much lower than its affinity for carbon monoxide, which consequently displaces O_2 on hemoglobin, reducing the oxygen- carrying capacity of blood .

Synthesis of Hemoglobin

The average normal hemoglobin content of blood is 16 g/dL in men and 14 g/dL

in women, all of it in red cells. In the body of a 70-kg man, there are about 900 g of hemoglobin, and 0.3 g of hemoglobin is destroyed and 0.3 g synthesized every hour . The heme portion of the hemoglobin molecule is synthesized from glycine and succinyl-CoA.

Catabolism of Hemoglobin

When old red blood cells are destroyed in the tissue macrophage system, the globin portion of the hemoglobin molecule is split off, and the heme is converted to biliverdin

In humans, most of the biliverdin is converted to bilirubin and excreted in the bile . The iron from the heme is reused for hemoglobin synthesis.
Exposure of the skin to white light converts bilirubin to lumirubin, which has a shorter half-life than bilirubin. Phototherapy (exposure to light) is of value in treating infants with jaundice due to hemolysis. Iron is essential for hemoglobin synthesis; if blood is lost from the body and the iron deficiency is not corrected, iron deficiency anemia results.

Anemias:
I.Defeciency of substrates which are necessary for RBC or Hb production like:

1. Iron deficiency anemia.
2. folic acid deficiency anemia(low intake) folic a. is necessary for DNA formation and maturation of RBCs.
3. B12 deficiency anemia. B12 is necessary for DNA formation of RBCs. deficiency due to low intrinsic factor deficiency (pernicious anemia).
4. membrane defects as in hereditary spherocytosis.
5. Haemolytic anemia eg :autoimmune Haemolytic anemia, erythroblastosis fetalis.
6. .Hemoglobinopathies.Thalassaemia and sickle cell anemia.
7. bone morrow infiltration like aplastic anemia and different forms of leukaemias.
8. Anemia of chronic disease .like chronic renal failure.

Effect of anemia on circulation:

1. Decrease the viscosity of blood.
2. increase work load on the heart .
3. In exercise there will be tissue hypoxia

Polycythemia:
Increase production of RBCs (count 6-8 milio/mm^3)

Human Blood Groups:

1. Agglutinogens - glycoproteins on the surface of blood cells; causes "agglutination" (clumping)

2. ABO Blood Groups - determined by presence or absence of Type A and Type B agglutinogen proteins on cell membrane

TYPE	GENES	PEOPLE	Antibodies	Receive Blood from:
type A	A/A, A/O, O/A	(30-40%)	Anti-B	A, O
type B	B/B, B/O, O/B	(l0-30%)	Anti-A	B,O
type AB	A/B or B/A	(3-5%)	none	A, B, AB, O
type O	no A or B	(40-50%)	Anti-A, Anti-B	O only

The Rh Group

The "Rh factor," named for the rhesus monkey because it was first studied using the blood of this animal, is a system composed primarily of the C, D, and E antigens, although it actually contains many more. Unlike the ABO antigens, the system has not been detected in tissues other than red cells. D is by far the most antigenic component, and the term "Rh-positive" as it is generally used means that the individual has agglutinogen D. The "Rh-negative" individual has no D antigen and forms the anti-D agglutinin when injected with D-positive cells. The Rh typing serum used in routine blood typing is anti-D serum. Eighty-five percent of Caucasians are D-positive and 15% are D-negative .Unlike the antibodies of the ABO system, anti-D antibodies do not develop without exposure of a D-negative individual to D-positive red cells by transfusion or entrance of fetal blood into the maternal circulation. However, D-negative individuals who have received a transfusion of D-positive blood (even years previously) can have appreciable anti-D titers and thus may develop transfusion reactions when transfused again with D-positive blood.

Platelets (thrombocytes - "clotting")

The platelets are small, granulated bodies that aggregate at sites of vascular injury. They lack nuclei and are 2-4 m in diameter . There are about 300,000/ml of circulating blood, and they normally have a half-life of about 4 days. The megakaryocytes, giant cells in the bone marrow, form platelets by pinching off bits of cytoplasm and extruding them into the circulation. Between 60% and 75% of the platelets that have been extruded from the bone marrow are in the circulating blood, and the remainder are mostly in the spleen. Splenectomy causes an increase in the platelet count (thrombocytosis).

. Their cytoplasm contains actin, myosin, glycogen, lysosomes, and **two types of granules**:

(1) **dense granules**, which contain the nonprotein substances that are secreted in

response to platelet activation, including serotonin, ADP and ATP.
(2) **α-granules**, which contain secreted proteins other than the hydrolases in lysosomes. These proteins include clotting factors.

Hemostasis (stoppage of blood flow after damage)

Steps of hemostasis:1. Vascular spasms (vasoconstriction at injured site)
2. Platelet plug formation (plugging the hole)
3. Coagulation (blood clotting - complex mechanism)

Vascular Spasms: first response to vascular injury - vasoconstriction is stimulated by:

a. compression of vessel by escaping blood
b. released chemicals by injured cells
c. reflexes from adjacent pain receptors

Formation of a Platelet Plug

After damage to endothelium of vessel

1. platelets become spiky and sticky in response
2. platelets attach to damaged vessel wall to plug it
3. platelets produce thromboxane A2 which causes granule contents release
4. serotonin release enhances vascular spasm
5. ADP stimulates accumulation platelets at site
6. prostacyclin - inhibits aggregation at other sites

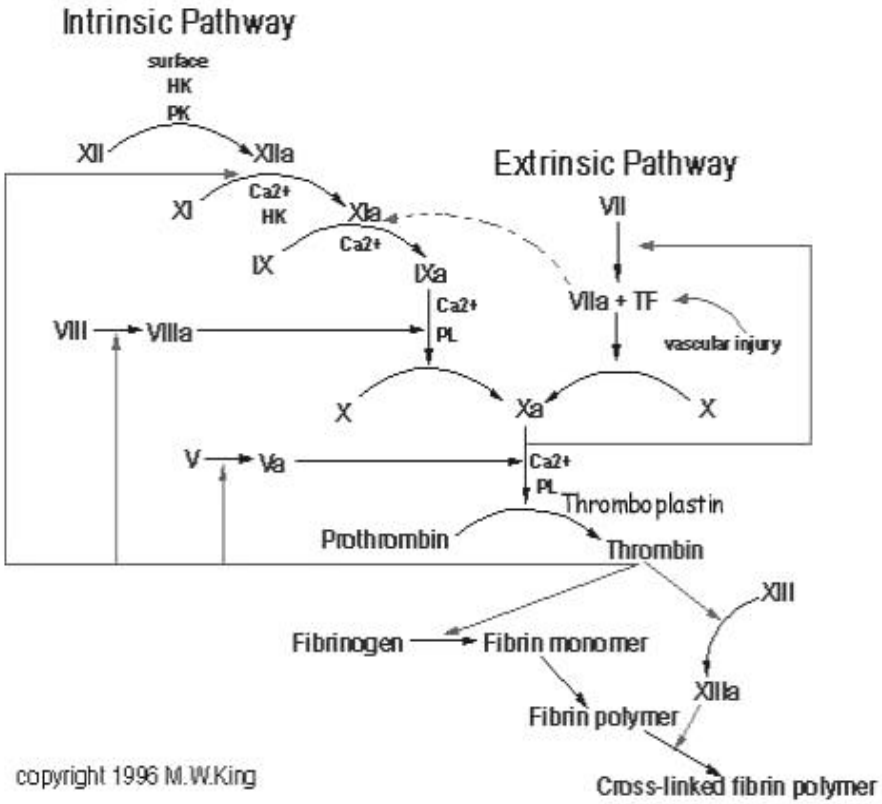
Coagulation (blood clotting)

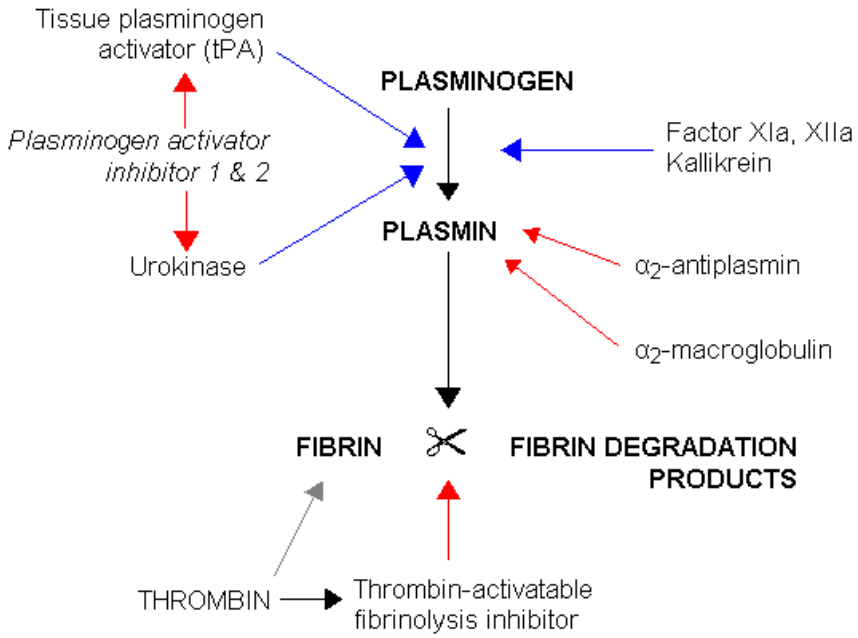
blood clotting factors

FACTOR	NAME
I	Fibrinogen
II	Prothrombin
III	Tissue factor or thromboplastin
IV	Calcium
V	Proaccelerin (Labile factor)
VII	Proconvertin (Stable factor)
VIII	Antihaemophilic factor A, Antihaemophilic globulin
IX	Antihaemophilic factor B, Plasma thromboplastin component, Christmas factor

FACTOR	NAME
X	Stuart-Prower factor
XI	Plasma thromboplastin antecedent, Haemophilia C, Rosenthal syndrome
XII	Hageman factor
XIII	Fibrin stabilising factor, Laki-Lorand factor

General Events in Clotting Is shown in the diagram





White blood cells, or leukocytes, are classified into two main groups: **granulocytes** and **nongranulocytes** .

Characteristic and Function

1. protection from microbes, parasites, toxins, cancer
2. 1% of blood volume; 4-11,000 per cubic mm blood

3 diapedesis - can "slip between" capillary wall

4. amoeboid motion - movement through the body
5. chemotaxis - moving in direction of a chemical
6. leukocytosis - increased "white blood cell count" in response to bacterial/viral infection

- The **granulocytes**, which include **neutrophils, eosinophils**, and **basophils**, have granules in their cell cytoplasm. **Neutrophils**, e**osinophils**, and **basophils** also have a multilobed nucleus.
- The **nongranuloctye** white blood cells, **lymphocytes** and **monocytes**, do not have granules and have nonlobular nuclei. They are sometimes referred to as mononuclear leukocytes. The lifespan of white blood cells ranges from 13 to 20 days, after which time they are destroyed in the lymphatic system." Leukocytes fight infection through a process known as phagocytosis. During phagocytosis, the leukocytes surround and destroy foreign organisms. White blood cells also produce, transport, and distribute antibodies as part of the body's immune response.

1. Neutrophils - destroy and ingest bacteria & fungi .
   a. most numerous WBC

b. defensins - antibiotic-like proteins (granules)
c. Have lobed nuclei
d. causes lysis of infecting bacteria/fungi

2. eosinophils - lead attack against parasitic worms
a. only 1-4% of all leukocytes
b. two-lobed, purplish nucleus
c. phagocytose antigens & antibodies complex

3. basophils - releases Histamine which causes inflammation, vasodilation, attraction of WBCs
a. Rarest of all leukocytes (0.5%)
b. have purple U or S shaped nucleus

Agranulocytes - WBCs without granules in cytoplasm

1. lymphocytes - two types of lymphocytes
a. T lymphocytes - (thymus) respond against virus infected cells and tumor cells.
b. B lymphocytes - (bone) differentiate into different "plasma cells" which each produce antibodies against different antigens
c. lymphocytes produce primarily in lymphoid tissues
d. very large purple nucleus
e. small lymphocytes in blood (5-8 microns)
f. larger lymphocytes in lymph organs (10-17 mic)

2. monocytes - differentiate to become macrophages; serious appetites for infectious microbes
a. largest of all leukocytes (18 microns)
b. dark purple, kidney shaped nucleus

Leukopoiesis and Colony Stimulating Factors (CSFs)

1. leukopoiesis - the production, differentiation, and development of white blood cells all cells derived from hemocytoblast
2. colony stimulating factors (CSF) - hematopoietic hormones that promote leukopoiesisIn response to an acute infection, trauma, or inflammation, white blood cells release a substance called colony-stimulating factor (CSF). CSF stimulates the bone marrow to increase white blood cell production. In a person with normally functioning bone marrow, the numbers of white blood cells can double within hours if needed

Normal values for total WBC

Total WBC: 4,000 - 11,000

- **Granulocytes** (or polymorphonuclears)
  - Neutrophils : 50 - 70% relative value
  - Eosinophils: 1 - 3% relative value
  - Basophils: 0.4% - 1% relative value
- **Agranulocytes** (or mononuclears)
  - Lymphocytes: 25 - 35% relative value
  - Moncytes: 4 - 6% relative value

Cardiovascular system.

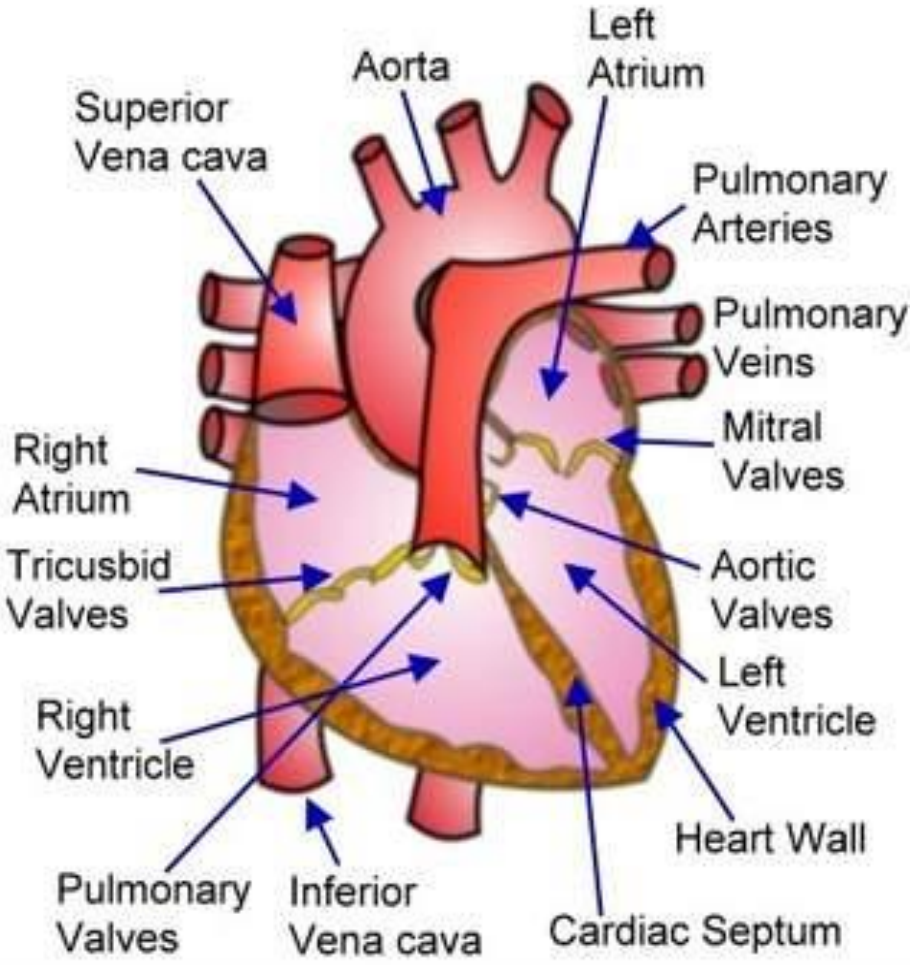
The heart

The heart is a muscular organ enclosed in a fibrous sac (the pericardium).The pericardial sac contains watery fluid that acts as a lubricant as the heart moves within the sac. The wall of the heart is composed of cardiac muscle cells, termed the myocardium. The inner surface of the wall is lined by a thin layer of endothelial cell called the endocardium. The heart is actually two separate pumps; a right heart which pumps blood through the pulmonary artery into the lung, and a left heart which pumps blood through the aorta into the peripheral organ. Each of these two pumps is consists of two chambers, an atrium and a ventricle, separated by atrioventricular valve (left: mitral valve and right: tricuspid valve). Blood exists from the right ventricle through the pulmonary valve to the pulmonary artery, and from the left ventricle through the aortic valve into the aorta.

Pulmonary and Systemic Circulations

Blood whose oxygen content has become partially depleted and carbon dioxide content has increased as a result of tissue metabolism returns to the right atrium. This blood then enters the ventricle, which pumps it into the pulmonary artery. The pulmonary arteries branch to transport blood to the lungs, where gas exchange occurs between the lung capillaries and the alveoli of the lungs. Oxygen diffuses from the air to the capillary blood; while carbon dioxide diffuses in the opposite direction. The blood that returns to the left atrium by way of the pulmonary veins is therefore rich in oxygen. The blood that is ejected from the right ventricle to the lungs and back to the left atrium completes one circuit: called **the pulmonary circulation.**

Oxygen-rich blood in the left atrium enters the left ventricle and is pumped into a very large, elastic artery; the aorta. The aorta ascends for a short distance, makes a U-turn, and then descends through the thoracic and abdominal cavities. Arterial branches from the aorta supply oxygen-rich blood to all of the organ systems and are thus part of the systemic circulation. As a result of cellular respiration, the oxygen concentration is lower and the carbon dioxide concentration is higher in the tissues than in the capillary blood. Blood that drains into the systemic veins is thus partially depleted of oxygen and increased in carbon dioxide content. These veins empty into two large veins; the superior and inferior venae cavae that return the oxygen-poor blood to the right atrium. This completes **the systemic circulation**.



Physiology of cardiac muscle

The heart is composed of three major types of cardiac muscle.

1- The atrial muscle.

2- The ventricular muscle.

3- Specialized excitatory and conductive muscle fibers; an excitatory system of the heart that helps spread of the impulse (action potential) rapidly throughout the heart.

Blood supply of the heart

The myocardial cells receive their blood supply through arteries that branch from the aorta, named coronary arteries.

Coronary veins drain into a single large vein, the coronary sinus, which drain into the right atrium.

The function of the heart valves

The atrioventricular valves (AV valves) are composed of thin membranous cusps (fibrous flaps of tissue covered with endothelium), which hang down in the ventricular cavities during diastole. After atrial contraction and just before ventricular contraction, the AV valves begin to close and the leaflets (cusps) come together by mean of backflow of the blood in the ventricles towards the atria.

The AV valves include:

- The mitral valve; the left AV valve; bicuspid valve, which consists of two cusps located between left atrium and left ventricle.
- The tricuspid valve; the right AV valve, which consists of three cusps, located between right atrium and right ventricle.

The function of AV valves is to prevent backflow (prevent regurgitation; leakage) of blood into the atria during ventricular contraction. Normally they allow blood to flow from the atrium to the ventricle but prevent backward flow from the ventricle to the atria. The atrioventricular valves contain and supported by papillary muscles.

The aortic and pulmonary valves each consist of three semilunar cusps that resemble pockets projecting into the lumen of aorta and pulmonary trunk. They contain no papillary muscle. During diastole the cusps of these valves become closely approximated to prevent regurgitation of blood from aorta and pulmonary arteries into the ventricles. During systole the cusps are open towards arterial wall, leaving a wide opening for ejection of blood from the ventricles. In other words, the pulmonary and aortic valves allow blood to flow into the arteries during ventricular contraction (systole) but prevent blood from moving in the opposite direction during ventricular relaxation (diastole).

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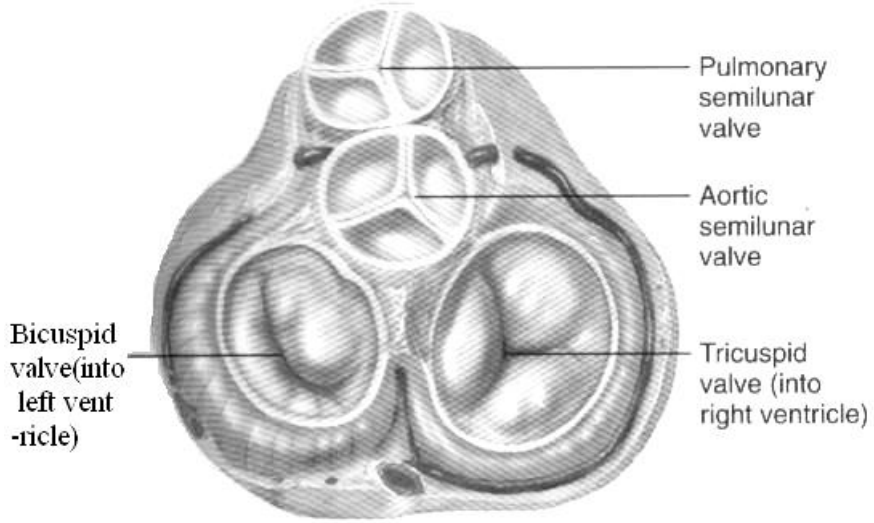

Function of papillary muscles

The AV valves (mitral and tricuspid) are supported by papillary muscles that attach to the flaps of these valves by the chordae tendineae. The papillary muscles originated from the ventricular walls and contract at the same time when the ventricular walls contract, but these muscles do not help the valves to

close or open. Instead, they pull the flaps of the valves inward, toward the ventricles to prevent too much further bulging of the flaps (cusps) backward

toward the atria during ventricular contraction, to prevent leakage of blood into the atria (keep the valve flaps tightly closed). In other words, contractions of papillary muscles prevent dash of the flaps of the AV valves into the atria which could be induced by high pressure produced by contraction of the ventricles.

The Cardiac cycle

Phases of the cardiac cycle:

The cardiac cycle starts by atrial systole followed by ventricular systole then by diastole of the whole heart.

1-Atrial systole (atria as a pump):

It is the first phase of cardiac cycle. Blood normally flows continually (passively) from the veins into the atria and about 75% of the blood in the atria flow directly into the ventricles even before the atrial contraction. Then, atrial contraction usually causes an additional 25% filling of the ventricles.

2- Isovolumetric contraction

It is ventricular contraction but without blood ejection (no emptying) just to close the AV valves and to open semilunar valves by the rise in intraventricular pressure (from 0 to 80 mmHg in the left ventricle). It is the isovolumetric contraction, which means only the tension is increasing in the ventricular muscle without shortening of the muscle and with no change in blood volume.

3-Ventricular ejection

The blood ejected from the ventricles into pulmonary trunk and aorta when the ventricular pressure rises and forces the semilunar valves open.
Left ventricular pressure rises above 80 mmHg.
Right ventricular pressure rises above 8 mmHg.

4-Isovolumetric relaxation:

Isovolumetric, or isometric relaxation; following ventricular systole, ventricular relaxation begins suddenly and ventricular pressure falls. The blood in the aorta and pulmonary trunk backflows toward the heart closing the semilunar valves. For another 0.03 to 0.06 second, the ventricular muscle continues to relax, even though the ventricular volume does not change giving rise to the period of isovolumic relaxation in which the intraventricular pressure falls rapidly back to their low diastolic levels. Meanwhile, the atria have been filling with blood. When the pressure exerted by the blood on the atrial side of AV valves exceeds that in the ventricles, AV valves forced open and the ventricular filling phase begins again for a new cycle of ventricular pumping.

Heart Sounds

When the stethoscope is placed on the chest wall over the heart, two sounds are normally heard during each cardiac cycle (1st & 2nd heart sounds). Heart sounds are associated with closure of the valves with their associated vibration of the flaps of the valves and the surrounding blood under the influence of the sudden pressure changes that develop across the valve.

1-The first heart sound (S_1): is caused by closure of the AV valves when ventricles contract at systole. The vibration is soft, low-pitched lub.
2-The second heart sound (S_2): is caused by closure of the aortic and pulmonary valves when the ventricles relax at the beginning of diastole. The vibration is loud, high-pitched dup.
3-The third heart sound (S_3): is caused by rapid filling of the ventricles, by blood that flow with a rumbling motion into the almost filled ventricles
4-The fourth heart sound (S_4): it is an atrial sound when the atria contract (at late diastole). It is a vibration sound (similar to that of S_3) associated with the flow of blood into the ventricle.

Heart murmurs

They are abnormal sounds, can be produced by blood flowing rapidly in the usual direction but through an abnormally narrowed valve (stenosis), by blood flowing backward through a damaged, leaky valve (incompetent, regurgitant valve) or by blood flowing between the two atria or two ventricles through a small hole: ASD (atrial septal defect), VSD (ventricular septal defect).

Properties of the cardiac muscle

The cardiac muscle has the property of:

- Autorhythmicity.
- Excitability and Contractility

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Autorhythmicity, Excitability and conductivity:

Electrical activity of the heart (action potential):
Specialized excitatory and conductive system of the heart: consists of:

1. Sinus node "SA" node: also called sinoatrial node, located in the right atrium. It is concerned with the generation of rhythmical impulse; it is the pacemaker of the heart that initiates each heart beat. This automatic nature of the heart beat is referred to as automaticity.
2. Internodal pathways conduct the impulse generated in SA node to the AV node.
3. The AV node (atrioventricular node), located near the right AV valve at the lower end of the interatrial septum, in the posterior septal wall of the right atrium. At which impulse from the atria is delayed before passing into the ventricles.
4. The AV bundle (bundle of His) conducts the impulse from the atria into ventricles.
5. The left and right bundles of purkinje fibers, which conduct the cardiac impulse to all parts of the ventricles. The purkinje fibers distribute the electrical excitation to the myocytes of the ventricles.

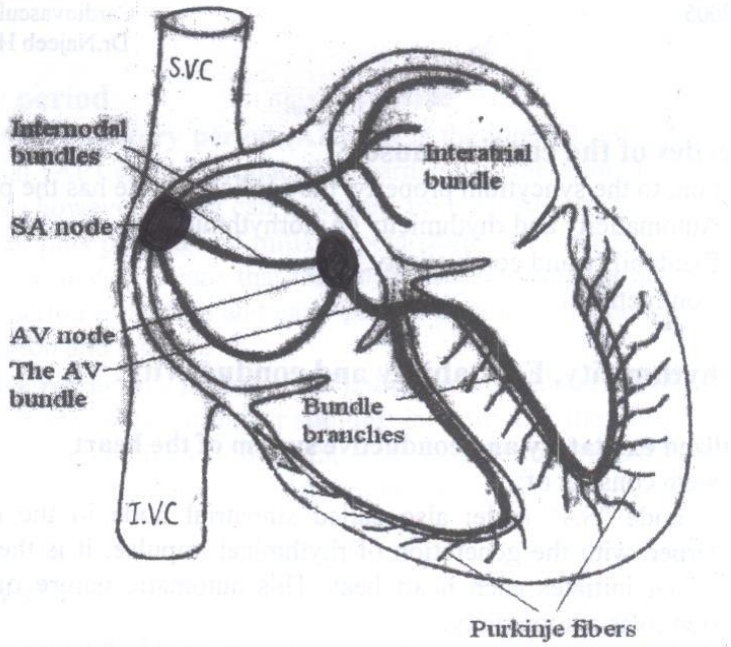


Figure: The cardiac conduction system.

The SA node as the pacemaker of the heart: (Autorhythmicity)

Autorhythmicity is the property of self-excitation (i.e. the ability of spontaneously generating action potentials independent of any extrinsic stimuli and regular generation of these action potentials. In other words, the cardiac impulse normally arises in the SA node, which has the capability of originating action potentials and functioning as pacemaker. This action potential then spreads from the SA node throughout the atria and then into and throughout the ventricles.

The contractile cardiac muscle cells don't normally generate action potentials but they can do in certain pathological conditions. This mean that all parts of the conduction system are able to generate a cardiac impulse; (autorhythmicity), but the normal primary pacemaker is the SA node, while the AV node is a secondary pacemaker and the Purkinje system is a tertiary (or latent) pacemaker. The AV node acts only if the SA node is damaged or blocked, while the tertiary pacemaker takes over only if impulse conduction via the AV node is completely blocked.

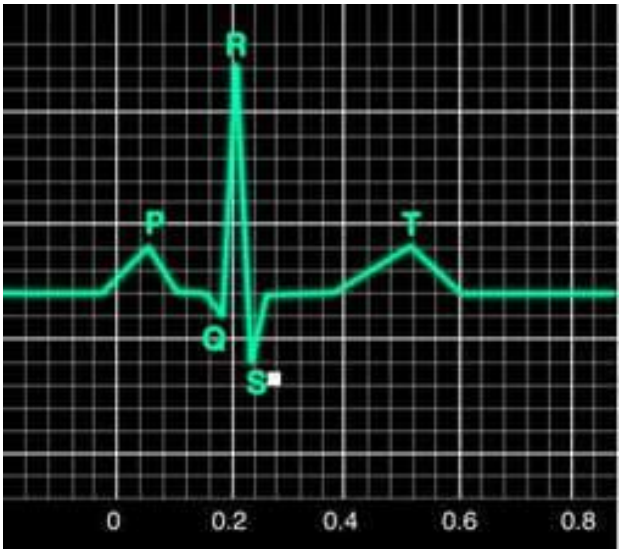
The SA node discharges at an intrinsic rhythmical rate of 100-110 times per minute (sinus rhythm). Under abnormal condition; the AV nodal fibers can exhibit rhythmical discharge and contraction at a rate of 40 to 60 times/minute. While those of purkinje fibers discharge at a rate between 15 and 40 times/minute.

Atrioventricular node (AV node):

The conductive system is organized, so that cardiac impulse will not travel from the atria into ventricles too rapidly. There is a delay of transmission of the cardiac impulse in the AV node to allow time for the atria to empty their blood into the ventricles before ventricular contraction begins.

Relationship of the ECG to the cardiac cycle (Timing):
The ECG (electrocardiogram) shows the P, QRS and T waves. They are electrical voltages generated by the heart and recorded by the ECG:

- P-wave is caused by atrial depolarization; this is followed by atrial contraction, which causes a slight rise in the atrial pressure curve after the P wave.
- About 0.16 second after the onset of the P wave, the *QRS waves* appear as a result of electrical depolarization of the ventricles, which initiates contraction of the ventricles and causes the ventricular pressure to begin rising, as shown in the figure. Therefore, the QRS complex begins slightly before the onset of ventricular systole.
- T-wave represents ventricular repolarization at which the ventricles begin to relax. Therefore, the T wave occurs slightly before the end of ventricular contraction.



Stroke volume (S.V): it is volume of blood eject from each ventricle on each beat.

Normal level 70 ml

It is depends on

1- heart rat

2-contractility

Cardiac output (C.O):it is volume of blood eject by each ventricle of heart per min.

C.V = Stroke volume S.V ml(L) × heart rat (H.R) beat per min.

Heart rate = the number of heart beats/minute (average; 72 beat/minute).

Cardiac index (C.I):it is relationship of cardiac output to body surface area

C.I= C.O/A

Venous return :quantity of blood returned from all over the body through the veins into right atrium in each min.

V.R=C.O

Pulse pressure :the difference between systolic blood pressure and diastolic blood pressure 120-80=40

Velocity of blood flow: can be expressed by

V=velocity = Q
/A Q=flow of blood A=surface area

Cardiac reserve (C.R): is maximum increase in cardiac output above the normal value

It is usually expressed in %

Adult 300-400 % Old age 200-250%

C.R increase in heart disease and decrease in heavy exercises

Lymphatic System

Microcirculation and Capillary System

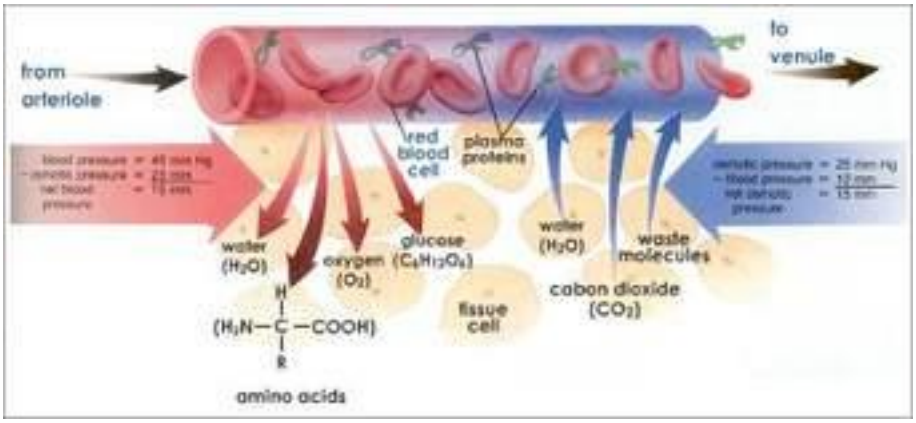
In general, each nutrient artery entering an organ branches six to eight times before the arteries become small enough to be called arterioles, .Then the arterioles themselves branch two to five times. at their ends where they supply blood to the capillaries. The arterioles are highly muscular ,the terminal arterioles do not have a continuous muscular coat, but smooth muscle fibers encircle the vessel at intermittent points. At the point where each true capillary a smooth muscle fiber usually encircles the capillary. This is called the precapillary sphincter. This sphincter can open and close the entrance to the capillary. The venules are larger than the arterioles and have a much weaker muscular coat. the pressure in the venules is much less than that in the arterioles

Exchange of Water, Nutrients, and Other Substances Between the Blood and Interstitial Fluid

Lipid-Soluble Substances Can Diffuse Directly Through the Cell Membranes of the Capillary Endothelium. If a substance is lipid soluble, it can diffuse directly through the cell membranes of the capillary without having to go through the pores. Such substances include *oxygen* and *carbon dioxide*. Because these substances can permeate all areas of the capillary membrane,

Water-Soluble Substances Diffuse Only Through Intercellular "Pores" in the Capillary Membrane.

Many substances needed by the tissues are soluble in water but cannot pass through the lipid membranes of the endothelial cells; such substances include *water molecules* themselves, *sodium ions*, *chloride ions*, and *glucose*. Despite the fact that not more than 1/1000 of the surface area of the capillaries is represented by the intercellular clefts between the endothelial cells, the velocity of thermal molecular motion in the clefts is so great that even this small area is sufficient to allow tremendous diffusion of water and water-soluble substances through these cleft-pores.



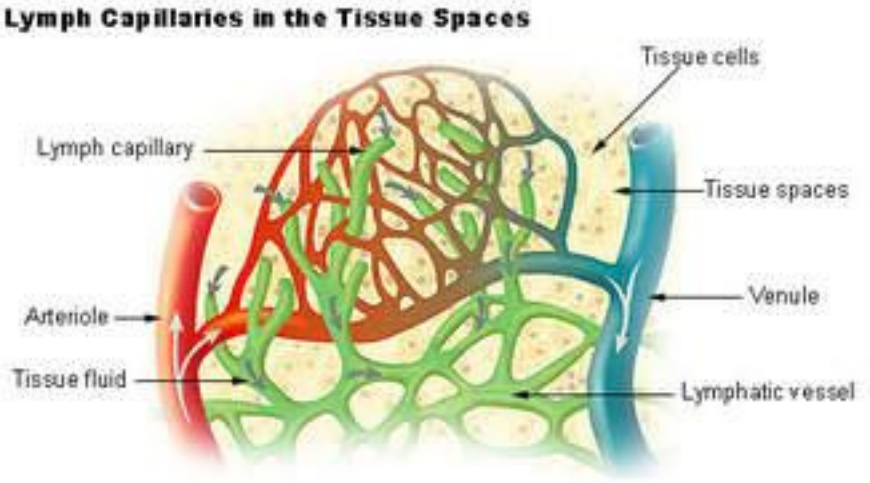
Lymphatic System

This circulation is concerned with return of the excess tissue fluid that is not reabsorbed at the capillaries back to the bloodstream. This fluid is called lymph,

1- it is similar to the plasma being an isotonic
2- colorless
3-having a pH of 7.4)
4-contains less protein and Ca2
5-has a higher A/G ratio (Albumin/Globulin ratio) since albumin is more easily filtered. Its average protein content is 3 gm %, but it varies in different organs and
6-it clots (as it contains fibrinogen and prothrombin)
7-it is rich in lymphocytes.

Lymph circulates in non-innervated vessels that form a lymphatic system. This system originates as minute lymphatic capillaries in the tissues (which are highly- permeable blind vessels lined by a single layer of endothelial cells) that drain the excess tissue fluid. These capillaries unite forming larger lymphatic vessels, which drain in the thoracic and right lymph ducts that open in the subclavian veins at the base of the neck.

The lymph nodes are located along the course of the lymphatic vessels, and such vessels have smooth muscle in their walls and contain valves that allow unidirectional flow toward their central end



Lymph Channels of the Body

Almost all tissues of the body have special lymph channels that drain excess fluid directly from the interstitial spaces. The exceptions include

1- the superficial portions of the skin,

2-the central nervous system,

3-the endomysium of muscles,

4- the bones.

this fluid eventually empties into lymphatic vessels then directly back into the blood through .

1- the thoracic duct: which collected Lymph from the left side of the head, the left arm, and parts of the chest in turn empties into the blood venous system at the junction of the left internal jugular vein and left subclavian vein

2- right lymph duct: which collected Lymph from the right side of the neck and head, the right arm, and parts of the right thorax enters the (much smaller than the thoracic duct), which empties into the blood venous system at the junction of the right subclavian vein and internal jugular vein.

The total quantity of all this lymph is normally only 2 to 3 liters each day. The fluid that returns to the circulation by way of the lymphatics is extremely important because substances of high molecular weight, such as proteins, cannot be absorbed from the tissues in any other way, although they can enter the lymphatic capillaries

Formation of Lymph

Lymph is derived from interstitial fluid that flows into the lymphatic's. Therefore, lymph as it first enters the terminal lymphatics has almost the same composition as the interstitial fluid. The protein concentration in the interstitial fluid of most tissues averages about 2 g/dl, and the protein concentration of lymph flowing from these tissues is near this value. Conversely, lymph formed in the liver has a protein concentration as high as 6 g/dl, and lymph formed in the intestines has a protein concentration as high as 3 to 4 g/dl. Because

about two thirds of all lymph normally is derived from the liver and intestines, the thoracic duct lymph, which is a mixture of lymph from all areas of the body, usually has a protein concentration of 3 to 5 g/dl. The lymphatic system is also one of the major routes for absorption of nutrients from the gastrointestinal tract, especially for absorption of virtually all fats in food, . Indeed, after a fatty meal, thoracic duct lymph sometimes contains as much as 1 to 2 per cent fat.
As the lymph passes through the lymph nodes, these particles are almost entirely removed and destroyed,

Rate of Lymph Flow
About 100 milliliters per hour of lymph flows through the *thoracic duct* of a resting human, and approximately another 20 milliliters flows into the circulation each hour through other channels, making a total estimated lymph flow of about 120 ml/hr. or 2 to 3 liters per day.

Effect of Interstitial Fluid Pressure on Lymph Flow.

factor that increases interstitial fluid pressure also increases lymph flow if the lymph vessels are functioning include
the following:

- Elevated capillary pressure.
- Decreased plasma colloid osmotic pressure.
- Increased interstitial fluid colloid osmotic pressure.
- Increased permeability of the capillaries.

Lymphatic Pump Increases Lymph Flow.

1. Valves exist in all lymph channels
2. contracts of the smooth muscle in the wall of the lymphatic vessels
3. Contracts of skeletal muscles
4. Contracts of diaphragm muscles
5. Pulsations of arteries adjacent to the lymphatic's vessels
6. Compression of the tissues by objects outside