INTRODUCTION TO HUMAN PHYSIOLOGY

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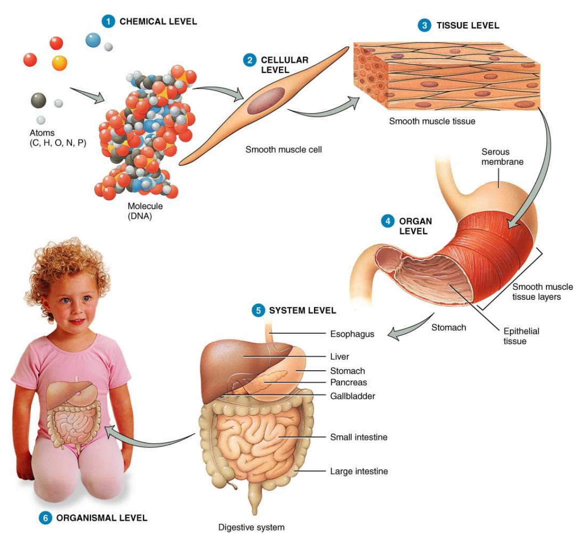
PHYSIOLOGY

- The goal of physiology is to explain the physical and chemical factors that are responsible for the origin, development, and progression of life.
- In human physiology, we attempt to explain the specific characteristics and mechanisms of the human body that make it a living being

LEVELS OF ORGANIZATION OF THE BODY

- The human body is organized into structural and functional levels of increasing complexity.
- Each higher level incorporates the structures and functions of the previous level
- The simplest level is the chemical level, and proceed to cells, tissues, organs, and organ system



Chemical Level

- The chemicals that make up the body may be divided into

1. Inorganic chemicals
2. Organic chemicals

Chemical Level cont'd

- Inorganic chemicals are usually simple molecules made of one or two elements other than carbon (with a few exceptions)
- Examples

1. Water (H2O)
2. Oxygen (O2)
3. Carbon dioxide (CO2)
4. Minerals such as iron (Fe), calcium (Ca), and sodium (Na)

Chemicals Level cont'd

- Organic chemicals are often very complex and always contain the elements carbon and hydrogen.
- Examples

1. Carbohydrates
2. Fats
3. Proteins
4. Nucleic acids.

Cellular Level

- The smallest living units of structure and function are cells.
- There are many different types of human cells, though they all have certain similarities.
- Each type of cell is made of chemicals and carries out specific chemical reactions

Tissue Level

- A tissue is a group of cells with similar structure and function.
- There are four groups of tissues

1. Epithelial tissues
2. Connective tissues
3. Muscle tissues
4. Nervous tissue

Tissues Level cont’d

1. Epithelial tissues

- These cover or line body surfaces and some are capable of producing secretions with specific functions.
- Examples
- The outer layer of the skin and sweat glands, walls of capillaries (squamous epithelium) and the kidney tubules (cuboidal epithelium)

Tissue Level cont’d

2. Connective tissues

- This connect and support parts of the body
- Some transport or store materials.
- Examples
- Blood, bone, cartilage, and adipose tissue

Tissue Level cont’d

3. Muscle tissues

- These are specialized for contraction, which brings about movement
- Skeletal muscles, cardiac muscles and smooth/visceral muscles

Tissues Level cont'd

4. Nerve tissue

- This is specialized to generate and transmit electrochemical impulses that regulate body functions.
- The brain and optic nerves are examples of nerve tissue

Organ level

- An organ is a group of tissues precisely arranged so as to accomplish specific functions.
- Examples include Kidneys, Bones, Liver, lungs and stomach.

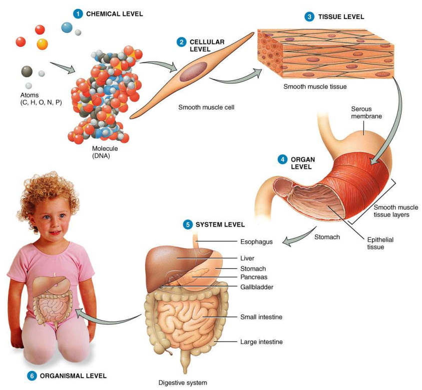
Organ level

- The stomach is lined with epithelial tissue that secretes gastric juice for digestion, Smooth muscle tissue in the wall of the stomach contracts to mix food with gastric juice and propel it to the small intestines and Nerve tissue carries impulses that increase or decrease the contractions of the stomach

Organ System level

- An organ system is a group of organs that all contribute to a particular function
- Examples include Urinary system, Digestive system and Respiratory system
- The urinary system consists of the kidneys, ureters, urinary bladder, and urethra.
- These organs all contribute to the formation and elimination of urine.

Organ System level cont'd



HOMEOSTASIS

- A condition in which the internal environment of the body remains relatively constant despite changes in the external environment.
- Examples would be the maintenance of body temperature and levels of glucose in the blood

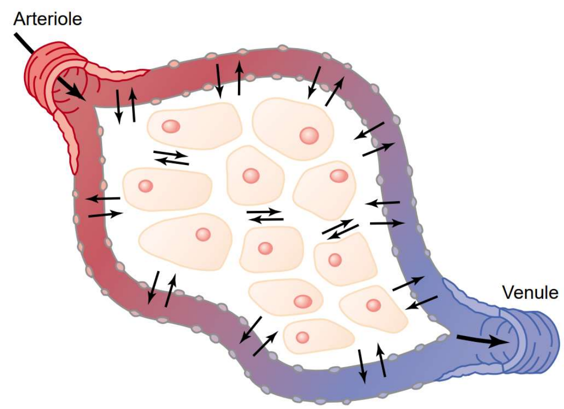
	Normal Value	Normal Range	Approximate Short-Term Nonlethal Limit	Unit
Oxygen	40	35–45	10–1000	mm Hg
Carbon dioxide	40	35–45	5–80	mm Hg
Sodium ion	142	138–146	115–175	mmol/L
Potassium ion	4.2	3.8–5.0	1.5–9.0	mmol/L
Calcium ion	1.2	1.0–1.4	0.5–2.0	mmol/L
Chloride ion	108	103–112	70–130	mmol/L
Bicarbonate ion	28	24–32	8–45	mmol/L
Glucose	85	75–95	20–1500	mg/dl
Body temperature	98.4 (37.0)	98–98.8 (37.0)	65–110 (18.3–43.3)	°F (°C)
Acid-base	7.4	7.3–7.5	6.9–8.0	pH

The Internal Environment

- About 60% of the adult human body is fluid, mainly a water solution of ions and other substances.
- Two thirds of this fluid is inside the cells and is called intracellular fluid (ICF)
- One third is in the spaces outside the cells and is called extracellular fluid (ECF)

The Internal Environment cont'd

- This ECF 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



Internal Environment cont'd

- In the ECF are the ions and nutrients needed by all cells to maintain cell life
- The ECF is also called the internal environment of the body, or the milieu intérieur

Internal Environment cont'd

- Cells are capable of living, growing, 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.

Distribution of ions in the ECF and ICF (Values are in mEq/L of H_2O)

Ion	Extracellular fluid	Intracellular fluid
Cations		
Na^+	142	14
K^+	5.5	150
Ca^{2+}	5	<1
Mg^{2+}	3	58
Anions		
Cl^-	103	4
HCO_3^-	28	10
PO_4^{3-}	4	75
Proteins	1 g/dL	5 g/dL

Homeostasic Mechanisms

- **Homeostatic mechanisms are designed to re-establish homeostasis when there is an imbalance**

Homeostasis cont'd

- **There are three components to a homeostatic system:**

1. **The Sensor which detects the stress.**
2. **The Control Center which receives information from the sensor and sends a message to adjust the stress.**
3. **The Effector which receives the message from the control center and produces the response which reestablishes homeostasis**

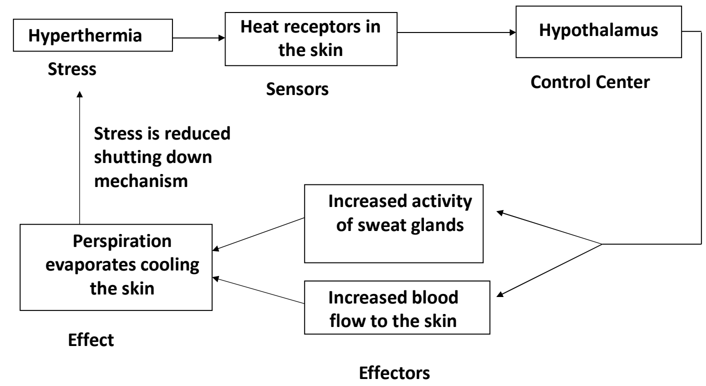
Characteristics of Homeostasic Mechanisms

1. **Negative feed back**
2. **Positive feed back**
3. **Feed forward/Adaptive control**

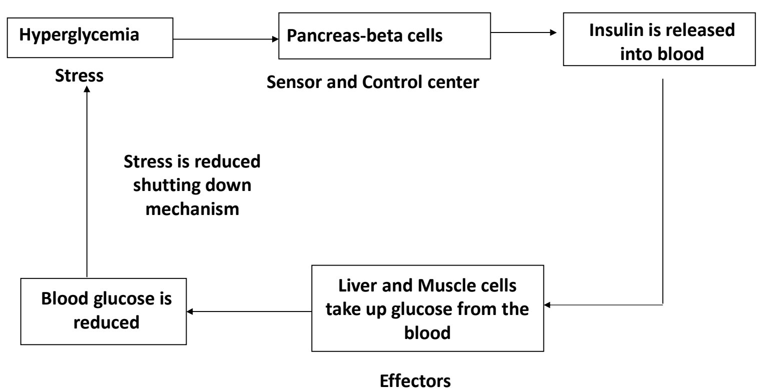
Negative feedback mechanisms

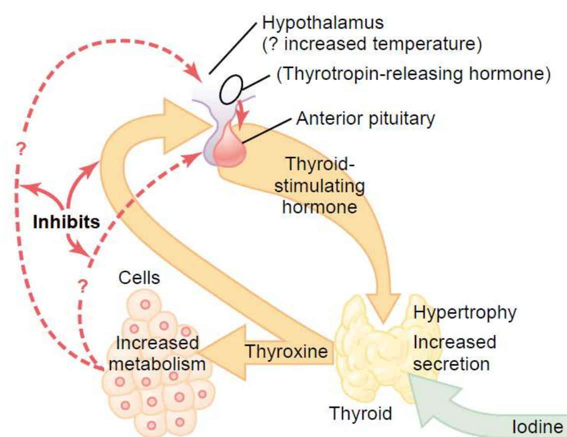
- This is the action of the homeostatic mechanism which occurs by inhibiting the deviation and reversing it back to normal

Homeostatic Regulation of Body Temperature through Negative Feedback



Homeostatic Regulation of Blood Sugar through Negative Feedback





Gain of a Control System

- The degree of effectiveness with which a control system maintains constant conditions is determined by the gain of the negative feedback

$$\text{Gain} = \frac{\text{Correction}}{\text{Error}}$$

Gain of a Control System cont'd

1. Example

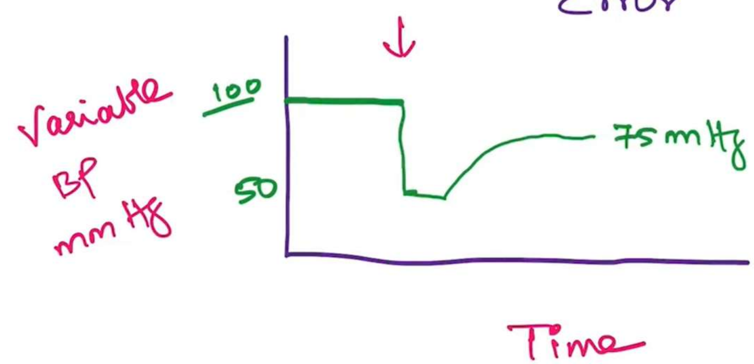
- In an experiment the mean blood pressure of a Rabbit was decreased from 100mmHg to 50mmHg. After 5 minutes the blood pressure came back to 75mmHg.
- Calculate the gain of the control system involved

Gain of a Control System cont'd

- STEPS

1. Draw the homeostatic response curve
2. Calculate the correction (final value after correction- change before correction)
3. Calculate the error (final value after correction- original set point)
4. Use the gain equation

$$\text{Gain} = \frac{\text{Correction}}{\text{Error}}$$



Gain of a Control System cont'd

2. Example

- **In an experiment the mean blood pressure of an adult male was increased from 100mmHg to 150mmHgby injecting a drug. After 5 minutes the blood pressure came back to 110mmHg.**
- **Calculate the gain of the control system**

Positive Feedback Mechanisms

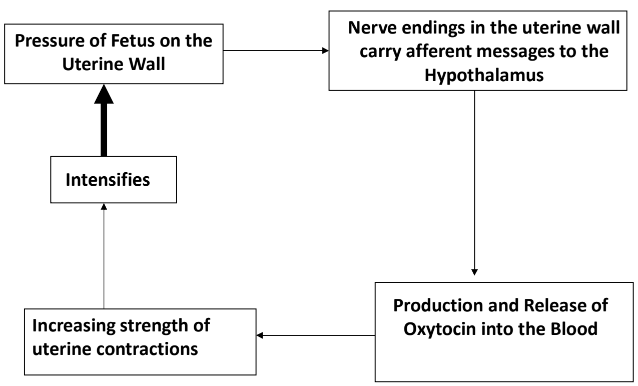
- **During a positive feedback process, the initial imbalance or stress is intensified rather than reduced as it is in negative feedback.**
- **Homeostatic systems utilizing positive feedback exhibit two primary characteristics:**

1. Time limitation

- **Positive feedback processes in the body that must be completed within a constrained time frame**

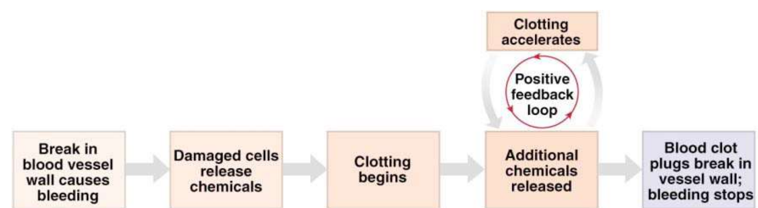
2. Intensification of stress

Homeostatic Regulation of Child Birth through Positive Feedback



The birth of the child will bring this process to a close. Other examples of positive feedback regulation occur during milk letdown and blood clotting.

Feedback in Coagulation



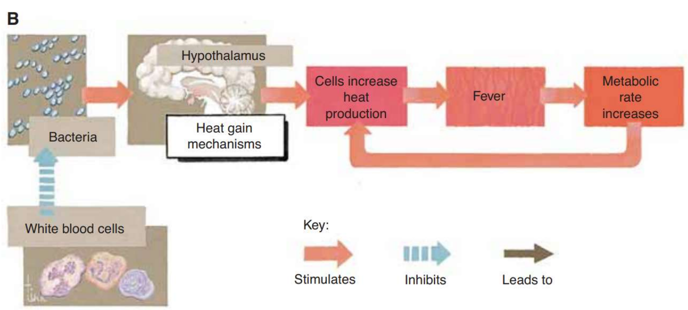
Positive feedback "mini-loops" are built into pathway to speed up production of chemicals needed to form the clot. Entire sequence of clotting is a negative feedback pathway:

Action potential

- The stimulus causes the Na+ channels to open, Na+ then diffuses rapidly into the nerve cell.
- Na+ influx causes the membrane potential to become positive
- The inside of the membrane is now positive relative to the outside

Harmful Effects of Positive Feedback

1. Fever can cause a positive feedback within homeostasis that pushes the body temperature continually higher.
2. If the temperature reaches 45 degrees centigrade cellular proteins denature bringing metabolism to a stop and death.



Positive feedback cont'd

3. Chronic hypertension can favor the process of atherosclerosis which causes the openings of blood vessels to narrow.

- This, in turn, will intensify the hypertension bring on more damage to the walls of blood vessels.

Adaptive Control/feed forward control

- Adaptive control system refers to a delayed type of negative feedback mechanism
- Some movements of the body occur so rapidly that there is not enough time for nerve signals to travel from the peripheral parts of the body all the way to the brain and then back to the periphery again to control the movement.

Adaptive Control cont'd

- Therefore, the brain uses a principle called feed-forward control to cause required muscle contractions.
- That is, sensory nerve signals from the moving parts apprise the brain whether the movement is performed correctly.

Adaptive Control/feed forward control cont'd

- If not, the brain corrects the feed-forward signals that it sends to the muscles the next time the movement is required.
- Then, if still further correction is needed, this will be done again for subsequent movements.

ROLE OF BODY SYSTEMS IN HOMEOSTASIS

Respiratory system

- Adequate amount of oxygen should be made available to the cells, and carbon dioxide and other metabolic end products must be removed.
- The respiratory system supplies the oxygen and removes carbon dioxide

Digestive system

- Adequate amount of different dissolved nutrients, including carbohydrates, fatty acids and amino acids, are absorbed from the ingested food into the ECF

Liver and other organs

- Fat cells, GIT – mucosa, kidneys, endocrine glands and the liver modify the chemical composition of substances absorbed from GIT

Musculo – Skeletal muscles

- Skeletal muscles enable the organism to move in search for nutrients, escape adverse conditions and prevent damage/destruction

Kidneys

- The kidneys removes from the plasma most other substances that are not needed by the body.
- These include metabolic end products such as urea, uric acid and excess water and ions

Nervous system

- Controls and coordinates bodily activities that require rapid responses
- Detects and initiates reactions to changes in external environment

Endocrine system

- Secreting glands of endocrine regulate activities that require duration rather than speed
- Controls concentration of nutrients and, by adjusting kidney function, controls internal environment’s volume and electrolyte composition

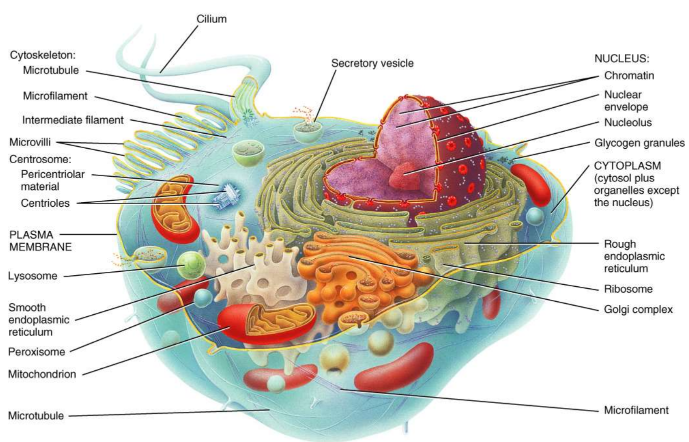
Reproductive system

?

To summarize, the body is actually a *social order of about 100 trillion cells* organized into different functional structures, some of which are called *organs*. Each functional structure contributes its share to the maintenance of homeostatic conditions in the extracellular fluid, which is called the *internal environment*. As long as normal conditions are maintained in this internal environment, the cells of the body continue to live and function properly. Each cell benefits from homeostasis, and in turn, each cell contributes its share toward the maintenance of homeostasis. This reciprocal interplay provides continuous automaticity of the body until one or more functional systems lose their ability to contribute their share of function. When this happens, all the cells of the body suffer. Extreme dysfunction leads to death; moderate dysfunction leads to sickness.

THE CELL

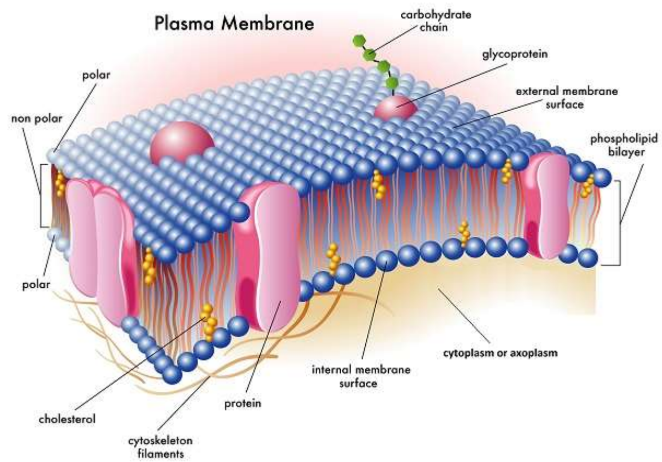
- **This is the smallest functional unit of the human body.**
- **It is the basic unit of the body**
- **Cells vary in size and shape, structure and function**
- **Various cells come together to form tissues**



Sectional view

THE CELL MEMBRANE

- **Also called plasma membrane**
- **It envelops the cell and composed almost entirely of proteins and lipids**
- **Most organelles of the cell are covered by membranes composed primarily of lipids and proteins.**
- **These membranes include the cell membrane, nuclear membrane, membrane of the endoplasmic reticulum, and membranes of the mitochondria, lysosomes, and Golgi apparatus**



Cell membrane cont'd

Components of the cell membrane

- Proteins in the cell membrane are glycoproteins

1. Integral proteins
2. Peripheral proteins

Cell membrane cont'd

1. Integral proteins

- Trans-membrane proteins embedded into the thickness of the membrane stretching from inside to outside

1. Cell junction proteins
2. Cell adhesion proteins
3. Carrier proteins
4. Hormone receptors
5. Channel proteins and antigen proteins.

Cell membrane cont'd

2. Peripheral proteins

- Are partially embedded into the membrane in the lipid layers.
- They do not penetrate the entire thickness of the membrane
- Act as antigens, enzymes and cell adhension molecules.

Cell membrane cont'd

Carbohydrates

- Are negatively charged therefore negatively charged substances do not directly move in and out of the cell.
- Carbohydrate act as cell junctions and receptors for some hormones.

Functions of cell membrane

1. Protective function

- Cell membrane protects the cytoplasm and the organelles present in the cytoplasm

2. Semi-permeability function

- Cell membrane acts as a Semi-permeable membrane, which allows some substances to pass through it and acts as a barrier for other substances

Functions of cell membrane cont'd

3. Absorptive function

- Nutrients are absorbed into the cell through the cell membrane

4. Excretory function

- Metabolites and other waste products from the cell are excreted out through the cell membrane

Functions of cell membrane cont'd

5. Gaseous exchange

- Oxygen enters the cell from the blood and carbon dioxide leaves the cell and enters the blood through the cell membrane.

6. Cell membrane is responsible for the maintenance of cellular shape and size.

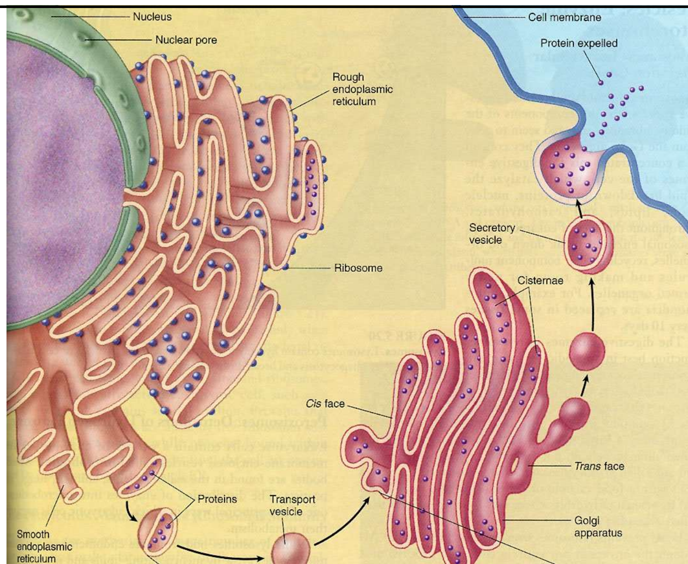
Cytoplasm

- **Jellylike material comprising of 80% water, carbohydrates, proteins, lipids, electrolytes and cell organelles.**

1. **Peripheral part of cytoplasm, just beneath the cell membrane = Ectoplasm**
2. **Inner part of cytoplasm, between the ectoplasm and the nucleus = Endoplasm**

ENDOPLASMIC RETICULUM

- **A network of tubular and flat vesicular structures in the cytoplasm interconnected with one another**
- **Attached to the ER are Ribosomes**
- **Substances formed in the cell enter the ER matrix and are then conducted to other parts of the cell**
- **Multiple enzymes are attached to ER thus provide machinery for major share of metabolic functions**



http://www.fredonia.edu/bio241/images/5.19_ER_and_Golgi.jpg

Rough endoplasmic reticulum

- **Part of the ER has attached to its outer surfaces, large numbers of minute granular particles called ribosomes.**
- **Where these are present, the reticulum is called the granular endoplasmic reticulum.**

Rough endoplasmic reticulum cont'd

1. These degrade worn out organelles
2. Act as a site of protein synthesis

Smooth Endoplasmic Reticulum

- Part of the ER has no attached ribosomes
- This part is called the agranular endoplasmic reticulum

1. The agranular reticulum functions for the synthesis of lipid substances

Smooth endoplasmic reticulum

1. Synthesis of lipid substances
2. Role in cellular metabolism
3. Storage and metabolism of calcium
4. Catabolism and detoxification of toxic substances

Golgi Apparatus

- It has membranes similar to those of the smooth endoplasmic reticulum
- It usually is composed of four or more stacked layers of thin, flat, enclosed vesicles lying near one side of the nucleus
- This apparatus is prominent in secretory cells

Golgi Apparatus cont'd

- Small transport vesicles or ER vesicles continually pinch off from the ER and shortly fuse with the Golgi apparatus
- The transported substances are processed in the Golgi apparatus to form lysosomes, secretory vesicles, and other cytoplasmic components

Lysosomes

- These are vesicular organelles that form by breaking off from the Golgi apparatus and then dispersing throughout the cytoplasm
- It is surrounded by a typical lipid bilayer membrane
- It is filled with large numbers of small granules which contain different hydrolase (digestive) enzymes.

Lysosomes cont'd

- The lysosomes provide an intracellular digestive system that allows the cell to digest the following;

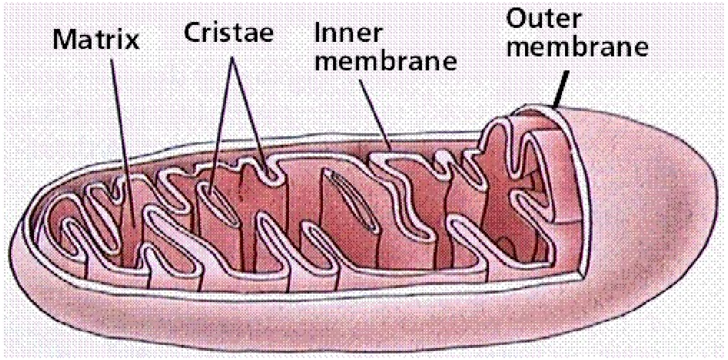
1. Damaged cellular structures
2. Food particles that have been ingested by the cell
3. Unwanted matter such as bacteria

Peroxisomes

- Peroxisomes are similar physically to lysosomes
- They are believed to be formed by self-replication or perhaps by budding off from the smooth endoplasmic reticulum
- They contain oxidases to oxidize many substances that might otherwise be poisonous to the cell

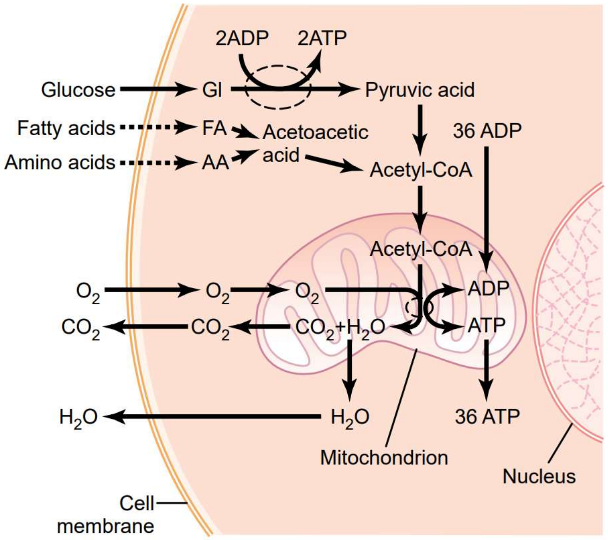
MITOCHONDRIA

- **Power house of the cell i.e. Extract energy from the nutrients**
- **Have a lipid bi – layer i.e. an outer and inner mitochondria membrane**
- **Have infoldings of the inner membrane which form shelves of oxidative enzymes**
- **The matrix contains enzymes that extract energy from nutrients**



Mitochondria cont'd

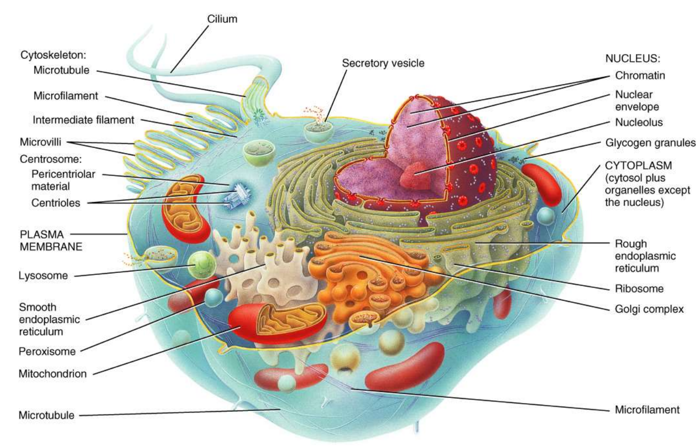
1. **Production of energy**
2. **Synthesis of ATP**
3. **Initiation of apoptosis**



THE NUCLEUS

- The nucleus is the control center of the cell
- It contains genes (DNA) which determine the characteristics of the cell's proteins
- The genes also promote the reproduction of the cell itself (mitosis)

Fig. 03.01



Sectional view

Functions of nucleus

1. Control of all the cell activities that include metabolism, protein synthesis, growth and reproduction.
2. Synthesis of tRNA and rRNA
3. Formation of subunits of ribosomes

Functions of nucleus cont'd

4. Sending genetic instruction to the cytoplasm for protein synthesis through messenger RNA (mRNA)
5. Control of the cell division through genes
6. Storage of hereditary information (in genes) and transformation of this information from one generation to another

CELL CONNECTIVITY, SIGNALING AND COMMUNICATION

Outline

- Cell connectivity – Tight/gap junctions and desmosomes.
- Cell signaling – electrical and chemical.
- Chemical Communication – receptor and second messenger systems.

Cell Connectivity

- Cell connectivity or Cell junction is the connection between the neighboring cells or the contact between the cell and extracellular matrix.
- It is also called membrane junction and allows signals to travel from one cell to another.

Cell Connectivity cont'd

- Types of Cell Junctions
  1. Tight junctions
  2. Gap junctions
  3. Desmosomes.

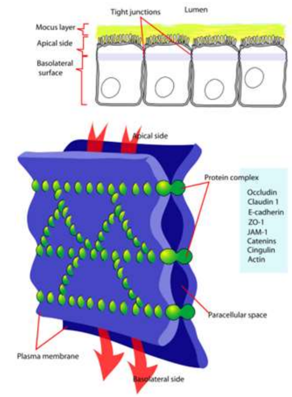
Tight junctions

- Are intercellular occluding junction that prevents the passage of large molecules.
- Also called zonula occludens
- It is the region where the cell membranes of the adjacent cells fuse together firmly.

Tight junctions cont'd

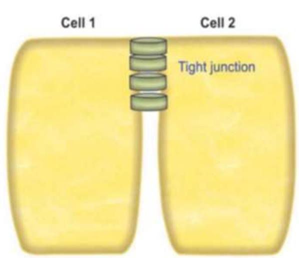
- This type of junction is present in the apical margins of epithelial and endothelial cells in

1. Intestinal mucosa
2. Wall of renal tubule capillary wall
3. Choroid plexus



Tight junctions cont'd

- **Proteins of Tight Junctions**
- Contains integral membrane proteins, such as occludin, claudin and junctional adhesion molecules (JAMs), Cingulin, Actin



Tight junctions cont'd

Functions of Tight Junctions

1. Strength and stability

- Tight junction holds the neighboring cells of the tissues firmly and thus provides strength and stability to the tissues.

2. Selective permeability (gate function)

- Tight junction forms a selective barrier for small molecules and a total barrier for large molecules.

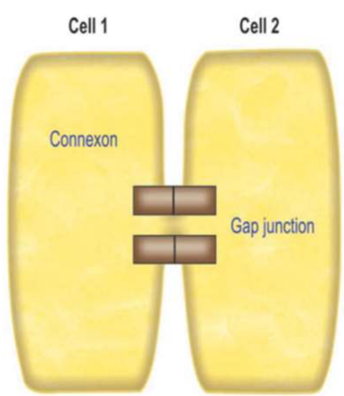
Gap junctions

- **Are intercellular junctions that allows passage of ions and smaller molecules between the cells.**
- **It is also called nexus.**
- **It is present in heart, basal part of epithelial cells of intestinal mucosa, etc.**

Gap junctions cont'd

- **Cytoplasm of two adjacent cells are connected by the channels formed by the membranes of both cells.**
- **So, the molecules move from one cell to another cell directly through these channels, without having contact with ECF.**
- **These channels are surrounded by 6 subunits of proteins called Connexins or connexons.**

Gap junctions cont'd



Gap junctions cont'd

- **Functions of Gap Junctions**

1. **It helps in rapid propagation of action potential from one cell to another cell.**
2. **The channel permits the passage of glucose, amino acids, ions and other substances, which have a molecular weight less than 1,000.**
3. **It helps in the exchange of chemical messengers between the cells**

Gap junctions cont'd

- Regulation of Gap Junctions

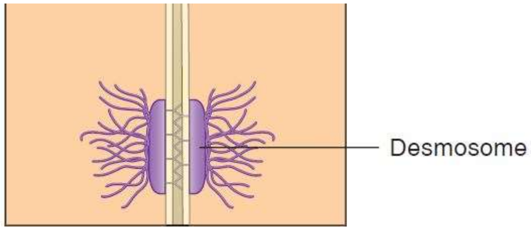
1. The diameter of each channel is regulated by the intracellular calcium ions, pH, electrical potential, hormones or neurotransmitters.

Desmosomes

- Are Anchoring junctions which provide firm structural attachment between two cells or between a cell and the extracellular matrix.
- It is a cell to cell junction, where the intermediate filaments connect two adjacent cells.
- Desmosomes are also called macula adherens.

Desmosomes cont'd

- The membranes of two adjacent cells, which oppose each other, are thickened and become spot-like patches.



Desmosomes cont'd

- Intermediate filaments are attached with the thickened patches.
- Some of these filaments are parallel to the membrane and others are arranged in radiating fashion.
- Desmosomes function like tight junctions.
- The trans-membrane proteins involved in desmosome are mainly Cadherins.

CELL SIGNALING

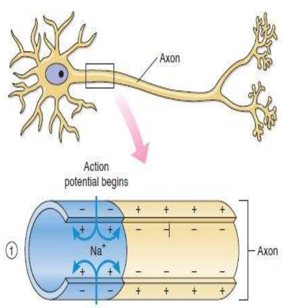
- Cells communicate by signaling to each other electrically and chemically
- Cell signaling refers to how cells communicate with each other.

Cell Signaling cont'd

- In certain specialized cases, signals can travel directly from one cell to the next because their plasma membranes are very close together, and their cytoplasm is continuous through tiny gap junctions that couple the cells together

Electrical Signaling;

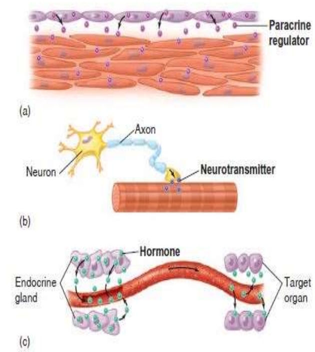
- The signaling cell transmits information in the form of changes in membrane potential along the length of the cell;
- The electrical signal is then transferred from the signaling cell (neuron) to the target cell, either in chemical form (neurotransmitter) or via gap junctions



Chemical Signaling

- Cells signal each other by releasing chemicals into the extracellular environment

1. Paracrine signaling
2. Synaptic signaling
3. Endocrine signaling.



Paracrine Signaling

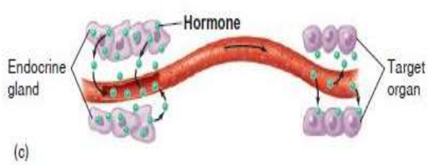
- In Paracrine signaling cells within an organ secrete regulatory molecules that diffuse through the extracellular matrix to nearby target cells
- A form of cell signaling in which the target cells are near to the signaling cells
- Example is seen in Tissue repair, blood clotting, responses to allergens

Synaptic Signaling

- In synaptic signaling a neuron innervates its target organ through a functional connection or synapse, between the axon ending and the target cell.
- The axon terminal of the neuron releases a neurotransmitter, which regulates a target cell

Endocrine Signaling

- In endocrine signaling, an endocrine gland secretes hormones into the blood, which carries the hormones to the target organs.
- Only the target cells for a particular hormone, however, can respond to the hormone

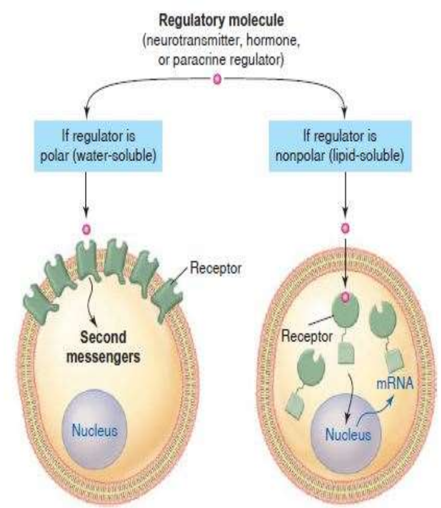


RECEPTOR AND SECOND MESSENGER SYSTEM

- For a target cell to respond to a hormone, neurotransmitter, or paracrine regulator, it must have specific Receptor Proteins for these molecules.
- A typical cell can have a few million receptor proteins.
- This great diversity allows the many regulatory molecules in the body to exert fine control over the physiology of our tissues and organs

Receptors cont'd

- These receptor proteins may be located on the outer surface of the plasma membrane of the target cells or they may be located intra-cellularly, in either the cytoplasm or nucleus
- The location of the receptor proteins depends on whether the regulatory molecule can penetrate the plasma membrane of the target cell

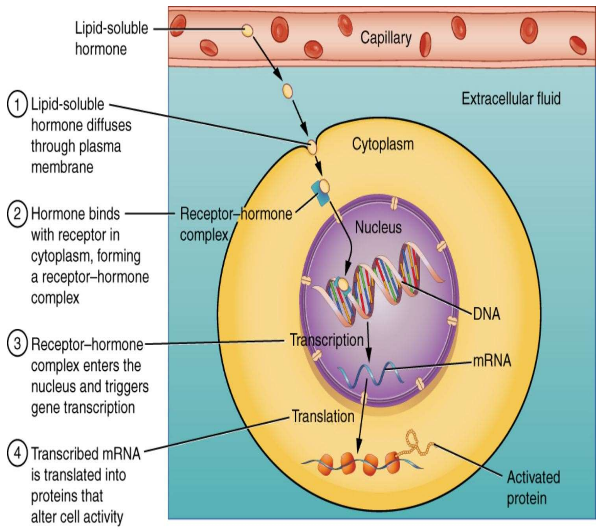


Receptors cont'd

- If the regulatory molecules are large or polar, such as epinephrine, acetylcholine, and insulin (a polypeptide hormone) cannot enter their target cells.
- In these cases, the receptor proteins are located on the outer surface of the plasma membrane.

Receptors cont'd

- If the regulatory molecule is nonpolar, it can diffuse through the cell membrane and enter the target cell
- Such regulatory molecules include steroid hormones, thyroid hormones.
- In these cases, the receptor proteins are intracellular in location.



SECOND MESSENGERS

- **Binding of polar regulatory molecules to extracellular receptor proteins triggers production of molecules produced within the cytoplasm which somehow changes the activity of specific proteins, including enzyme proteins, within the cytoplasm**

Second Messengers cont'd

- **This feature is accomplished by means of intermediaries, known as second messengers, activated in the cytoplasm from the receptor proteins in the plasma membrane**

Second Messengers cont'd

- **Second messengers are intracellular signaling molecules released by the cell in response to exposure to extracellular signaling molecules (hormones – the first messengers)**
- **Second messengers trigger physiological changes at cellular level such as proliferation, differentiation, migration, survival, apoptosis and depolarization**

Second Messengers cont'd

- Second messengers are thus a component of signal-transduction mechanisms, because extracellular signals (hormones) are transduced into intracellular signals (second messengers)
- The only direct effect of the first messenger has on the cell is to activate its specific membrane receptor.
- The second messenger does the rest

Second Messengers cont'd

- Second messengers may be ions (most commonly Ca2+) from the ECF or molecules produced within the cytoplasm in response to binding of polar regulatory molecules to their receptors in the plasma membrane
- One important second-messenger molecule is cyclic adenosine monophosphate (cyclic AMP, or cAMP)

Second Messengers cont'd

- The second messenger systems that are activated through coupling of hormone–receptor complexes by G-protein include:

1. Adenylyl cyclase - cAMP system
2. Guanyl cyclase - cGMP system
3. Membrane phospholipase - phospholipid system
4. Calcium - calmodulin system

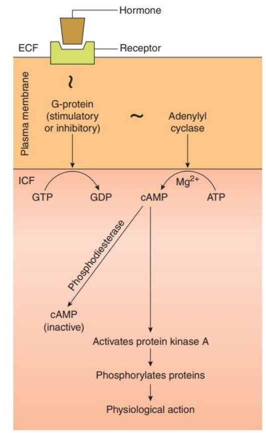
1. Adenylyl cyclase–cAMP system

1. Protein hormone (first messenger) binds with receptor on plasma membrane
2. Hormone-receptor complex activates a membrane protein called the G-protein
3. Activated G-protein activates membrane protein (adenylyl cyclase enzyme)

1. Adenylyl cyclase–cAMP system

1. Adenylyl cyclase catalyzes the conversion of ATP to cAMP (second messenger)
2. cAMP activates protein kinase A
3. Protein kinases A phosphorylates proteins in the cytoplasm that carried out the required cellular or physiological response.

1. Adenylyl cyclase - cAMP system



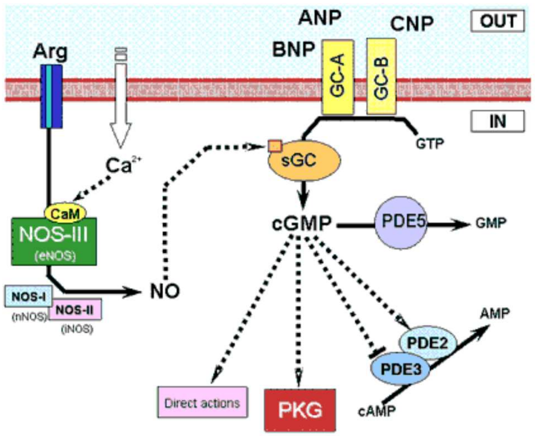
2. Guanylate cyclase - cGMP system

1. Protein hormones such as NO and ANP binds with receptor on plasma membrane
2. Hormone-receptor complex activates the G-protein
3. Activated G-protein activates Guanyl cyclase enzyme

2. cGMP system cont’d

- Enzyme guanylate cyclase produces cGMP from GTP
- cGMP exerts its biochemical response through an enzyme protein kinase G, which initiates a cascade of subsequent enzyme activations

2. cGMP system cont'd



3. Calcium -Calmodulin second messenger System

- **This operates in response to the entry of calcium into the cells.**

1. **Calcium entry may occur due to changes in membrane potential that open calcium channels or when a hormone interact with membrane receptors & open calcium channels.**

3. Calcium -Calmodulin System cont'd

3. **Upon entering a cell, calcium ions bind with the protein calmodulin**
4. **Calmodulin has 4 calcium sites, and when 3 or 4 of these sites bind with calcium, it activates or inhibits of protein kinases.**

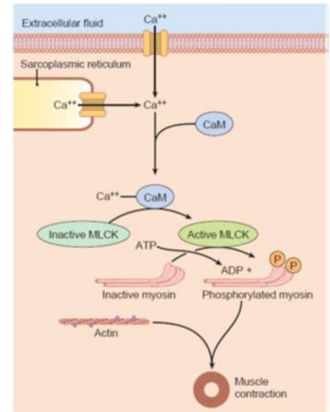
3. Calcium -Calmodulin System cont'd

5. **Activation of calmodulin-dependent protein kinases causes, phosphorylation, activation or inhibition of proteins involved in the cell's response to the hormone.**

3. Calcium -Calmodulin System cont'd

6. For example, one specific function of calmodulin is to activate myosin light chain kinase, which acts directly on the myosin of smooth muscle to cause smooth muscle contraction

3. Calcium -Calmodulin System cont'd



4. Membrane phospholipase - phospholipid system or IP3 mechanism

- Hormones which exert their response through this system include catecholamines, PDGF, GnRH, TRH, oxytocin
- Hormone binds to a receptor in the plasma membrane

1. The hormone - receptor complex via a G-protein activates the membrane enzyme phospholipase C

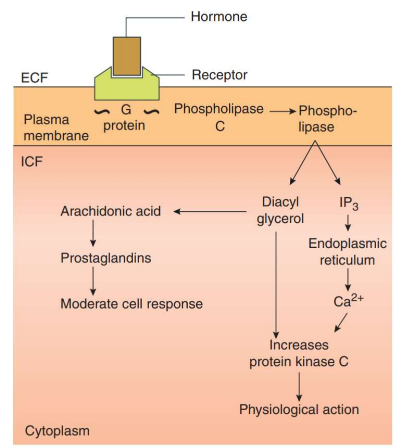
4. IP3 mechanism cont'd

2. Activated phospholipase C then releases diacylglycerol and inositol triphosphate (IP3) from the membrane phospholipid
3. IP3 mobilizes Calcium from the endoplasmic reticulum.
4. Calcium ions and DAG together activate protein kinase C.

4. IP3 mechanism cont'd

5. Activated protein kinase C phosphorylates proteins and causes specific physiological action
6. DAG also yields arachidonic acid, which serves as a substrate for rapid synthesis of prostaglandins that modulate cell response.

4. IP3 mechanism cont'd



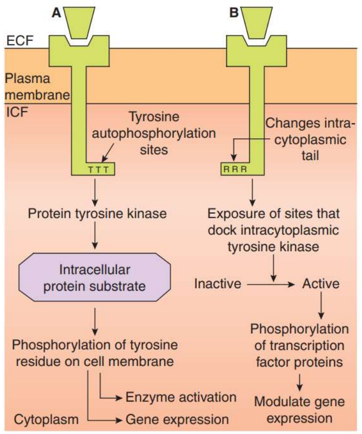
4. ACTION OF HORMONE VIA TYROSINE KINASE ACTIVATION

- Hormones such as HCS, erythropoietin, GH, insulin, NGF, prolactin act by activating tyrosine kinase system
- The receptors have an extracellular hormone binding portion, a single transmembrane portion and an intracytoplasmic C-terminal portion

Tyrosine kinase system cont'd

- Binding of hormone to the receptor changes its conformation and exposes sites on its intracellular portion that are capable of receptor autophosphorylation at specific tyrosine sites.
- This sets into motion a cascade of events leading to enzyme activation and gene transcription

Tyrosine kinase system cont'd



Tyrosine kinase system cont'd