Principles of Human Physiology

Foundation Module

For
1st Year Medical Students
Alexandria University

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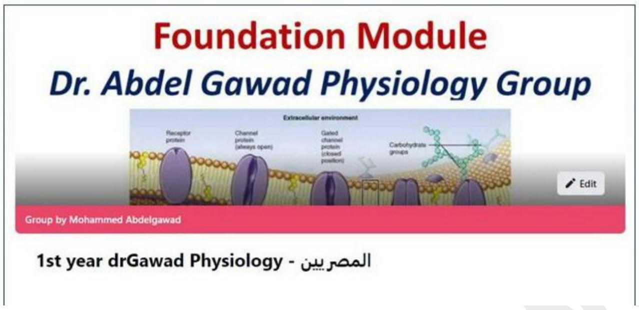

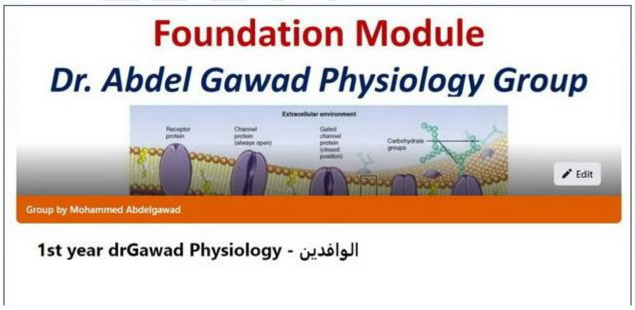

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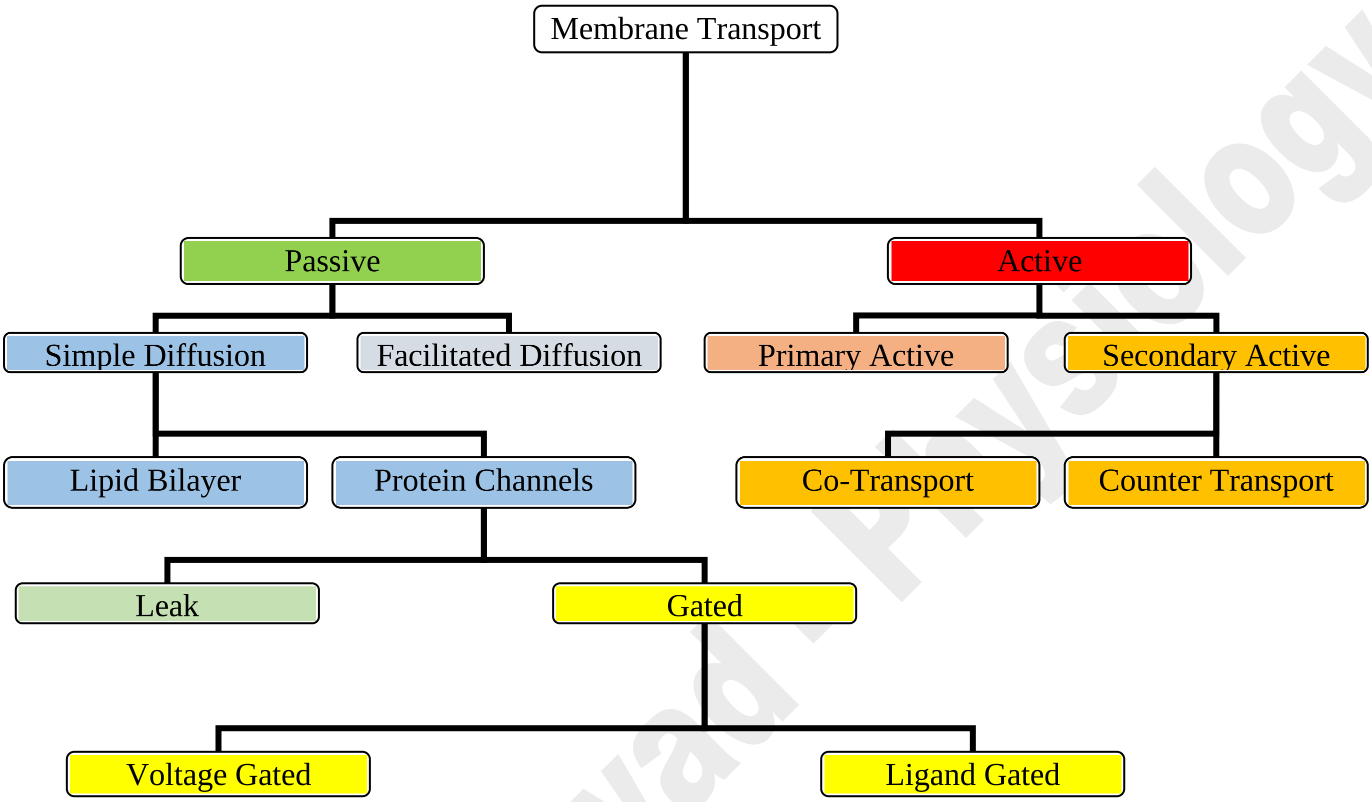
Part 1:

A- Cell Membrane Transport

Transport through the cell membrane:

Transport through the cell membrane occurs by passive or active transport.



I- Passive Transport:

Definition:

It is the transport of molecules through the cell membrane ***from*** areas of high concentration ***to*** areas of low concentration (i.e., down concentration gradient or downhill)) ***by the aid of*** the kinetic energy of the molecules

Types of Passive transport:

- Simple diffusion
- Facilitated diffusion

1. Simple diffusion:

Definition:

It is the transport of substances either through:

a- the lipid bilayer or

b- through the channel proteins of the cell membrane

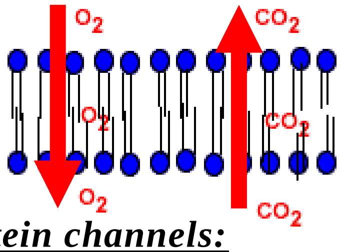
Types:

a- Simple diffusion through the lipid bilayer:

- Non-polar and lipid-soluble molecules e.g. oxygen, carbon dioxide, and fat-soluble vitamins:

i- oxygen diffuses from the blood into the cells.

ii- carbon dioxide diffuses in the opposite direction.



b- Simple diffusion through protein channels:

- Diffusion of small water soluble molecules e.g. electrolytes

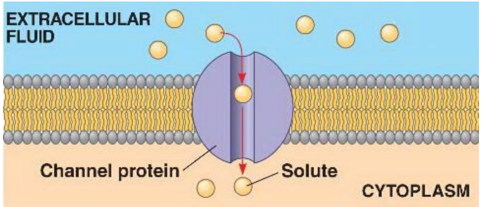
- The channels are highly selective:

- the sodium channel is specifically selective for passage of sodium ions.

- the potassium channel is selective for potassium transport.

-Types of the channel according to presence or absence of a gate:

1- leak channels: continuously opened.

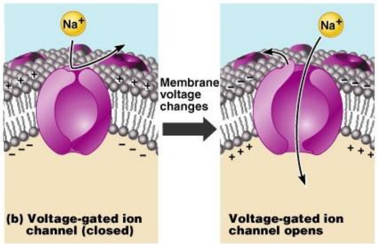


<u>*2- Gated channels:*</u> Controlled by gates:

- Two types of gated channels are present:

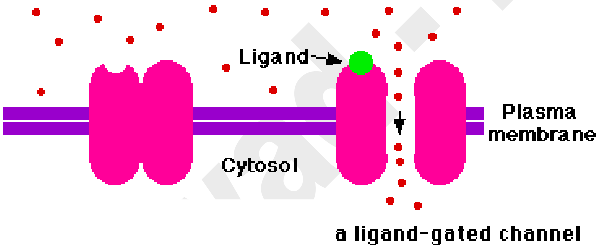
<u>*a- Voltage gated ion channel:*</u>

These channels open or close according to changes in membrane voltage (potential)



<u>*b- Chemical (ligand) gated ion channels:*</u>

These channels open or close by binding to a ligand (chemical substance) e.g. acetylcholine sodium gated channel at the neuro muscular junction.



Factors affecting the rate of simple diffusion (lipid bilayer or protein channel):

<u>*1- Surface area of the membrane:*</u>

The greater the surface area of the membrane the higher the rate of diffusion.

<u>*2- Concentration gradient:*</u>

Increase in concentration difference of the substance on both sides of the membrane increases the rate of diffusion from high to low concentration.

<u>*3- Electrical gradient:*</u>

Ions passed from positively charged area to negatively charged one

<u>*4- Pressure gradient:*</u>

Molecules diffuse from areas of high pressure to areas of low pressure

<u>*5- Permeability of the membrane*</u>:

The rate of diffusion increases by increasing the *permeability of the membrane*.

Membrane Permeability:

Definition

It is the rate of transport through a unit area of the membrane for a given concentration difference.

Factors affecting the permeability of the membrane

1. The number of channels.
2. The resistance of the channel.
3. The molecular weight (M.W.) of the diffusing substance (inverse relation with permeability)
4. The temperature:

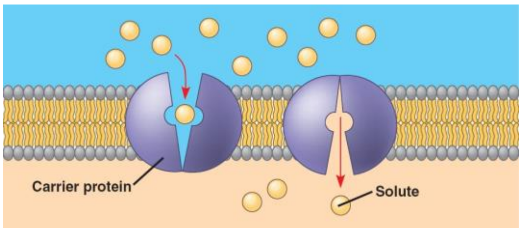
   Increase in temperature → increase in motion of ions → increase the permeability.
5. The thickness of the membrane: The greater the thickness of the membrane the lesser will be the permeability.

2. Facilitated (carrier-mediated) diffusion:

Definition: transported substance uses a specific carrier protein

Mechanism: substance combines with a carrier, forming a complex that passes through the membrane, then it splits from the carrier to the other side

Occurs with: It occurs in cases of large sized polar lipid insoluble particles such as sugars and amino acids.



Factors affecting facilitated diffusion:

1- the availability of the carrier,

2- high concentration gradient of the substance through the membranes,

3- rapid combination and splitting of the carrier with the transported substance,

4- saturation of the carrier.

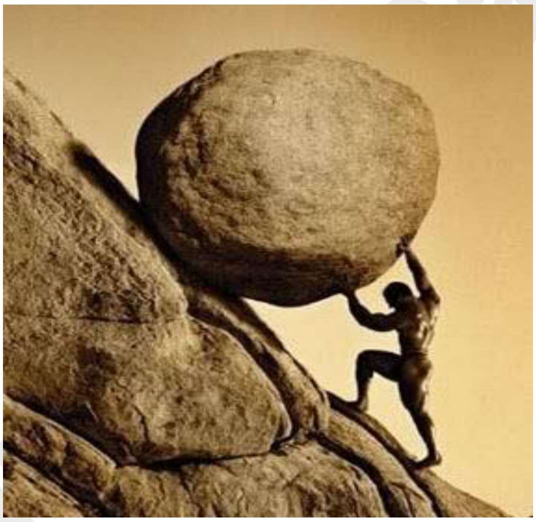
N.B. glucose is normally in higher concentrations in the blood than in the cells

Molecules which ***can diffuse*** through the membrane	Molecules which ***cannot diffuse*** through the membrane
1- Non-polar Lipid soluble e.g. oxygen and carbon dioxide (through lipid bilayer) 2- Small water soluble molecules e.g. electrolytes.(through channels) 3- large molecules e.g. glucose and amino acids (by facilitated diffusion)	The large molecules with high molecular weights e.g. proteins, which pass by a process called vesicular transport (pinocytosis).

II- Active Transport

Definition:

- Active transport is the movement of substances across the membrane against energy gradients (uphill).
- It requires an additional source of energy derived from the cell.



Types of Active transport:

- Primary active transport
- Secondary active transport

1. Primary active transport:

Definition: It requires energy derived directly from breakdown of adenosine triphosphate (ATP) or creatine phosphate

Sodium - potassium (Na-K) pump:

The most important example of a 1ry active transport is the sodium-potassium pump.

Definition: It is a transport process that pumps sodium ions outward of the cell and at the same time pumps potassium ions from the outside to the inside of the cell against their concentration gradient.

Mechanism of action:

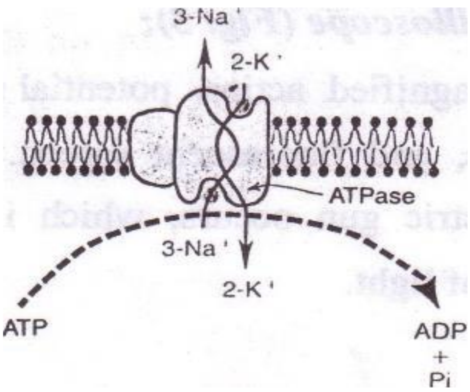
- Na-K pump is a carrier protein formed of a complex of two separate globular proteins:

- a larger one called the 'a' subunit,
- a smaller one; the 'b' subunit.

- The larger protein has three specific features:

- It has 3 receptor sites for binding sodium ions on the inner surface.
- It has 2 receptor sites for potassium ions on the outside surface.
- It has an ATPase enzyme activity.

- When potassium ions bind to the receptor sites on the outside of the carrier protein and the sodium ions bind on the inside receptors → the ATPase enzyme activated → This then cleaves one molecule of ATP → liberate a high energy phosphate bond → This energy causes a conformational change in the carrier protein → move the sodium ions to the outside and potassium ions to the inside.



Importance of the Na+-K+ Pump:

1. This pump is responsible for maintaining the sodium and potassium concentration differences across the cell membrane:

   The concentration of K inside the cell is higher than that outside, and the reverse is true of Na^+ → Na^+ and K leak continuously through leakage channels in the membrane along their concentration gradient that will disturb their normal distribution → the Na-K pump works to drive Na^+ back to out of the cell and pump K back into the cell, against their concentration gradient.
2. It maintains a negative electrical voltage inside the cells.
3. Maintenance of intracellular potassium is necessary for protein metabolism.
4. It keeps the osmotic equilibrium and controls cell volume.

2. Secondary active transport:

Mechanism:

- There is carrier existing in the lipid layer of the membrane, which has two binding sites:

  a- one site for one sodium ion moves with their concentration gradient

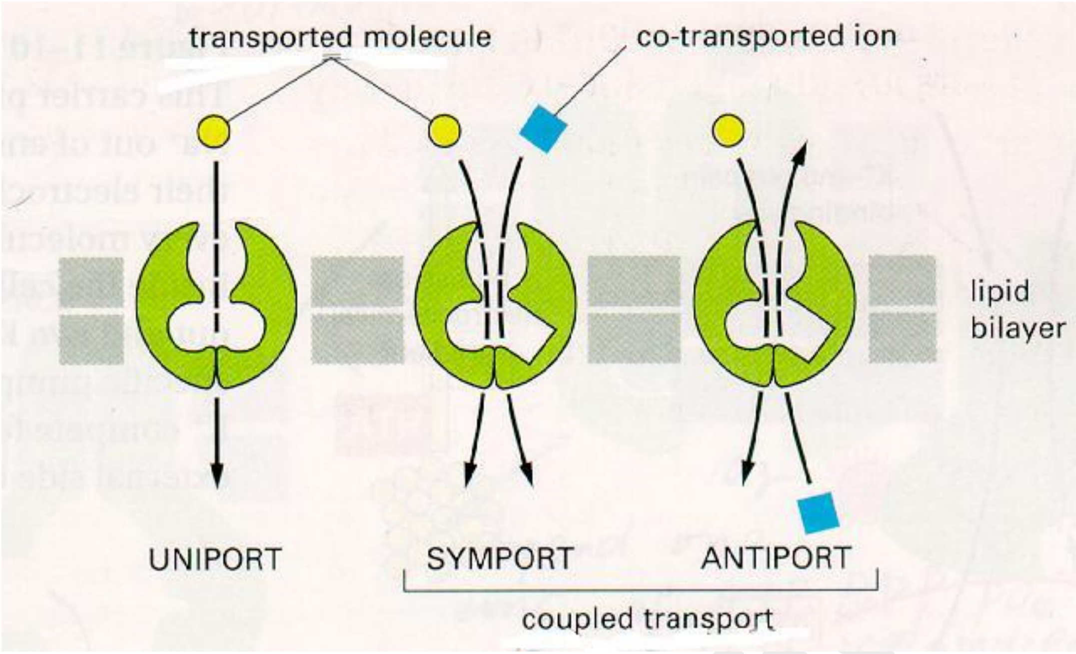
  b- other site used by another molecule (e.g. glucose, galactose or amino acids) to move against their electrochemical gradient.

- The energy supplied for glucose, galactose or amino acids in this process comes from the movement of the sodium along its electrochemical (concentration) gradient.

Types:

a- If the two transported substances are moved in the same direction, the system is a symport system (Co-transport). E.g. Sodium-Glucose co-transport and Sodium-amino acids co-transport.

b- If the transported substances cross the membrane in opposite directions, the system is an antiport system (Counter-transport). E.g. sodium-calcium counter-transport, sodium-hydrogen counter-transport.

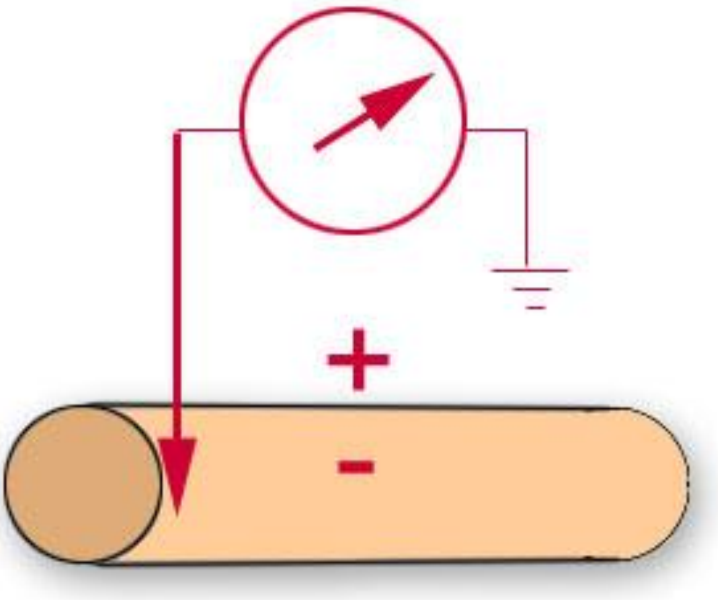


Resting Membrane Potential (Polarized State)

Normal Value:

- Resting membrane potential ranges from - 50 to - 100 millivolts (mV), depending on cell type.

- The minus sign before the voltage indicates that the inside of the cell is negative compared to its outside.



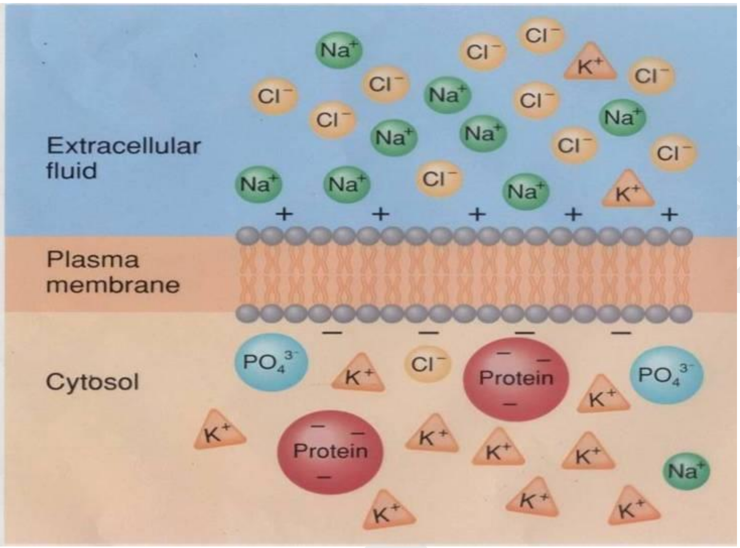
Causes of resting membrane potential (i.e. why RMP is negative?):

1. Selective permeability across the cell membrane:

- ions distribution:

a- K and protein anions predominate inside body cells

b- the extracellular fluid contains relatively more Na^+, Cl - and HCO_3^-.



- K & Protein: The plasma membrane is permeable to *K* because of leakage channels, but absolutely impermeable to the protein anions → potassium diffuses out of the cell along its concentration gradient but the protein is unable → the membrane interior is more negative.

- *Sodium* is moved to the cell interior by its concentration gradient.

- The membrane is much more permeable to K^+ than to Na^+ although diffusion of K^+ across the plasma membrane is resisted somewhat by the positive charge on the cell exterior.

- *Cl* does not contribute to the resting membrane potential because its entry is resisted by the negative charge of the interior due to protein anions.

2. Active Na^+-$K^\pm$ pump (Electrogenic Nature of the Na-K Pump):

- The fact that the Na-K pump moves three Na ions to the exterior for every two K ions to the interior creates positivity outside the cell and negativity on the inside *(membrane potential).*

- Na+-K pump is said to be electrogenic because *it creates an electrical potential across the cell membrane*.

Body fluid exchange

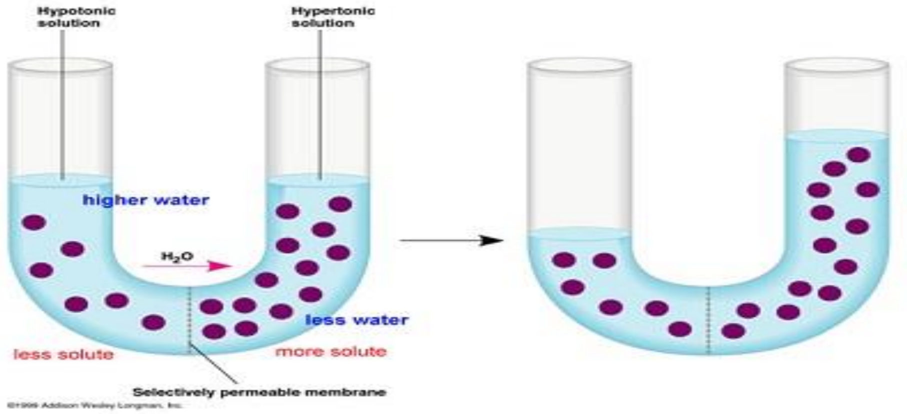
- The exchange of body fluids is affected by two major forces: osmosis and filtration.

1. Osmosis:

Definition of osmosis:

- It is the diffusion of a solvent, such as water, through a selectively permeable membrane to the other side in which there is higher concentration of the solute to which the membrane is impermeable.

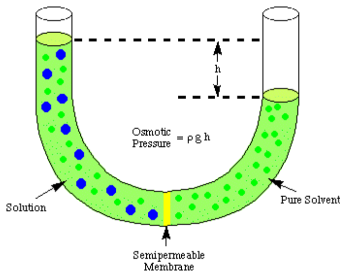
- It is determined by the number of particles per unit volume of fluid, not by the mass of the particles.

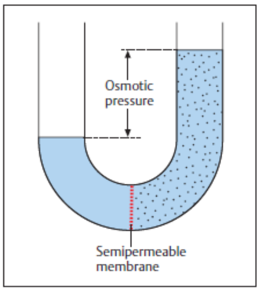


Osmotic pressure:

- It is the pressure needed in the concentrated solution to prevent water movement from the diluted side.

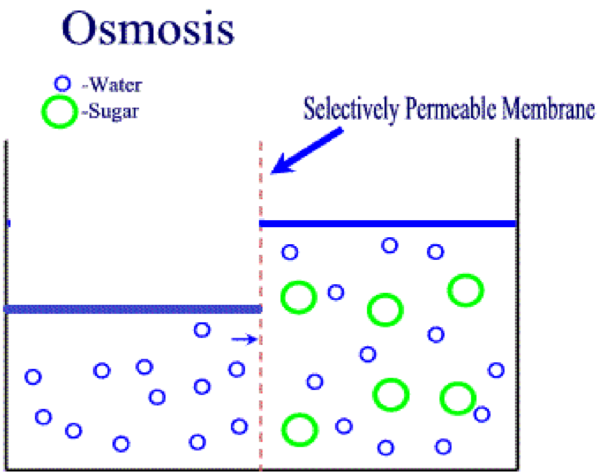
- It is determined by the number of particles per unit volume of fluid, not by the mass of the particles.





Osmole:

- it is the concentration of a solution in terms of numbers of particles.
- One osmole = 1 gram MW of osmotically active undissociated solute e. g. Glucose.
- Osmole = 1000 milliosmole



Osmolality:

- def:

- is the number of osmoles (solutes) per kilogram of solution.

- Value:

- normal osmolality of the extracellular and intracellular fluids is about 300 milliosmoles/kilogram of water.

Osmolarity:

- def:

- it is the total concentration of all osmoles (solutes) per liter of solution i.e. it is the osmolar concentration

- expressed as osmoles/L of solution.

- N.B. Osmotic imbalances cause cells to swell or shrink.

Tonicity:

- Definition:

- It is the ability of a solution to change the shape of cells by altering their internal water volume.

- Types:

a- isotonic solutions:

- def:

solutions with the same concentrations of non-penetrating solutes as those found in cells

- e.g.

0.9% saline or 5% glucose.

- Effect on cell:

Cells exposed to such solutions retain their normal shape and exhibit no loss or gain of water.

b- hypertonic solutions:

- def:

solutions with a higher concentration of non-penetrating solutes than seen in the cell

- e.g.

a strong saline solution.

- Effect on cell:

Cells immersed in hypertonic solutions lose water and shrink.

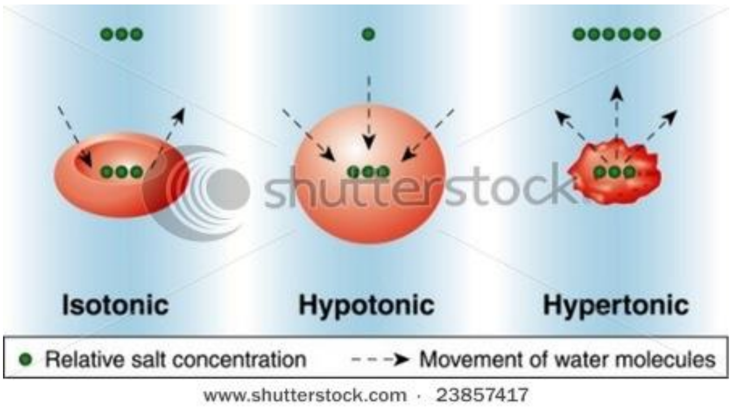
c- hypotonic solution:

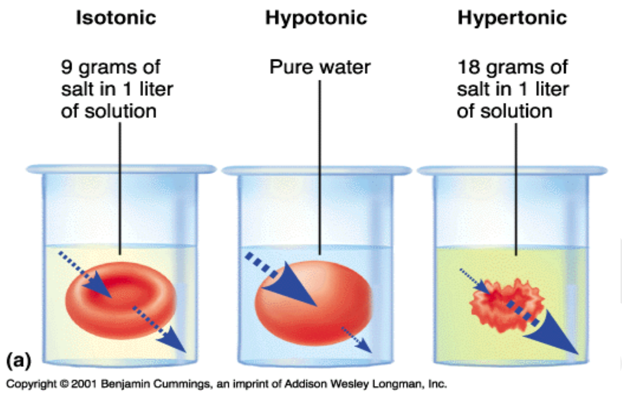
- def:

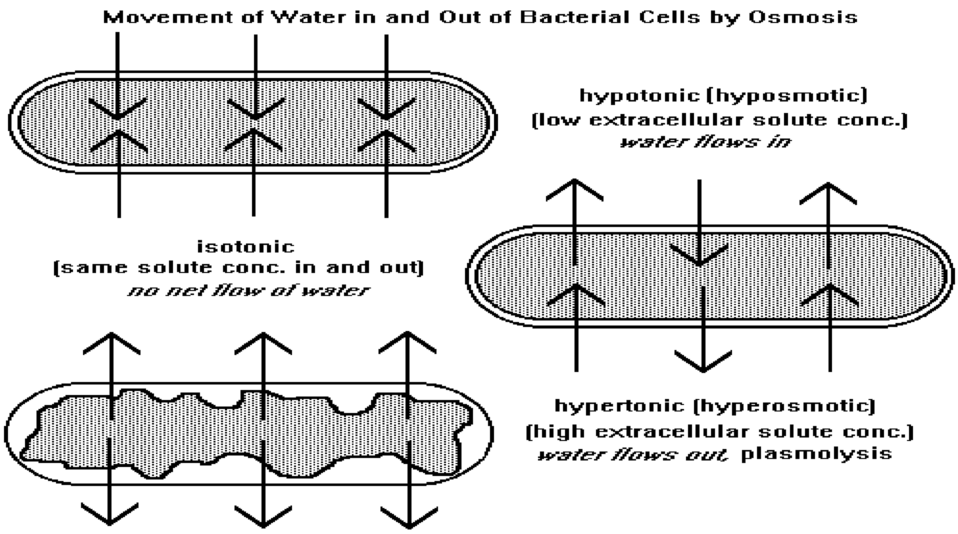
Solutions contain a lower concentration of non-penetrating solutes) than cells.

- Effect on cell:

Cells placed in a hypotonic solution swell rapidly as water rushes into them.







2. Filtration:

- def: It is the process that forces water and solutes through a membrane or capillary wall by the hydrostatic pressure.

- Like diffusion, filtration is a passive transport process.

Part 1:
B- HOMEOSTASIS

Physiology is the science that seeks to explain the physical and chemical mechanisms that are responsible for the origin, development, and progression of life. Each type of life, from the simplest virus to the largest tree or the complicated human being, has its own functional characteristics.

The science of human physiology attempts to explain the specific characteristics and mechanisms of the human body that make it a living being.

The fact that we remain alive is the result of complex control systems. Hunger makes us seek food, and sensations of cold make us look for warmth. Other forces cause us to seek fellowship and to reproduce. The fact that we are sensing, feeling, and knowledgeable beings is part of this automatic sequence of life; these special attributes allow us to exist under widely varying conditions, which otherwise would make life impossible.

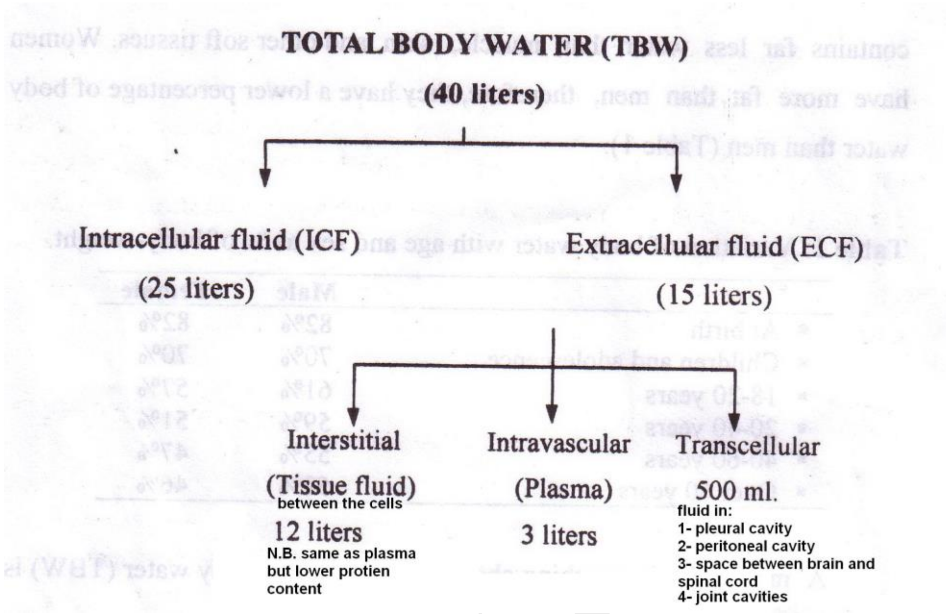
The human body consists of many systems e.g. cardiovascular, respiratory, nervous etc., each system is made of organs; each organ is made of tissues, which in turn are made up of cells. The cell is the living unit of the body. Each cell is specifically performing one or few particular functions.

The fundamental living unit of the body is the cell. Although the many cells of the body often differ markedly from one another, all of them have certain basic characteristics that are alike.

Composition of the human body

The human body is composed of:

I- Water:



- About 60% of the young adult male body weight is fluid.

- However, the amount of body water decline with age and is affected by the quantity of body fat.

- A man, who is weighing about 65 kg, has total body water (TBW) equals to 40 liters.

- TBW (40 L) is subdivided into:

a- Intracellular; inside the cells (ICF): it is about 2/3 of the total body water (25 liters).

b- Extracellular; outside the cells (ECF): it is about 1/3 of the total body water (15 liters).

ECF is further subdivided into:

i- Interstitial (between the cells): in the tissue spaces (12 liters).

ii- Intravascular (inside the blood vessels): it is the blood plasma (3 liters).

iii- Transcellular (500 ml): it is found in special compartments in the body such as in the pleura, and in the joint cavities.

II- Proteins:

- 18% of the body weight is protein

- found in the structure of all tissues, but the largest amount is found in skeletal muscles.

III- Fats:

- 15% of the body weight is fat which constitutes the main energy stores of the body,
- found around abdominal viscera, in subcutaneous tissues and in the structure of the central nervous system. Phospholipids are found in the structure of cell membranes.

IV- Minerals:

- 7% of the body weight is minerals,
- Minerals are present in relatively small quantities with the exception of calcium.
- Minerals and electrolytes concentrations in the intracellular fluid are different from those in extracellular fluid.

- The concentration of major cations and anions in body fluids (mmol/L):

	Extracellular fluid	Intracellular fluid
Cations (mmol/L)		
Na^+	145	10
K^+	4	145
Ca^{++}	5	1
Mg^{++}	2	40
Total (+)	**156**	**196**
Anions (mmol/L)		
Cl^-	105	3
HCO_3^-	28	10
Protein	17	45
$HPO_4^=$	6	138
Total (-)	**156**	**196**

- Special mechanisms for transporting ions through the cell membranes maintain the ion concentration differences between the extracellular and intracellular fluids.

The extracellular fluid contains a large amount of sodium and chloride ions but only a small amount of potassium. The opposite is true of the intracellular fluid. However, the concentrations of phosphates and proteins in the intracellular fluid are considerably greater than those in the extracellular fluid.

These differences are extremely important to the life of the cell.

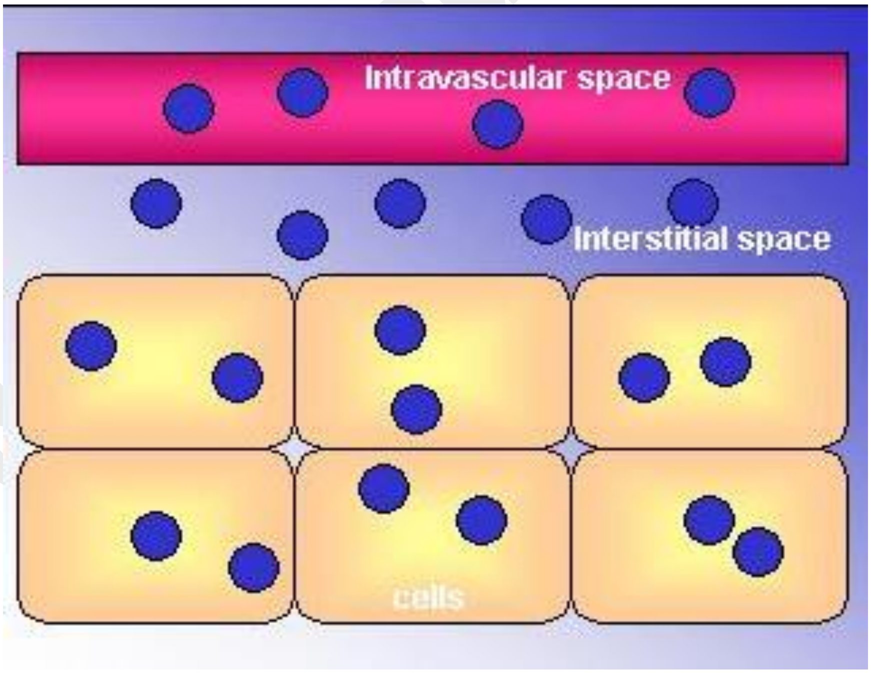
Homeostasis

Definition:

is the ability of the body to maintain constant conditions in its internal environment in spite of changes in the surroundings.

The internal environment:

- def: All cells are surrounded by the same environment (the extracellular fluid) which contains the ions and nutrients needed by the cells to maintain cell life.
- There is continuous exchange between the intravascular and interstitial fluid to keep the internal environment constant.
- Extracellular fluid is in constant motion throughout the body. Fluid moves from blood to tissues and opposite by diffusion through capillary walls.



N.B. Cells are capable of living and performing their special functions as long as the proper concentrations of oxygen, glucose, different ions, amino acids, fatty substances, and other constituents are available in this internal environment.

The various ions, nutrients, waste products, and other constituents of the extracellular fluid are normally regulated within a range of values, rather than at fixed values.

: Important constituents and physical characteristics of extracellular fluid:

	Normal Value	Normal Range	Approximate Short-Term Nonlethal Limit	Unit
Oxygen (venous)	40	35-45	10-1000	mm Hg
Carbon dioxide (venous)	45	35-45	5-80	mm Hg
Sodium ion	142	138-146	115-175	mmol/L
Potassium ion	4.2	3.8-5.0	1.5-9.0	mmol/L
Calcium ion	1.2	1.0-1.4	0.5-2.0	mmol/L
Chloride ion	106	103-112	70-130	mmol/L
Bicarbonate ion	24	24-32	8-45	mmol/L
Glucose	90	75-95	20-1500	mg/dl
Body temperature	98.4 (37.0)	98-98.8 (36.6 - 37.1)	65-110 (18.3-43.3)	°F (°C)
Acid-base	7.4	7.3-7.5	6.9-8.0	pH

Normal ranges:

- Note the narrowness of the normal range for each one.
- Values outside these ranges are often caused by illness, disease, injury, or major environmental challenges, and some abnormalities may cause death:
  1. An increase in the body temperature of only 11°F (7°C) above normal can lead to a vicious cycle of increasing cellular metabolism that destroys the cells.
  2. A normal pH value is 7.4. Lethal values only about 0.5 on either side of normal.

Homeostatic Control Mechanism

Definition:

The homeostatic mechanisms are the regulatory mechanisms that tend to correct any deviation from normal in response to changes in the external or internal environment.

N.B.

- Each cell benefits from homeostasis, and in turn, each cell contributes its share toward the maintenance of constant internal environment i.e. communication within the body is essential for homeostasis.
- If one or more systems of the body lose this function, all the cells of the body suffer.
- Moderate dysfunction leads to sickness whereas extreme dysfunction leads to death.

The control systems of the body:

- The body depends mainly on two major control systems for the regulation of all its functions:

a- The nervous system;

- responsible to the functions that need *rapidity of execution*:

    e.g. applying a hot object to the hand causes immediate flexion of the arm to withdraw it from such harmful hot object.

- The nervous system is composed of three major parts:

a. the sensory input portion: detect the state of the body or the state of the surroundings.
b. the central nervous system (or integrative portion), composed of:

    i- Brain: store information, generate thoughts, and determine reactions that the body performs in response to the sensations.

    ii- Spinal cord
c. the motor output portion: to carry out one's desires.

- An important segment of the nervous system is called autonomic system. It controls subconsciously many functions of the internal organs.

b- The endocrinal system

- composed of many endocrine glands and several organs and tissues that secrete hormones into the blood stream.

- Hormones are transported through ECF to different body organs to help regulate cellular function.

- Endocrine system is concerned with the functions that do *not need rapidity of execution*

- e.g.

  a. thyroid hormone increases rate of chemical reactions in all cells
  b. insulin controls glucose metabolism

N.B. Many interrelationships exist between the endocrine and nervous system.

- Characteristics of Control Systems:

All homeostatic control mechanisms have at least three main components:

stimulus → receptor (first component) → afferent pathway (nerve) → center (second component) → efferent pathway (nerve) → effector (third component) → response (feedback, which may be positive or negative)

I- The first component, the receptor,

- is a sensor that monitors the environment and responds to the change (stimulus), by sending information (input) to the second component along the afferent pathway.

II- The second component, the control centre,

The center analyzes the input it receives from the receptor and then determines the appropriate response.

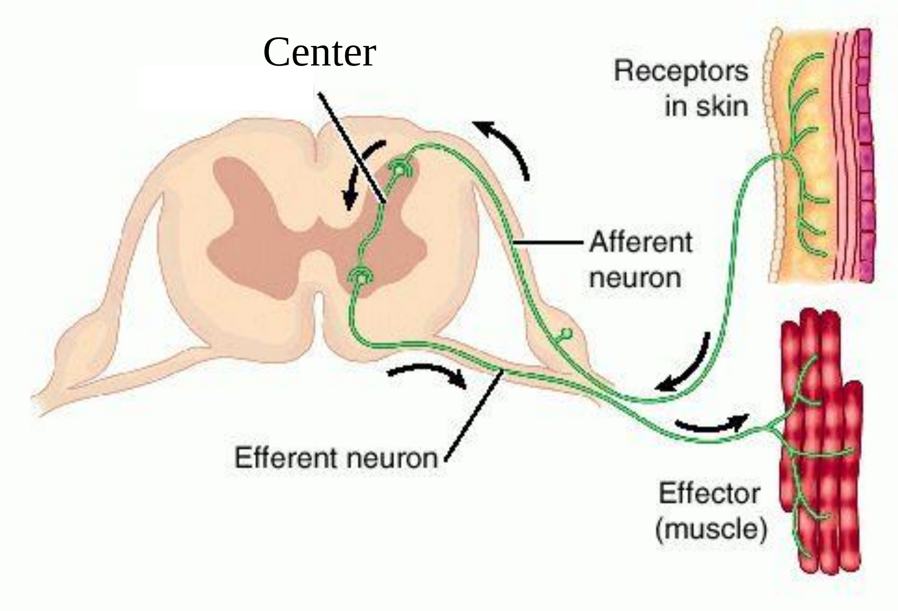
III- The third component, the effector,

- Information flows from the centre to the effector along the efferent pathway to give response.

- The result of the response is feedback. Types of feedback:

  a- depressing stimulus (negative feedback) so that the whole control mechanism is shut off

  b- enhancing stimulus (positive feedback) so that the reaction continues at an even faster rate.



Negative Feedback Mechanisms:

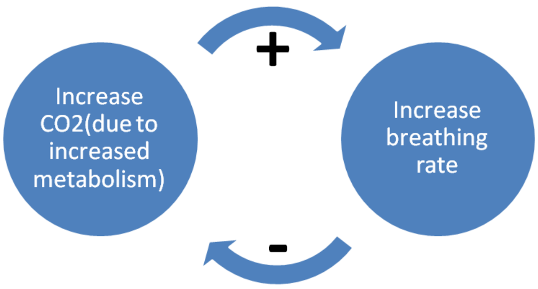
- def: In these systems, the output (response) is opposite to the original stimulus. The output shuts off the original stimulus or reduces its intensity.

- Importance: have the goal of preventing sudden severe changes within the body.

- e.g.CO2 feedback mechanism:

If the concentration of carbon dioxide in the extracellular fluid increases (due to increase activities of the cells) → it will stimulate the rate of breathing, and the excess of carbon dioxide is washed out → This, in turn, decreases the extracellular fluid carbon dioxide concentration.

- N.B. Most homeostatic control mechanisms are negative feedback mechanisms.

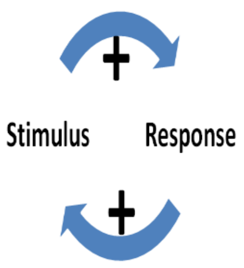


Positive Feedback Mechanisms:

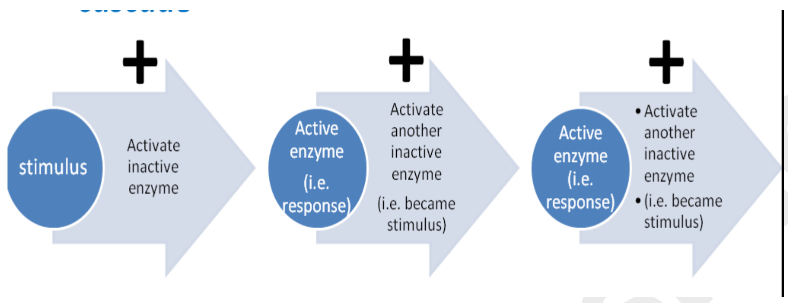
- Definition:

- In positive feedback mechanisms, the response enhances the original stimulus.

- two types: "vicious cycle" & "cascades".



• vicious circle



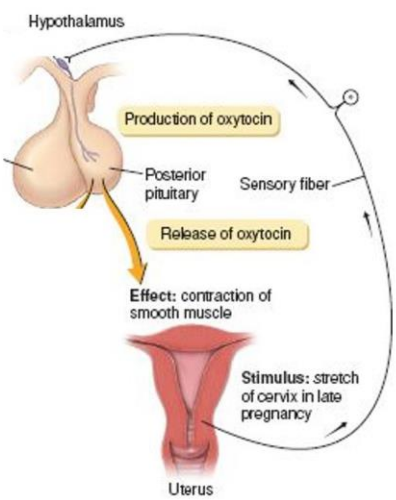
• cascade

- E.g.

a- Vicious circle positive feedback: Childbirth

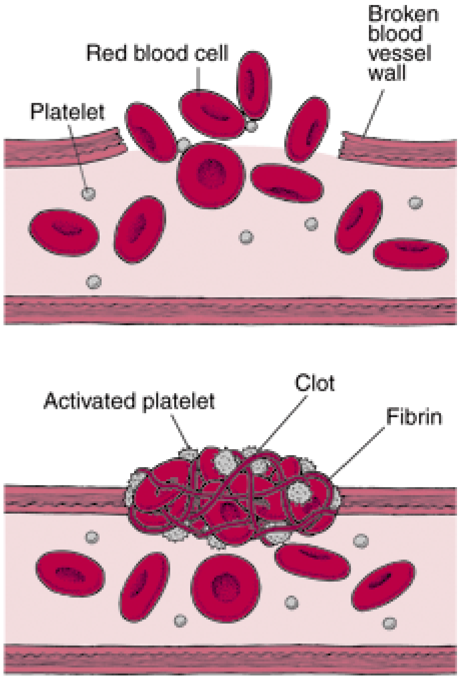
When uterine contractions become strong enough to push the baby's head through the cervix → stretched cervix → sends signals to the pituitary gland → secrete the oxytocin hormone → circulates in the blood → reach the uterine muscles → causing even more powerful contractions.

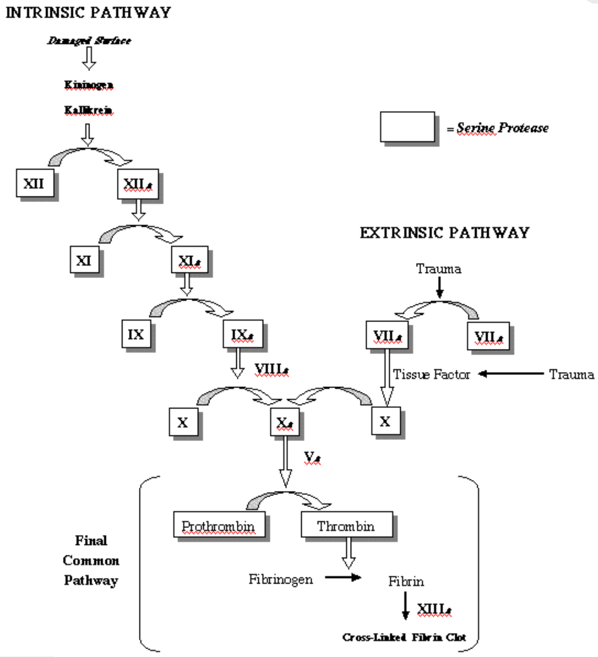
So uterine contractions stretch cervix, and cervical stretch causes stronger contractions. When this process becomes powerful enough, baby will born.



b- Cascade positive feedback: Blood clotting:

- Mechanism: Multiple enzymes (clotting factors) are activated within clot itself → these activated enzymes will act on other inactive enzymes → then activate them, and so on → more blood clotting until bleeding stopped.

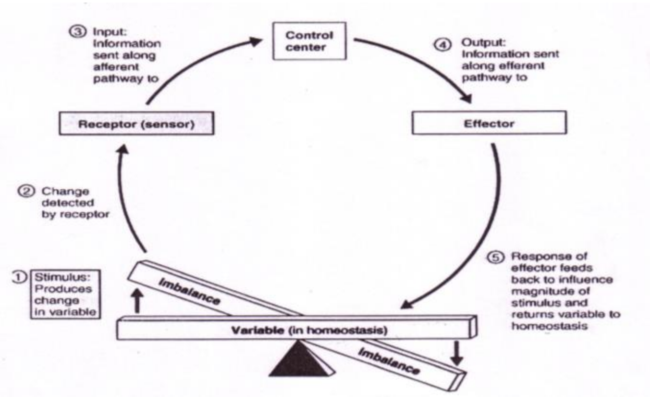




N.B. In contrast to negative feedback controls, which maintain physiological function within narrow ranges, positive feedback mechanisms control infrequent events that do not require continuous adjustments.

Homeostatic Imbalance:

Homeostasis is so important that most of the diseases can be regarded as a result of its disturbance, a condition called homeostatic imbalance.



Integration of body functions

- There is a functional relationship between the various systems of the body.

- A good example for this integration is during **muscular exercise**, many systems act to increase the oxygen needs of the active muscles and to remove the waste products as CO_2 and the heat liberated during exercise, to enable the muscles to act for a long time without fatigue, as follow:

1- Cardiovascular changes:

The functions of the heart are increased. The blood that carries the oxygen and nutrients to the active muscles and removes the waste product from it is also increased

2- Respiratory changes:

There is increase rate of respiration. This will lead to increase oxygen delivered to the body and wash excess CO2.

3- Temperature regulation:

During muscular exercise the heat production is increased, which stimulates the heat losses mechanisms.

4- Muscle coordination:

During muscular exercise the adjustment and smoothness of movements are obtained via certain parts in the brain.

Part 2:
Autonomic nervous system

THE NERVOUS SYSTEM - Introduction

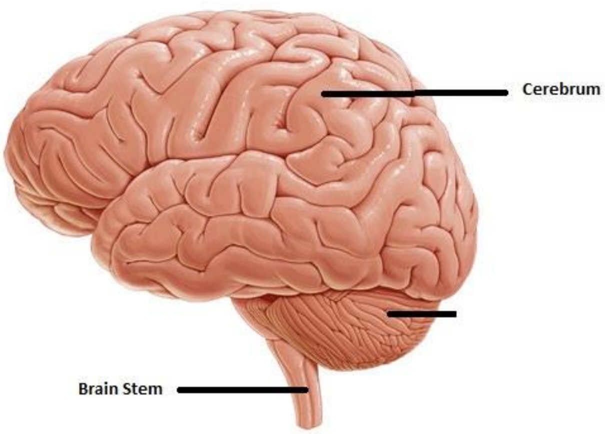
- In the human body, there are two main control systems: the endocrine system and the nervous system, both coordinate the functions of various systems in order to maintain homeostasis.
- The endocrine system: exerts a relatively slow control, through secreting hormones, which regulate growth and metabolic processes within the cells.
- The nervous system: exerts rapid control by serving three broad functions: sensory, integrative and motor.
  - First, it senses changes within the body and in the outside environment; this is its sensory function.
  - Second, it interprets the changes; this is its integrative function.
  - Third, it responds to the interpretation by initiating action e.g.muscular contractions or glandular secretions, this is its motor function.

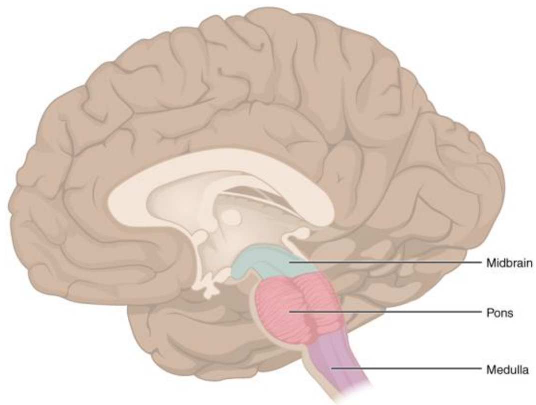
THE NERVOUS SYSTEM - Classification

●*Anatomical classification of the nervous system:*

I-Central nervous system (CNS):

a- brain



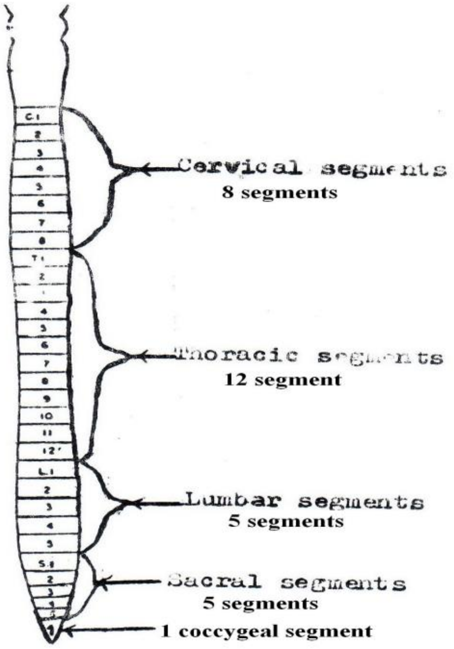


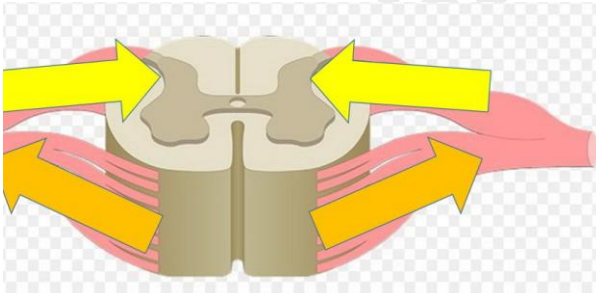
b- spinal cord

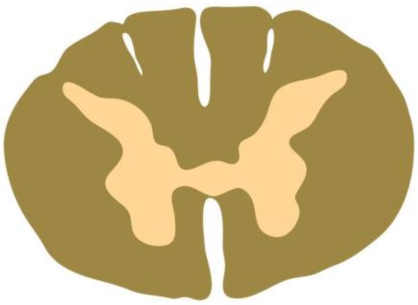
- The spinal cord is divided into 31 segments with a pair of spinal nerves arising from each segment. Each spinal nerve arises from the spinal cord by 2 roots:

a) <u>Dorsal (afferent sensory) root:</u>
Fibers of which originate in the peripheray from sensory receptors and terminate in the dorsal horn. Cell bodies of these afferent fibers are located outside the spinal cord in clusters called dorsal root ganglia.

b) <u>Ventral (efferent motor) root:</u>
Fibers of which originate in the ventral horn and travel to the periphery where they form synapses with skeletal muscles.
The connections between neurons inside the CNS is called synapse







- In cross section, the spinal cord shows a central butter fly-shaped area of grey matter with 3 projections called horns: dorsal, lateral and ventral.
- The grey matter is surrounded by white matter, which consists of groups of myelinated axons.
- These groups of fibers run longitudinally through the cord, some descending to relay information from the brain to the spinal cord, others ascending to transmit information to the cortex.

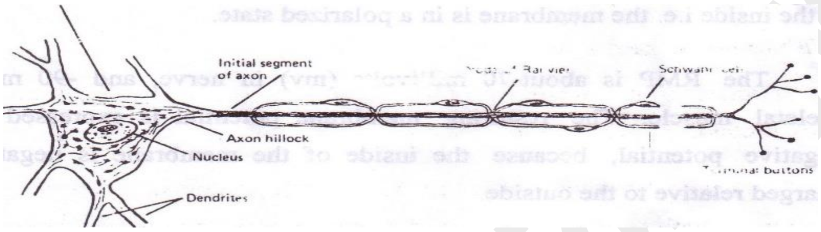
II-Peripheral nervous system: (peripheral nerves arise from CNS)

a-Cranial nerves: 12 pairs arising mostly from the brain stem.

b-Spinal nerves: 31 pairs arising from the spinal cord, one pair for each segment.

N.B. Unit structure of PNS:

Is the nerve cell or neuron.



•*physiological (functional) classification of PNS:*

a) Somatic nervous system

control body voluntary movements of skeletal muscles

b) Autonomic nervous system

control involuntary of viscera & glands

•*Reflex action (the unit function of the nervous system):*

- Definition:

Is an unavoidable beneficial inborn response brought about by a stimulus (a sudden change of the external or internal environment)

- Types of reflex action:

1. Somatic reflex action: if the responding tissue is skeletal muscle.

- Examples:

1- painful stimulus to the hand→ rapid flexion of the arm.

2- Foreign object (an insect) touches the eye-lashes→ the lids are quickly closed.

2. Autonomic (visceral) reflex action: internal organs or viscus.

- Examples:

1-Stretching of the urinary bladder with large amount of urine → contraction of the bladder as well as relaxation of the urinary sphincter → micturition.

2- Gastrointestinal tract movement

• Reflex arc (the pathway of reflex action):

	Somatic reflex arc	autonomic reflex arc
1-receptor (very excitable & sensitive structure stimulated by slight changes in the external or internal environment)	skin	viscus (organ)
2-afferent neuron (sensory) (carries impulse from receptors to central nervous system i.e. sensory)	The same	The same
3-center (one or more neuro-neural junction or synapse -interneurons-, present inside the CNS)	the anterior horn cell (A.H.C) of the grey matter	the lateral horn cell (L.H.C) of the grey matter (it is the start of preganglionic neuron)
4-efferent neuron (motor) (carries impulses from the CNS to the effector organ i.e. motor)	Somatic motor neuron Thick myelinated type Aα→ fast conduction velocity (100m/sec)	Two neurons, with a synaptic connection (ganglia) a- preganglionic neuron → preganglionic fibers (thin myelinated type B, with conduction 10m/sec) b- postganglionic neuron → postganglionic fibers (unmyelinated C fiber, with conduction 1m/sec)
5-effector organ	skeletal muscle	plain, cardiac muscles and gland

Synapse:

It is the site of contact between 2 neurons i.e. the site of contact between the axon terminals of one neuron and the cell body or dendrites of another neuron. There is no cytoplasmic continuity between neurons.

THE AUTONOMIC NERVOUS SYSTEM

•*Anatomical classification (divisions) of ANS:*

Preganglionic neuron of the ANS starts in:

1. Cranial autonomic outflow:

- From the midbrain, medulla oblongata, pons.
- cranial nerves III, VII, IX & X.

2. Thoracolumbar autonomic outflow:

- From T1 to L2.

3. The sacral autonomic outflow:

- S 2,3,4.

•*Physiological (Functional) classification of ANS:*

a) The sympathetic: thoracolumbar outflow

b) The parasympathetic: craniosacral outflow (cranial & sacral outflows have complementary physiological action.

AUTONOMIC GANGLIA

- ***Definition:*** aggregation of cell bodies of neurons outside the CNS.

- ***Classification:***

	Lateral (paravertebral) ganglia	**Collateral (prevertebral) ganglia** (Coleiac, superior and inferior mesenteric ganglia)	**Terminal (peripheral) ganglia**
site	- on each side of the vertebral column → sympathetic chains (2 in number) i.e. located near the spinal cord - contains one ganglion for each segmental nerve, except in the cervical region → ganglia fused to form three ganglia (the superior, middle and inferior cervical ganglia).	between the sympathetic chain and the organ of supply	Near or embedded in the innervated organs
Relay of	Preganglionic sympathetic fibers of head, neck, thorax.	preganglionic sympathetic fibers of abdominal and pelvic viscera	Preganglionic parasympathetic fibers
Preganglionic fibers	short as the ganglia is near from spinal cord	in-between	long as the ganglia is away from the spinal cord
Post ganglionic fibers	long as the ganglia is far from organ	in-between	short as the ganglia is near or sometimes on the organ

•functions of the autonomic ganglia:

1. act as distributing centers:

a- sympathetic system

preganglionic fibers synapse → activate many postganglionic neurons → generalized sympathetic effects over wide areas of the body (widespread distribution of impulse)

b- Parasympathetic system

Preganglionic fibers synapse → activate only few postganglionic neurons → localized discrete parasympathetic activities

2. Site of relay (synapse):

Autonomic ganglia are cell stations for relay of preganglionic fibres coming from CNS.

3- Release of Chemical transmitter:

- Acetylcholine is the mediator at all preganglionic endings (sympathetic and parasympathetic).
- It is responsible for transmission of nerve impulse from preganglionic to postganglionic neurons (synaptic transmission).

N.B. Each preganglionic fiber relays once only, though it may pass through several ganglia

SYMPATHETIC NERVOUS SYSTEM

	Center (LHC)	Pregang fibers	Ganglia (symp chain)	Post ganglionc fibers	Effector organs / viscera (function of sympathetic NS)	
Head & neck				Pass along the branches of the carotid artery	**I – Eye:**	Motor to all dilatation of pupil (mydriasis) retraction of eye lids → wide palpebral fissure protrusion of eye ball (exophthalmos)
					2- lacrimal gland *Blood vessels*	vasoconstriction → atrophic or no secretions
					II- Salivary gland: *1- Trophic secretory fibers*	Secretory → saliva (viscid, small in volume, rich in organic matter)
					2-bld vessels	vasoconstriction
					IV- Cerebral vessels :	Under normal physiological conditions sympathetic has little influence on cerebral autoregulation. Its role is more evident under pathological conditions as hypertension.
Thorax					**I- Heart:** *1-cardiac muscle properties* →	Excitation → increase of heart rate and force of contraction
					2- coronaries →	Vasodilator → increase the blood supply and O2 to the cardiac muscle
					II- Lung: *1-plain (smooth) muscle of the bronchi and bronchioles* →	Inhibitory → broncho-dilatation.
					2- the pulmonary blood →	Slight vasoconstriction

	Center (LHC)	Preganglionic fibers	Ganglia (collateral gang)	Postganglionic fibers	Effector organs / viscera (function of sympathetic NS)	
Abdomen (Greater splanchnic nerve)				Except adrenal medulla	1- Visceral Bld vessels:	Vasoconstriction
					2-smooth ms of wall & sphincters of stomach, small intestine & proximal ½ of colon	inhibitory of smooth ms and motor to sphincters → food retention.
					3-smooth ms & sphincters of Oddi o of gall bladder:	inhibitory of smooth ms and motor to sphincters → bile retention
					4-Smooth ms of splenic capsule:	Motor to smooth muscle → contraction → blood rich in RBCs & O2
					5-Liver:	Glycogenolytic: conversion of glycogen into glucose → ↑ bld glucose level
					6-Adrenal medulla:	Secretion of adrenaline and noradrenalin
Pelvis (Lesser splanchnic nerve)				Lesser splanchnic runs with blood supply of pelvic organs	1- Visceral Bld vessels:	Vasoconstriction
					2-smooth ms &sphincters of distal half of the colon and rectum:	inhibitory of smooth ms and motor to internal anal sphincters → feaces retention
					3-smooth ms (detrusor ms) &sphincters of urinary bladder:	inhibitory of smooth ms and motor to internal urethral sphincters → urine reten
					4-smooth muscle of male sex organs (epididymis, ejaculatory ducts, seminal vesicles &prostate)	Motor → ejaculation of semen (in males).
					5-smooth muscle of uterus:	contraction or relaxation depending on the stage of menstrual cycle, the ovarian hormonal level, pregnancy and other factors.

	Center (LHC)	Preg fibers	Ganglia	Post ganglionic fibers	Effector organs / viscera (function of sympathetic NS)
H&N, thorax, abdomen, pelvis, upper limb and upper limb parities					**1- cutaneous blood vessels:** vasoconstriction **2-Sweat glands:** secretion of sweat **3-erector pilae muscle:** motor causing erection of hair in animals **4-skeletal muscle:** a- vasodilatation of *bld vessels* → increase blood flow and O_2 supply b- increase muscle *glycogenolysis*

•Functions of the sympathetic system

I-Sympathetic tone:

-definition: It is the basal rate of activity of the sympathetic system i.e. under basal conditions the sympathetic system is continuously active and discharge impulses to the innervated organs.

- Main function: Tonic sympathetic charge to arterioles maintains arteriolar wall halfway → arterial pressure → good distribution of blood to tissues.

II-Role of sympathetic nervous system in emergencies i.e. fight and flight i.e. stress:

- Emergency (physical or mental, e.g. hypothalamus activation by fear or severe pain) **→ mass discharge of sympathetic** (wide spread, large portions of sympathetic discharge throughout the body) **→ alarm or stress response** (wide spread reaction and extra-activation throughout the body increases the ability of the body to perform vigorous muscle activity).

- Sympathetic stimulation during the stress response produces the following effects:

1- eye: dilatation of pupil.

2- CNS:

a- increase mental activity

b-reinforces alert, aroused state by action of catecholamine on reticular formation.

3- heart:

a- cardiac muscle properties: Excitation → increase heart rate and contraction

b- Coronaries: Vasodilator → increase blood supply and O_2 to the cardiac muscle

4- Vascular system: raise blood pressure

N.B. 3,4 → provide better perfusion of the vital organs and muscles

5- lung: plain muscle of the bronchi and bronchioles → Inhibitory → broncho-dilatation → ensure better lung ventilation and more O_2 supply to the blood

6- Spleen: Motor to splenic capsule → contraction & squeeze → blood rich in RBCs → increase blood volume and O_2 supply to organs.

7- liver: Glycogenolytic: conversion of glycogen into glucose → increase glucose in blood → more energy

8- increase free fatty acids → more energy

9- Adrenal medulla: Secretion of adrenaline and noradrenalin → potentiates sympathetic stimulation.

10- skin: constriction of bld vessels (limits bleeding/hemorrhage if wounded)

11- Sweat gland: increase sweat secretion → evaporation → heat loss from body

12- muscles: increase blood supply, oxygen supply and glucose delivery to muscles.

13- The blood is shifted from the peripheral and unimportant organs as skin and spleen to the more important organs as heart, CNS and skeletal muscles

14- Increase **cellular metabolism** throughout the body.

III-Sympathetic activation may occur in isolated portions of the system

e.g. heat regulation:

The sympathetic control sweating and blood flow in the skin without affecting other organs.

To Conclude

<u>- The cell bodies</u> of the preganglionic neurons of sympathetic nervous system are found in the inter-mediolateral gray matter of the spinal segments T1 to L2

<u>- Preganglionic fibers on entering the ganglionic chain, a preganglionic fiber may have one of three courses</u>

<u>1- Relay in sympathetic chain:</u>

- Other preganglionic fibers pass up or down the chain to establish synaptic connections with postganglionic neurons in ganglia belonging to more superior or inferior segments

<u>2- The preganglionic fibres may pass without interruption</u> through the chain into the splanchinc nerves to reach the collateral ganglia (Coleiac, superior and inferior mesenteric ganglia) then to abdomen and pelvis.

N.B. The postganglionic fibres arising from these ganglia run with the blood vessels to supply the smooth muscle of the abdominal and pelvic viscera, to the glands of the gut, and to the blood vessels of the abdominal viscera.

N.B. the term splanchinic is usually used to describe organs in the abdominal cavity (visceral organs)

<u>3. Some preganglionic fibres</u> of the splanchnic nerve <u>directly innervate</u> secretory cells of the adrenal medulla.

The adrenal medulla is the only sympathetic effector organ known to be directly innervated by preganglionic fibres.

PARASYMPATHETIC NERVOUS SYSTEM

Cranial outflow

(Supply head, thorax, and abdomen)

	Center (cranial N.nuclei)	Preganglionic fibers	Ganglia (terminal ganglia)	Post ganglionic fibers	Effector organs / viscera (function of parasympathetic NS)	
Oculomotor (3rd cranial)					**Eye:** Muscles:	Motor to all constriction of pupil (miosis) accommodation for near vision (increase power of lens)
Facial (7th cranial)					**1-lacrimal gland**	1- secretory fibers stimulation 2- vasodilatation of bld vessels → tears
					2-Nasopharyngeal glands & soft palate	1- secretory fibers stimulation 2- vasodilatation of bld vessels.
					3-sublingual & submaxillary glands	1- secretory fibers stimulation 2- vasodilatation of bld Vessels → saliva (copious watery, rich in electrolytes)
					4- Tongue	Vasodilatation of bld
Glossopharyngeal (9th cranial)					**1-parotid gland**	1- secretory fibers stimulation 2- vasodilatation of bld Vessels → saliva (copious watery, rich in electrolytes)
					2-Tongue	Vasodilatation of bld vessels of post 1/3

	Center (cranialN. nuclei)	Preganglionic fibers	Ganglia (terminal ganglia)	Post ganglionic fibers	Effector organs / viscera (function of parasympathetic NS)	
Vagus (10th cranial)					**1-Heart**	
					a-heart properties	inhibition →↓contractility of atria only, rythmicity, excitability and conductivity
					b- coronaries	Vasoconstriction → reduction of the blood supply and O2 consumption of the cardiac muscle
					2-Lung	
					a-plain (smooth) muscle of the bronchi and bronchioles	Motor → broncho-constriction.
					c-bronchial mucous membrane	Secretory → mucus
					3-GIT	
					a- smooth ms and sphincters of oesophagus, stomach, small intestine, proximal half of large intestine, GB(sphincter of Oddi)	Motor to muscle and inhibitory to sphincter
					b-stomach cells	secretion → gastric juice, rich in HCL & enzymes
					c-pancreatic cells	secretion → a- pancreatic juice rich in enzymes c-beta cells of islets of Langerhans → insulin

Sacral outflow

(Supply pelvic viscera and external genitalia)

	Center (LHC)	Preganglion fibers	Ganglia (terminal ganglia)	Post ganglionc fibers	Effector organs / viscera (function of parasympathetic NS)	
Sacral outflow (pelvic nerve)					1-wall & sphincter of distal half of colon and rectum	Motor to wall and inhibitory to internal anal sphincter → defecation
					2-wall & sphincter of urinary bladder	Motor to wall and inhibitory to internal urethral sphincter → micturition
					3- seminal vesicle & prostate	Secretory → semen
					4-blood vessel of erectile tissue in penis in males, vulva & clitoris in females	vasodilatation → erection (nervous erigens)

N.B. Erectile tissue of penis in males, vulva & clitoris in females are the only vascular system in pelvis that is supplied by parasympathetic.

N.B. external urethral and anal sphincters are skeletal muscles and are supplied by somatic spinal nerve called pudendal nerve

•Functions of parasympathetic system

I-Anabolic nervous system

1- It favors digestion and absorption of food by:

a- ↑ activity of intestinal musculature

b- ↑ gastric acid secretion

c- Relaxing pyloric sphincter.

i.e. it is concerned with the vegetative aspects of day-to-day living

2- Prepares body for recovery and repair:

The activity of parasympathetic is continues and even increases during rest and sleep

N.B. sympathetic nervous system is a catabolic system

II-localized action of parasympathetic system

- Most functions of parasympathetic system are specific and localized:

a- decrease heart rate without affecting other systems

b- Secretion may be mainly from mouth glands, in other instances secretion is mainly from stomach cells

c- Rectal emptying reflex takes place, without affecting other parts of bowel to a major extent

Para-sympathetic Tone:

Definition:

- It is continuous mild parasympathetic impulses (activity) even during rest.

Target Tissues:

• Sino-Atrial Node (SAN, = Vagal tone on the heart):

- Leading to decrease in the intrinsic high rhythm of the heart from 120 to 70-90 during rest to preserve energy of the heart.
- So,
  - ↑ Heart rate → produced by ↓ vagal tone.
  - ↓ Heart rate → produced by ↑ vagal tone.

▲ **Paradoxical fear :** when there is no escape route or no way to win (failure of sympathetic).

- Causes massive activation of parasympathetic division.
- loss of control over urination and defecation .

Organs with Dual Innervation

Most visceral organs receive dual innervation—they are innervated by both sympathetic and parasympathetic fibers. In this condition, the effects o the two divisions of the autonomic system may be antagonistic, complementary, or cooperative.

Antagonistic Effects:

The effects of sympathetic and parasympathetic innervation on :

- The pacemaker region of the heart ,where stimulation of sympathetic fibers increases the heart rate, whereas the parasympathetic fibers stimulation decreases the heart rate.
- The digestive tract, where sympathetic nerves inhibit intestinal movements and secretions, while the parasympathetic nerves do the reverse.

Synergistic effects

- The effects are complementary when sympathetic and parasympathetic stimulation produce similar effects as on salivary secretion.
- The secretion of watery saliva is stimulated by parasympathetic nerves, whereas sympathetic nerves stimulate the constriction of blood vessels throughout the digestive tract. The resultant decrease in blood flow to the salivary glands causes the production of a thicker, more viscous saliva.

Complementary effects

- The effects are cooperative when sympathetic and parasympathetic stimulation produce different effects that work together to promote a single action as on the reproductive system.
- Erection of the penis, for example, is due to vasodilation resulting from parasympathetic nerve stimulation, whereas ejaculation is due to stimulation of sympathetic nerves.

Organs Without Dual Innervation:

Although most organs receive dual innervation, **some receive only sympathetic innervation. These include:**

- Sweat glands.
- Piloerector muscle.
- Blood vessels all over the body except the penis.
- Dilator pupillae muscle.
- Blood vessels of the skeletal muscles.
- Adrenal medulla
- Capsule of the spleen

In these cases, regulation is achieved by increases or decreases in the tone (firing rate) of the sympathetic fibers. For example, constriction of cutaneous blood vessels is produced by increased sympathetic activity that stimulates alpha- adrenergic receptors, and vasodilation results from decreased sympathetic nerve stimulation.

Organs that receive *only parasympathetic supply:*

- The lacrimal gland,
- Ciliary muscle (for accommodation for near vision), and
- The nasopharyngeal gland.

Sympathetic nervous system versus parasmpathetic nervous system compariso chart:		
	sympathetic nervous system	parasympathetic nervous system
Origin	Thoracolumbar outflow (T1-L2)	Craniosacral outflow III, VII, IX, X S2,3,4
Preganglionic fibers	Short, from spinal cord to sympathetic chain. -Synaps & activates many postganglionic fibers.	Long, from brain or spinal co to ganglia in effector organ. -Synaps & activates few postganglionic fibers.
Ganglia	-*Lateral* (paravertebral)	*Terminal* ganglia
	-*Collateral* (prevertebral)	
Post- ganglionic fibers	Long, from sympathetic chain to the effector organ	Short, because ganglia are embedded in effector organ
Functionally	-- catabolic -- prepare the body for vigorous muscle activity (fight & flight) --Action is wide spread	-- Anabolic -- Concerned with vegetative aspects of day to day living -- action is localized and discrite
Chemical transmitter	Mainly noradrenaline	Acetylcholine

CHEMICAL TRANSMISSION IN THE AUTONOMIC NERVOUS SYSTEM

• Definition:

Transmission of nerve impulse by releasing chemical substance at:

1- Autonomic ganglia between preganglionic and postganglionic neurons

2- between postganglionic neurons and the autonomic effectors

N.B. somatic neuromuscular transmission is also chemically transmitted by acetylcholine that depolarizes the end plate.

• principle autonomic chemical transmitters:

1- Acetylcholine

2- Norepinephrine (noradrenaline)

• The autonomic fibers are classified into:

1- Cholinergic: secreting acetylcholine at their terminals.

2- Adrenergic: secreting noradrenaline at their terminals

ACETYLCHOLINE & CHOLINERGIC FIBERS

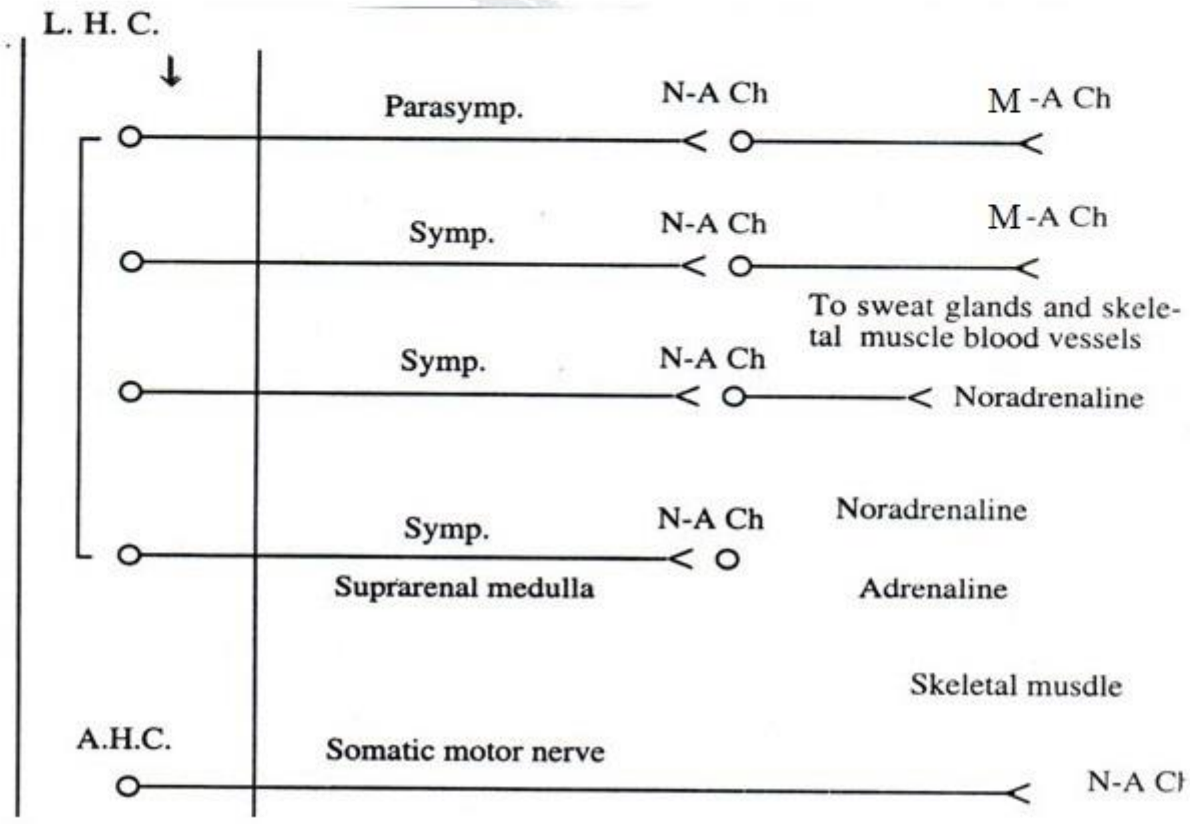
•site of synthesis, storage, release & action of Ach (i.e. site of cholinergic nerve fibers)

a-Autonomic NS

At Preganglionic fibers of	At Postganglionic fibers of
1-all sympathetic and parasympathetic preganglionic neurons i.e. all autonomic ganglia 2- adrenal medulla	1- all parasympathetic postganglionic neurons 2- sympathetic postganglionic nerve endings of: a- sweat glands b- Blood vessels in the skeletal muscles.

b- Somatic system

Somatic motor nerve fibers to the skeletal muscle (myoneural junction).



• *Acetylcholine (cholinergic) receptors:*

I-Muscarinic receptors:

- activated by muscarine and acetyl choline

- effect of their action: can be either excitatory or inhibitory

- They are present on:

1- All effector cells supplied by parasympathetic postganglionic neurons

2- On the surface of:

a- sweat glands

b- Blood vessels in the skeletal muscles.

Both are supplied by sympathetic postganglionic nerve endings.

II- Nicotinic receptors:

- activated by small doses of nicotine and acetyl choline.

- effect of their action: always excitatory

- They are present on the surface of:

1- Autonomic nerves:

a- all sympathetic and parasympathetic postganglionic neurons i.e. all autonomic ganglia

b- Adrenal medulla

2- Somatic nerves: on the membranes of skeletal muscle fibers: supplied by somatic motor nerve (myoneural junction).

N.B. The reason for these names is that muscarine, a drug that activates only the muscarinic receptors but will not activate the nicotinic receptors; whereas nicotine in small dose will activate only nicotinic receptors. Acetylcholine activates both of them.

• Action of acetylcholine:

1-actions produced by stimulation of the muscarinic receptors:

Because both acetylcholine and muscarine have similar effects on muscarinic receptors, so these actions are described as muscarine like actions of acetylcholine, e.g. stimulation of all postganglionic parasympathetic endings and sympathetic postganglionic endings to sweat glands and skeletal blood vessels.

2- Actions produced by stimulation of the nicotinic receptors:

Because both acetylcholine and nicotine have similar effects on the nicotinic receptors, so these actions are described as nicotine-like actions of acetylcholine, e.g.

- Stimulation of the autonomic ganglia.
- Secretion of adrenaline and noradrenaline at adrenal medulla.
- Contraction of skeletal muscles due to stimulation at the motor end plates.

SYMPATHETIC TRANSMISSION
Catecholamines: Noradrenaline (Norepinephrine), Adrenalin (Epinephrine)

•*site of synthesis, storage and release (i.e. site of adrenergic nerve fibers)*

All sympathetic postganglionic nerve endings except:

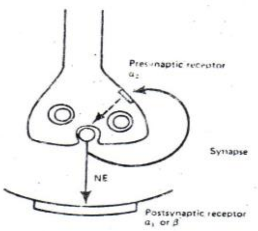
a- sweat glands

b- Blood vessels in the skeletal muscles.

•*Adrenergic receptors:*

Adrenergic receptors

- **Alpha adrenergic receptors**
  - Responding to: noradrenaline and adrenaline but higher affinity for noradrenaline
  - alpha-1
    - on effectors
      - Mainly excitatory: V.C., spleen contraction …etc
      - Except on intestinal muscles → relaxation
  - alpha-2
    - on presynaptic nerve terminal
      - Prevent excessive or prolonged neurotransmitter (NA) release
- **Beta-adrenergic receptors**
  - Responding to: adrenaline and slight response to nor adrenaline
  - Beta-l receptors:
    - their stimulation produces excitatory effects
      - chiefly in the heart, increase cardiac rate and strenght of contraction.
  - Beta2 receptors:
    - Their Stimulation produce inhibitory effects.
      - smooth muscle of bronchioles, gastrointestinal tract, urinary bladder



•Action of Noradrenaline and adrenaline:

- Noradrenlaine:

1- Excite mainly alpha-receptors, but excites the beta-receptors to slight extent as well.

2- Thus noradrenaline released by the sympathetic adrenergic nerve endings is responsible for various sympathetic effects.

3- Noradrenaline secreted by the adrenal medulla has the same effects on the different organs, except that its action lasts for longer time because it is slowly removed from the blood.

- Adrenaline:

- excites both types of receptors approximately equally.

- N.B. Therefore, the relative effects of noradrenaline and adrenaline on different effector organs are determined by the types of receptors in the organs e.g. if they are all beta-receptors, adrenaline will be the more effective excitant.

•Differences between Noradrenaline and adrenaline:

	Adrenaline	**Noradrenaline**
Receptors	Excite both types of receptors approximately equally.	-Excite mainly alpha-receptors. -Excite the beta receptors to slight extent.
Blood vessels	Weak vasoconstriction	Strong Vasoconstriction
Cardiac stimulation	More than noradrenaline	Less than adrenaline
Smooth muscles of bronchioles & intestine	More inhibitory effect (so it is used in bronchial asthma)	Inhibitory effect
Metabolic effect	More than noradrenaline	Less than adrenaline

-value and role of the adrenal medulla to the function of the sympathetic NS:

- Organs are stimulated in two different ways simultaneously:

1- Directly by sympathetic nerves.

2- Indirectly by the medullary hormones.

These two means of stimulation support each other and can usually substitute each other.

- total loss of the two adrenal medulla has a little effect on sympathetic nervous system because the direct pathways still can perform all the necessary duties.

CONTROL OF AUTONOMIC FUNCTIONS

I- Spinal cord:

Simple autonomic reflexes such as (micturation and defection)

Simple autonomic reflexes such as (micturition and defection) are integrated in the spinal cord, e.g.: "Stretching of the full urinary bladder sends impulses to the sacral cord, and this in turn causes contraction of the bladder as well as relaxation of the urinary sphincter, thereby promoting micturition."

II- Brain stem:

Many areas in the reticular substance of the medulla, pons and midbrain, as well as many special nuclei, control different autonomic functions; such as arterial blood pressure, respiration ,heart rate, glandular secretion in the gastrointestinal tract and many others.

III- Higher control (i.e. above brain stem):

The autonomic centers in the lower brain stem acts as relay stations for control activities initiated at higher levels of the brain.

1- Hypothalamus:

a-Stimulation of anterior hypothalamic nuclei → parasympathetic response

b-stimulation of posterior hypothalamic nuclei → sympathetic response

2- Cerebral cortex:

- Sites: Area 6 & 8, limbic lobe and prefrontal area.
- Action: affects both sympathetic and parasympathetic functions.

3- Reticular formation: Responsible for the tone of sympathetic and parasympathetic (i.e. normal functions during basal rate of activity).

N.B. The higher areas of the brain can alter functions of the whole autonomic nervous system or portion of it, strongly enough to cause severe autonomic induced disease such as: peptic ulcer, constipation or diarrhea, heart palpitation, hypertension: is known as psychosomatic effect.