

ULTRASTRUCTURE OF THE EUKARYOTIC CELL

The cell is the living functional unit of all organisms. An organism may be composed of one cell only (Unicellular) e.g. Bacteria and Algae or of several cells (Multicellular) e.g. Man. The cell exists in two forms:

1. Eukaryotic cell, which has a nucleus that is enclosed in a nuclear envelope and several membrane-limited compartments e.g. the human cell.
2. Prokaryotic cell which has no nucleus and is devoid of membrane-limited compartments e.g. the bacterial cell.

Structure of the Eukaryotic Cell (See Fig. C1)

A broad spectrum of morphological and functional specializations of cells occurs in the multicellular organisms. However, all Eukaryotic cells conform to a basic structural model.

Thus the eukaryotic cell is composed of two basic parts; the Cytoplasm and the Nucleus.

THE NUCLEUS

This is the largest organelle of the cell often located in the central part of the cytoplasm and enclosed in a double-layered nuclear membrane. Its shape usually corresponds to the shape of the cell in which it is found. It contains a nucleolus/nucleoli (which produces ribosomal subunits) and chromatin (DNA). The latter is the genetic material implicated in cell division and in the synthesis of several molecules particularly proteins. The nucleus as the control centre of the cell contains the blueprint for all cellular structure and activities and in its absence the cell can neither function nor survive. The nuclear envelope is perforated by pores (3000-4000), which facilitate communication between the nucleus and the cytoplasm. Attached to the outer membrane of the nuclear envelope are polyribosomes. This membrane is also continuous with the rough endoplasmic reticulum of the cytoplasm.

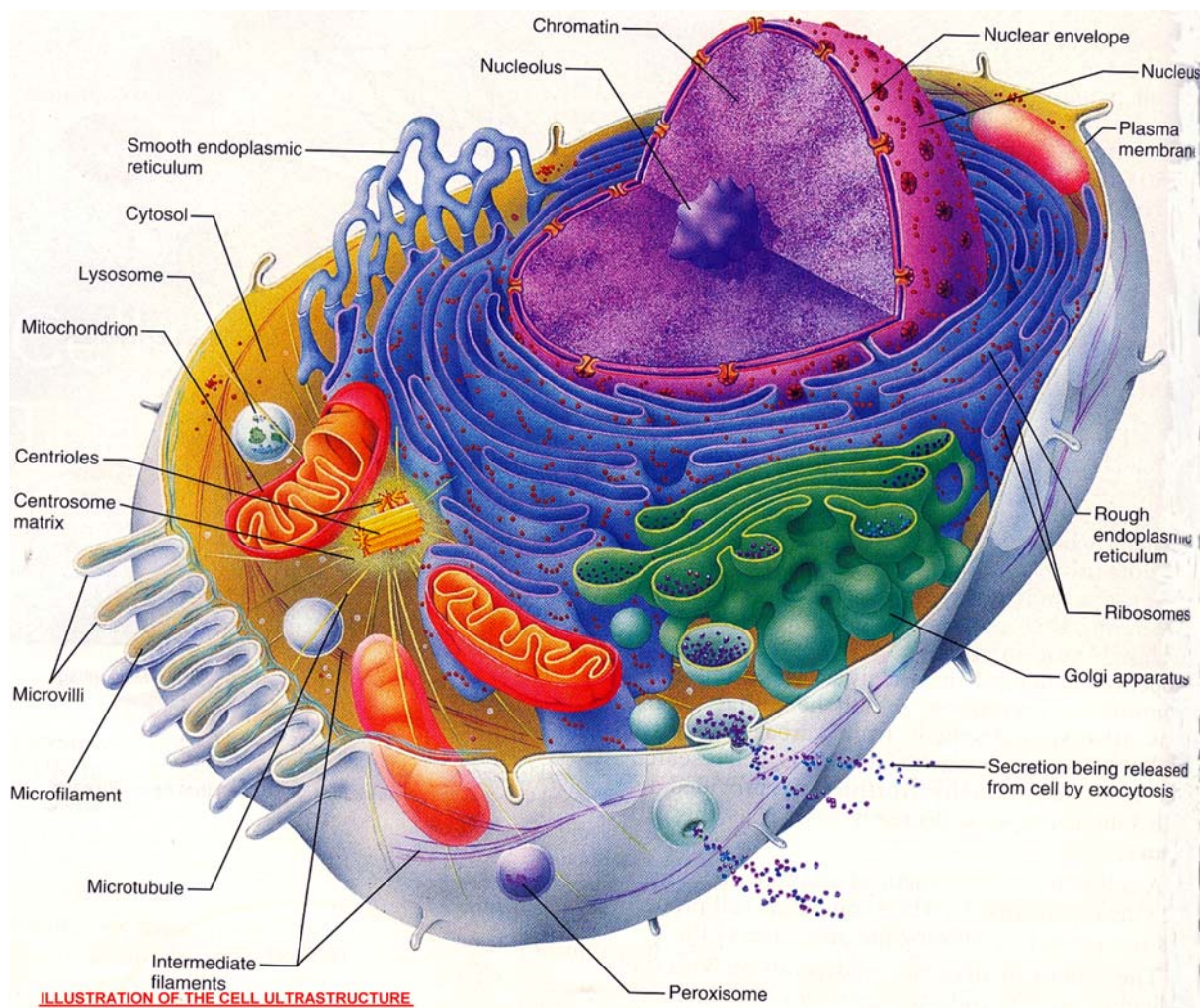
THE CYTOPLASM.

The fluid component of the cytoplasm is the Cytosol (pH 7.2) while the metabolically active contents of the cytoplasm are the Organelles. Apart from being metabolically active, organelles are permanent residents of the cell which would survive cell division i.e. they reappear in the daughter cells following cell division. Organelles occur in two forms, freely within the cytosol or enclosed in membrane. The cytoplasm also contains substances which are not metabolically active. These are called Inclusion Bodies.

Inclusion bodies are the transitory residents of the cytoplasm not involved in cell metabolism and do not survive cell division. They comprise mainly accumulated metabolites, lipid droplets, pigments and minerals and are sporadically distributed in body cells.

The eukaryotic cell is enclosed in a limiting membrane called the Plasma membrane or the Plasmalemma.

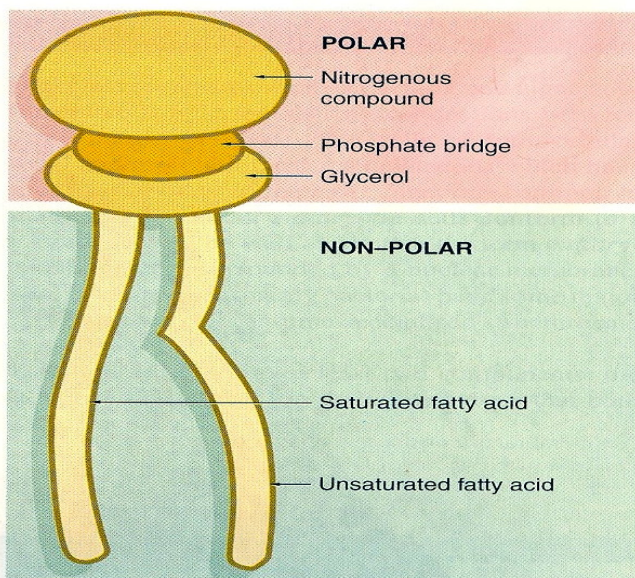
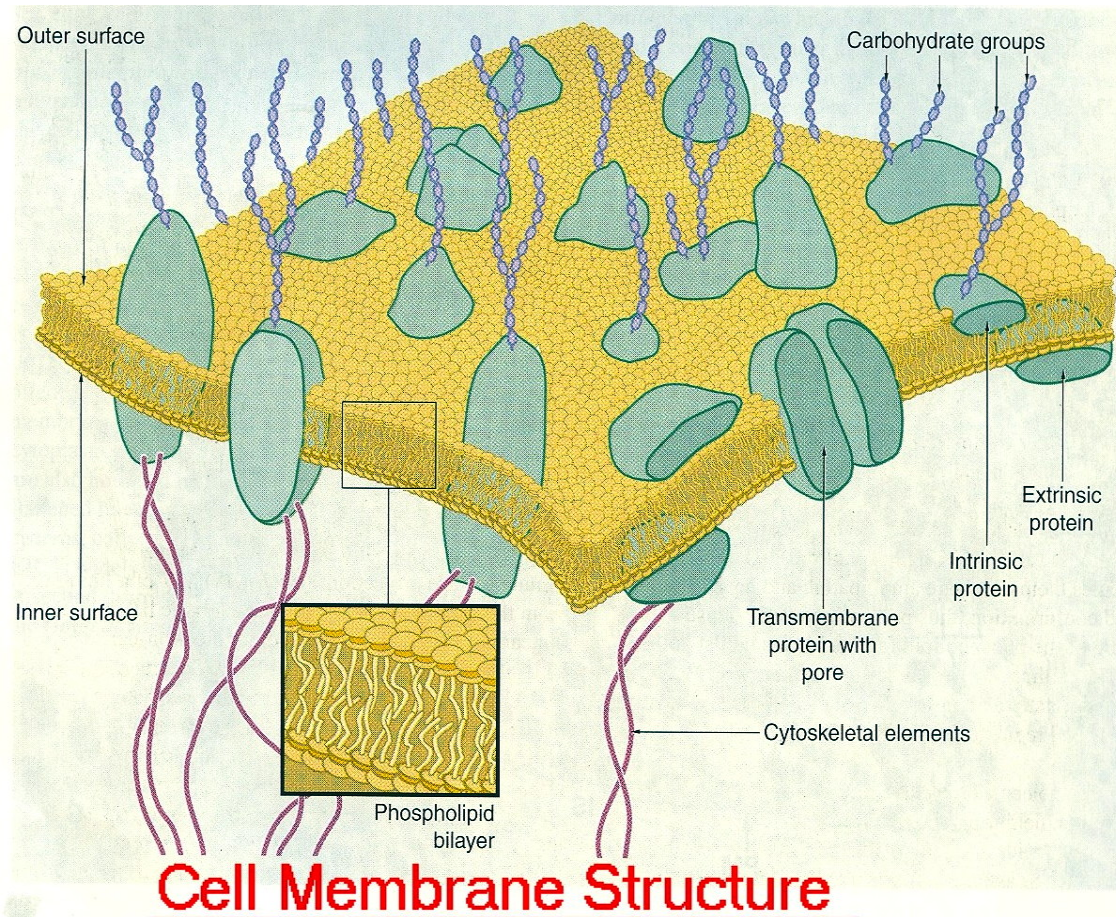
Fig C1: Ultrastructure of the cell



THE PLASMALEMMA Fig. C 2

The Plasmalemma is the physical external boundary of the cell. It is composed of Phospholipids, Protein, Carbohydrate and Cholesterol which are intricately organised into a trilaminar structure. The cell membrane as well as the membranes surrounding the organelles ranges from 7.5 to 10 nanometre in thickness. The 3-layered structure, referred to as the **Unit Membrane structure** is formed from two phospholipid layers; the fatty acid nonpolar (Hydrophobic) tails of the two phospholipids are located in the middle layer while the polar (Hydrophilic) head are located on either side of the middle layer (see Fig. C2). The proteins of the cell membrane account for 50% (w/w) of the membrane and occur in two forms, viz. integral proteins which traverse the thickness of the membrane and peripheral proteins which are adsorbed to the outer or inner surfaces of the membrane. While the peripheral proteins are involved in cell recognition and interactions, integral proteins regulate passage of material and active transport of specific molecules across the membrane.

Fig. C 2 The Plasmalemma



Phospholipid Structure

The cholesterol is embedded within the phospholipid fatty acid chains where it restricts their movements and also modulates the fluidity and movements of other contents of the membrane.

The carbohydrate contents of the membrane are attached to the lipids and proteins as glycolipids and glycoproteins respectively. Some of the carbohydrates of the glycoprotein constitute the glycocalyx on the outer surface of the membrane. Others are receptors involved in adhesion, cell recognition and responses to protein hormones. Others yet are attached to the cytoskeletal components of the cytoplasm for maintenance of cell shape and integrity.

In summary, the principal functions of the Plasmalemma are:

1. Communication through receptors on the outer surface
2. Intercellular connectivity which facilitates boundary flexibility, support of cell structure and protects cellular contents.
3. Provision of physical barrier between the intra and extra cellular compartments.
4. Selective permeability which regulates entry/exit of materials across the membrane.

Transmembrane Trafficking

Apart from active transport and passive diffusion across the membrane, other mechanisms are utilized in traversing the cell membrane. Amongst these is:

Endocytosis which occurs in three forms, viz.

1. Phagocytosis (Cell eating): This process entails bulk passage through the membrane by infoldings and fusion of parts of the membrane as in Macrophages and Neutrophils.
2. Fluid-phase endocytosis (Cell drinking): In this process, fluids and which may contain some solids are taken into the cell through infoldings and fusion of cell membrane.
3. Receptor-mediated Endocytosis: In this process, a ligand attaches to its receptor and the complex formed is endocytosed.

Exocytosis: This is the reverse of endocytosis as materials are moves out of the cell compared to endocytosis. It entails the fusion to the cell membrane of membrane-enclosed materials with subsequent discharge of the material into the extracellular space. This process is aided by certain membrane proteins and often triggered in many cells by transient increase in cytosolic calcium ions.

CYTOPLASMIC ORGANELLE

Organelles are the metabolically active and permanent residents of the cell. Organelles exist in two forms; membrane-bound and not bound by membrane. The principal cytoplasmic organelles include:

- **The Mitochondrion**

Mitochondria are membrane-bound enzyme storage organelles. Mitochondrial enzymes are involved in aerobic respiration, production of ATP and heat energy for maintenance of body temperature. The mitochondrion is enclosed in two sheets of membrane. An outer sieve-like unfolded membrane and an

inner membrane which is thrown into long finger-like folds called cristae. The number of cristae corresponds to the cell's energy needs. The space between the two membranes is the intermembranous space while the space deep to the inner membrane is referred to as the matrix. Mitochondria are eosinophilic, elongated rod-like organelles measuring 0.5 to 1 micron in diameter and 5 to 10 micron in length. They are widely distributed in all cells but occur abundantly in cell with very high energy needs (Heart muscles and kidney cells). Integral proteins of the outer and inner membrane provide channels for selective passage of small molecules, while enzymes in the matrix and on the surface of the inner membrane are involved in the production of ATP for the cell. The Matrix also contains chromosomes DNA, ribosomes, messenger RNA and Transfer RNA which are utilized in the synthesis of small amount of proteins for use within the matrix. However the bulk of the proteins required in the mitochondrion is synthesised in the cytosol. The mitochondrial matrix also contains granules which store calcium ions. The mitochondrion produces about 100 molecules of ATP per second.

Clinical Correlates

Muscle tissues are most commonly affected by mitochondrial deficiency diseases because of their high-energy metabolism. Most mitochondrial diseases often result from chromosomal defect in the nucleus or in the mitochondrion. Hereditary mitochondrial diseases are usually maternal in origin because only very few paternal mitochondria are left in the zygote following fertilization.

RIBOSOMES

Ribosomes are small, electron-dense particles not enclosed in membrane and are located in the cytosol. Measuring about 20-30 nanometer they are basophilic and stained by all basic dyes.

Ribosome is composed of rRNA and about 80 different proteins. It usually occur in two subunits, large and small subunits. The rRNA of the ribosome is synthesised in the nucleus while its protein is synthesised in the cytosol.

Ribosomes are involved in protein synthesis. While cytosolic proteins (free proteins) are synthesised by polyribosomes, secretory and endoplasmic reticulum proteins are synthesised on the membrane of rough endoplasmic reticulum.

Ribosomes occur in three forms:

- In isolated particles
- Assembled in cluster on mRNA strand to form **Polyribosome**
- Adsorbed to the membrane of endoplasmic reticulum through their large subunit to form **Rough Endoplasmic Reticulum**.

Protein synthesis by ribosomes also implicates: mRNA, tRNA and rRNA.

LYSOSOME

- What is it? Membrane-bound organelle
- Functions:
 - a. site of intracellular digestion
 - b. Site of turnover of cellular components
- Contents: Contains up to 40 different acid Hydrolytic enzymes (pH – 5)
- Distribution: Found in cells involved in extensive phagocytic activities, e.g. Macrophages and Neutrophil
- Nature of Lysosomal Enzymes:

Most of these are acid hydrolases and are involved in breaking down a wide range of macromolecules, they include:

 - a. Proteases
 - b. Nucleases
 - c. Phosphatases
 - d. Phospholipases
 - e. Sulfatases
 - f. Beta Glucuronidases

These enzymes are inactive in the Cytosol because of Cytosol pH of 7.2

- Sources of Lysosomes: Its membrane is derived from Golgi apparatus while the enzymes are synthesised in the endoplasmic reticulum

AUTOPHAGOSOME:

Organelles and certain cytoplasmic components might become enclosed in membrane and subsequently fused with lysosome to form **Autolysosome**. This phenomena is referred to as **Autophagy**.

HETEROLYSOSOME

This is the product of the fusion of lysosome with membrane-bound endocytosed material.

RESIDUAL BODY

This is heterolysosome containing indigestible materials such as lipofuscin granules of the neuron and heart muscles.

UTILIZATION OF LYSOSOMAL ENZYMES

- a. For intralysosomal digestion
- b. For Extracellular digestion/destruction e.g. osteoclast breakdown of bone matrix
- c. Metabolism of several substrate all over the body

CLINICAL CORELATES

Lysosomal diseases: These are diseases resulting from accumulation of substances that could not be metabolised due to the absence of lysosomal enzymes. Examples include:

- **Metachromatic Leukodystrophy:** Absence of Lysosomal sulphatases leads to accumulation of Sulphated cerebroside
- **I-Cell Disease (Inclusion cell disease):** Absence of Golgi phosphorylation enzyme leading to transfer of non-phosphorylated enzymes into lysosomes; These enzymes are released into the blood stream living the lysosome empty to form large inclusion body.

PROTEASOMES

- **What are they?** These are cytoplasmic protein complexes, the size of ribosomes. They are involved in the removal of denatured or non-functional polypeptides as well as proteins no longer required by the cell. They also restrict or terminate the activities of some proteins (Enzymatic proteins). This function could be referred to as protein quality control.
- **What is the structure?** Cylindrical unit made up of 4 rings each containing 7 proteins. At each end of the proteasome is a regulatory particle which contains ATPase
- **What is its Mechanism of Action?** Proteasome recognises proteins destined for destruction and are coupled to **UBIQUITIN MOLECULE**. With the aid of the ATPase the protein-Ubiquitin complex is broken down to peptides and Ubiquitin molecules which are then released into the cytosol for reuse. The peptides could be broken down into amino acids to build other protein molecules such as antigen presenting complexes

- **CLINICAL CORELATES**

Failure or absence of proteasome action may lead to aggregation of non-functional protein which invariably might lead to cell damage and release of products of cell damage into the extracellular space as in Alzheimer and Huntington disease of the brain.

PEROXISOME/MICROBODIES

What are they? Peroxisomes are membrane-bound organelles which contain various enzymes and utilise oxygen without the production of ATP. Measuring about 0.5 micron in diameter they **oxidise organic substrate** by the removal of hydrogen ions, leading to the production of H₂O₂. This is immediately broken down by **peroxisomal catalase** to prevent its toxic effect on the cell. The oxygen atom released from this process is utilized in oxidation of other potentially toxic substances/drugs in the liver (Ethyl alcohol) and kidneys. Peroxisomes are also implicated in lipid metabolism (Beta oxidation of long-chain [18 carbon and over] fatty acids).

Source of Peroxisome:

Peroxisomal enzymes are synthesised on polyribosome while the membranes originate from endoplasmic reticulum

CLINICAL CORELATES:

- **Zellweger Syndrome:** This is characterised by deficiency of peroxisomal enzyme leading to muscular, liver, kidney and nervous system lesions. In this condition the peroxisome is empty.
- **X-Linked Adrenoleukodystrophy:** This is characterised by failure of Beta oxidation of long-chain fatty acid. This fatty acid accumulates leading to damage to myelin sheaths in the nervous system.

THE ENDOPLASMIC RETICULUM (ER)

This organelle is made up of anastomosing network of intercommunicating channels/cisternae/sacs enclosed in a continuous membrane.

ER occurs in two forms, namely Rough and Smooth which are also interconnected. While the cisternae of smooth ER are tubular in shape, those of Rough ER are flattened. The roughness on the surface of rough ER is due to the adsorption of polyribosome on their outer surface. Polyribosome also impacts the basophilic staining characteristic on RER. Furthermore, its membrane is continuous with that of the nuclear envelope.

Distribution and Functions of RER

RER is prominent in protein synthesising cells such as; Pancreatic acinar cells, cells of the endocrine glands, plasma cells, fibroblast etc.

Proteins synthesised in RER are stored in Lysosomes or granules; stored temporarily before exocytosis or used as integral membrane proteins.

Smooth Endoplasmic Reticulum (SER)

This is ER not bound to polyribosomes but continuous with RER and are less abundant in cell containing RER.

Distribution and Functions of SER

SER is found in all cells where they are involved in:

- The synthesis phospholipids and cholesterol used in all cellular membranes including membranes of organelles.

They occur in abundance in other cells where they are involved in:

- Sequestration and release of Calcium ions a vital process in muscular contraction
- Biosynthesis of Lipids required for synthesis of steroid hormones
- Detoxification of potentially harmful compounds such as alcohol and barbiturates

GOLGI APPARATUS (COMPLEX)

This is a complex of smooth membranous saccule usually located between the apical membrane and the nucleus of the secretory cell. Within its saccule are various enzymes implicated in processing proteins synthesised in the endoplasmic reticulum. The Golgi apparatus receives transport vesicles containing proteins from the endoplasmic reticulum and packages modified proteins into condensing vesicles for transportation to other organelle or to the cell membrane for release of modified proteins as secretory products. Protein modification occurring in the Golgi apparatus includes concentration, glycosylation, sulfation, phosphorylation and proteolysis.

THE CYTOSKELETON

This is composed of a complex of microtubules, microfilaments (Actin Filaments), and Intermediate Filaments.

- **Microtubules**

These are tubular protein subunits involved in cellular shape, cell division, intra and extra cellular movements and transport of substances in the cytoplasm of the cell. Microtubules are widely distributed within the cytoplasm where they occur in various forms which include:

- a. Cytoplasmic microtubules for intracellular transport of materials including organelles
- b. Centrioles which are involved in cell division
- c. Mitotic spindles which are involved in cell division
- d. Cilia and Flagella which are motile structures implicated in cellular motion
- e. Basal bodies which are located at the bases of cilia and flagella and are involved in the configuration of these structures.

- **Microfilaments/Actin Filaments**

Microfilament is a double-stranded helix of globular protein subunits which is widely distributed in all body cells and is involved in the structural integrity and contractility of the cell as well as movement of organelles in the cytosol. Actin filaments are also implicated in cell cleavage during cell division.

Actin filament is seen in two forms in the cell viz. polymerised F-Actin and free Globular G-Actin.

F-Actin filaments are involved in:

1. Muscular contraction in collaboration with myosin filaments
2. Cell shape integrity and locomotion (stress fibres of crawling cells)
3. Movement of organelles and other cytosolic contents (cytoplasmic streaming)
4. Cellular cleavage in mitotic cells

• **Intermediate Filaments**

As the name implies, intermediate filaments are intermediate in size to microtubules and microfilaments (10-12 nanometer in diameter). They are more stable structurally than Microtubules/filament and are composed of variable protein subunits depending on their localization and functions

Examples of intermediate filaments include:

1. **Keratin** of epithelial cell for strength and protection
2. **Vimentin** of the mesenchymal cell for structural integrity
3. **Desmin** of the muscle cell for structural integrity
4. **Neurofilament** of the nerve cell for structural integrity
5. **Lamins** of all cell nuclei also for structural integrity

CLINICAL CORRELATES:

Immotile cilia Syndrome: This results from abnormalities in the microtubular structure leading to immotile cilia and flagella as in male sterility and chronic respiratory infection.

Tumor Diagnosis: Identification of the intermediate filament in a tumor cell would facilitate the knowledge of tumor type in tumor studies.

Antimitotic Alkaloids: These substances arrest cell division by interfering with the organization of mitotic spindles. They are thus used in cancer therapy to prevent cell proliferation

- **Centrosome/Centrioles:**

The centrosome is the region of the cytosol situated between the nucleus and the Golgi apparatus. It accommodates the Centrioles which are two cylindrical shaped microtubular structures oriented at right angles to one another. Each cylinder is made up of nine triplets of parallel microtubules. Centrioles are implicated in organizing the microtubules of the cell as in the organization of mitotic spindles during cell division. They also form the basal bodies of cilia and flagella

INCLUSION BODIES

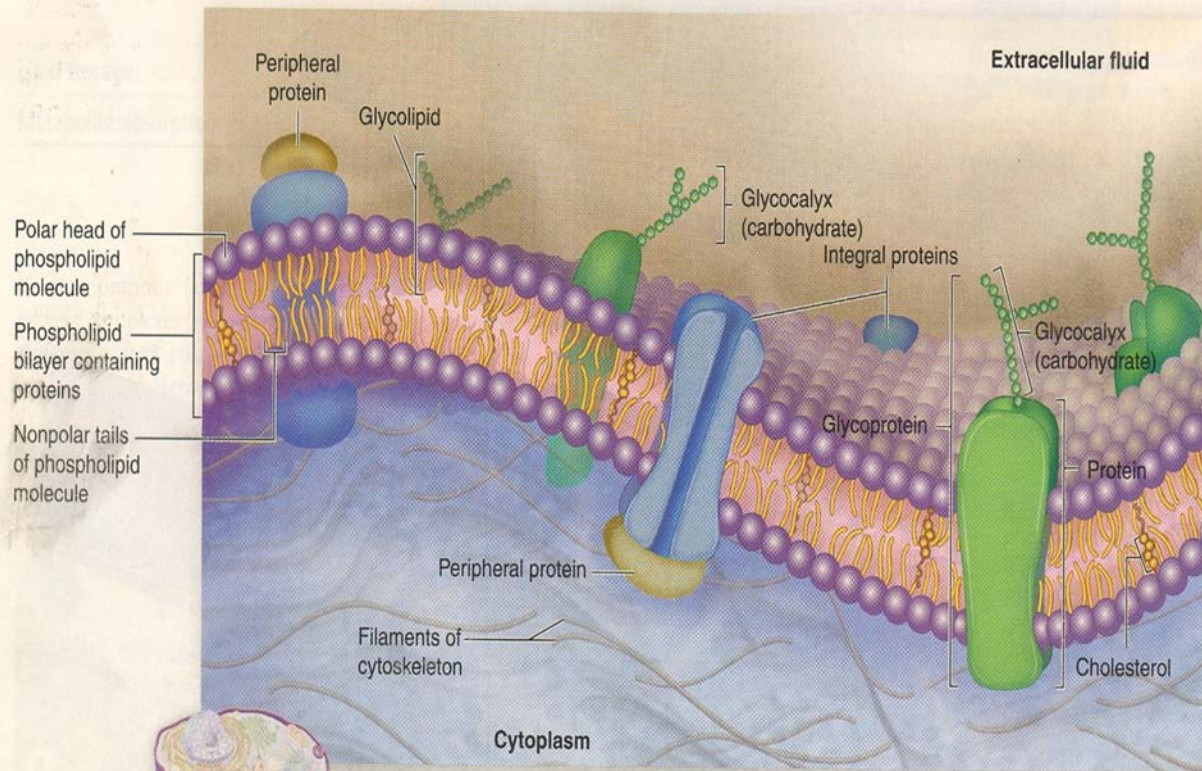
Inclusion bodies are the transitory residents of the cytoplasm not involved in cell metabolism and do not survive cell division. They comprise mainly accumulated metabolites, lipid droplets and pigments and are sporadically distributed in body cells.

Examples of Inclusion Bodies Include:

- Fat droplet of the adipocytes, liver cells and cells of the adrenal cortex
- Glycogen granules, which occurs in form of carbohydrate polymer for glucose storage in various cells. They are PAS-positive and not enclosed in membranes
- Membrane bound secretory vesicles or granules containing proteins to be released out of the cell by exocytosis
- Pigments: These include:
 1. Lipofuscin, golden-brown pigments which are found only in stable and non-dividing cells where they accumulate progressively with age and thus used to determine cell's age. They derived from the residual bodies following lysosomal digestion.
 2. Melanin Pigments: These are localized in the epidermis, locus coeruleus and the substantia nigra
- Minerals: These include:
 1. Calcium and Magnesium in the pineal gland (brain sand)
 2. Zinc in the hippocampus
 3. Iron in the oculomotor nucleus

Fig. C 3

The Plasmalemma



Functions of plasma membrane

- 1. Communication:** Contains receptors that recognize and respond to molecular signals
- 2. Intercellular connection:** Establishes a flexible boundary, protects cellular contents, and supports cell structure
- 3. Physical barrier:** Phospholipid bilayer separates substances inside and outside the cell
- 4. Selective permeability:** Regulates entry and exit of ions, nutrients, and waste molecules through the membrane