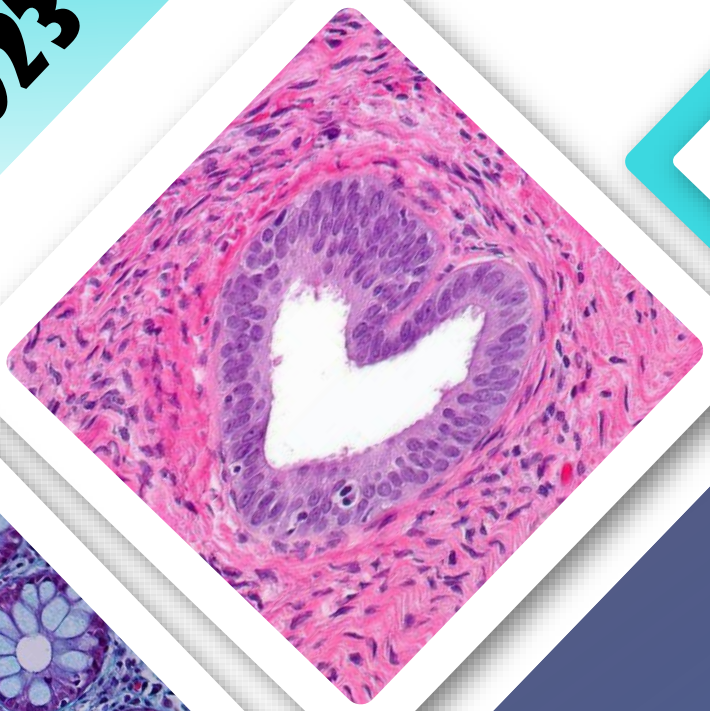
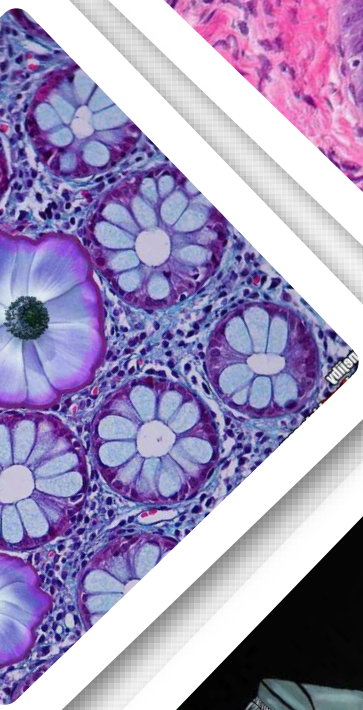
2023





For Medical Students

HISTOLOGY

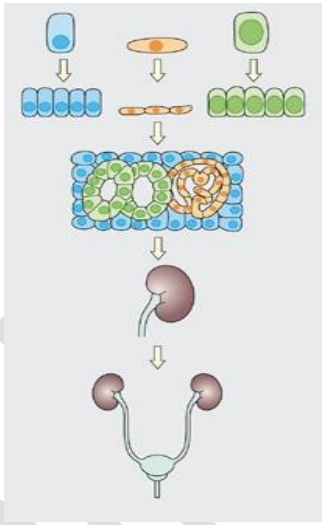
Dr. Iman Nabil

نبراس
Nebras

Foundation Module

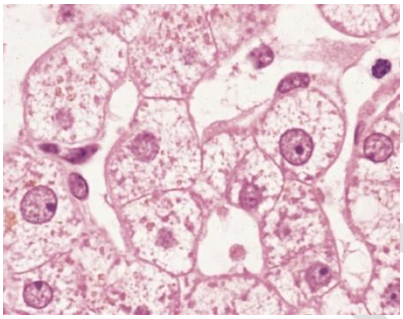
FOUNDATION MODULE

- The cell is the functional & structural unit of the body.
- A group of cells with similar structure & function will form tissues.
- These tissues are grouped to form organs.
- A group of organs collect to form the body systems.



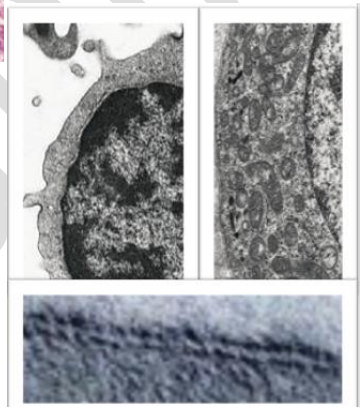
Cell Membrane

Plasma membrane = Plasmalemma



LM: It cannot be seen by light microscope *because* it is too thin to be seen *but* the condensation of the stain on the outer surface of the cell membrane marks its.

EM:

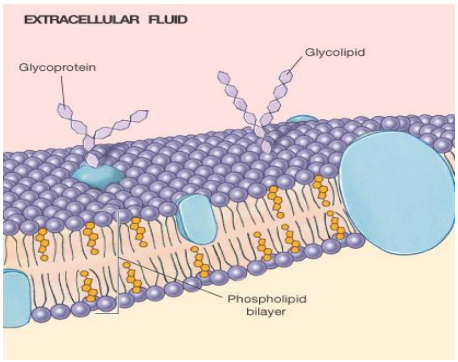


1- **At Low Magnification:** thin dense line (خط رفيع غامق) 8 - 10 nm in thickness.

2- **With Higher Magnification:** a **trilaminar structure,** (3 طبقات) with an outer (= extracellular leaflet) (الورقية الوجه للجزء الخارجي من الخليه) and an inner (= cytoplasmic leaflet) (غمقه) electron dense lines and a middle electron (فتحه) lucent zone in between.

The entire structure is known as the unit membrane.

Molecular structure of the Cell membrane:

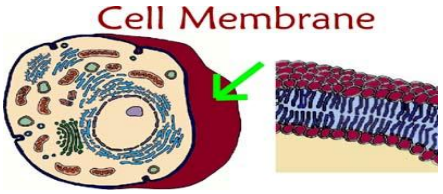


3 Components: (مكونات)

1-**Lipid molecules:** (الدهون) **a- phospholipids b- cholesterol**

2- **Protein molecules.** **3- Carbohydrate molecules**

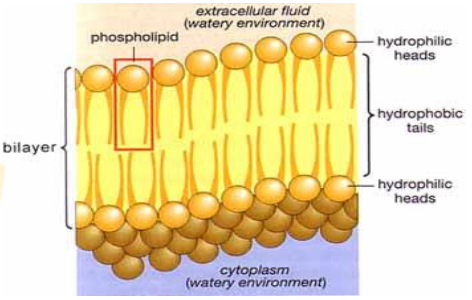
The cell membrane & almost all the membranes surrounding the membranous organelles have the same structure except for minor differences.



1- Lipid Molecules

A- Phospholipids:

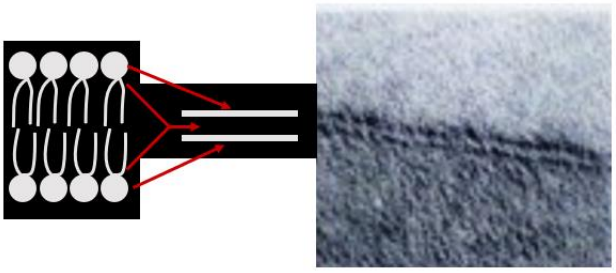
- Each phospholipid molecule consists of:



1- **One polar hydrophilic head:** faces the aqueous media on either side of the membrane.

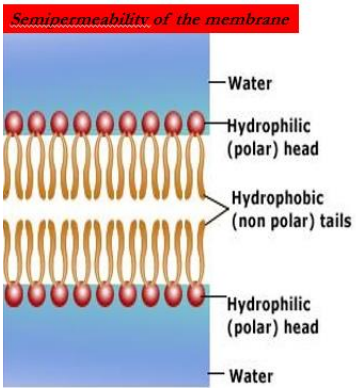
2- **Two long non-polar hydrophobic tails (fatty acids):** project towards the center of the membrane facing each other. They form weak non-covalent bonds with each other, holding the bilayer together.

Why does the cell membrane appear as a trilaminar structure? **Deposition of osmium in the hydrophilic heads**



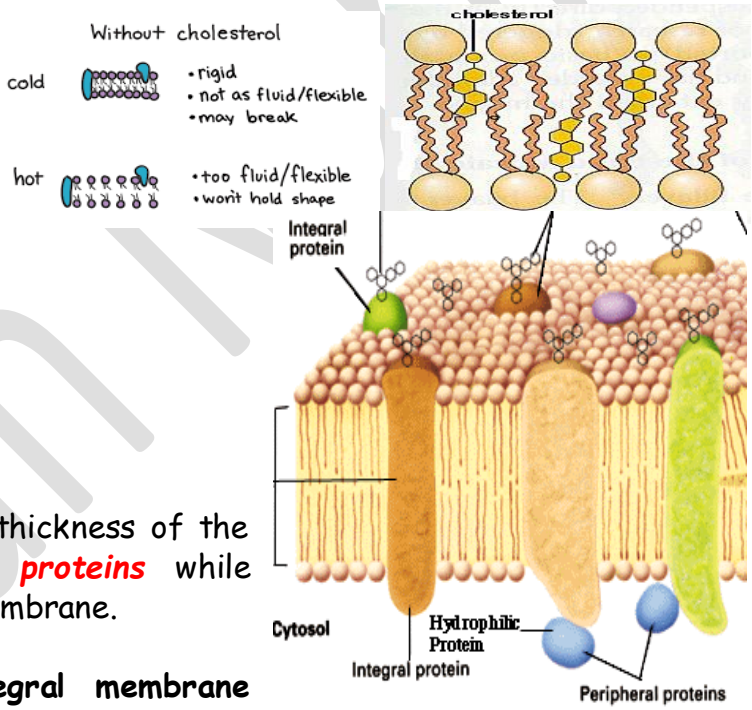
Functions of Phospholipid molecules:

- **Prevent passage of:**
  1. Water soluble substances.
  2. Polar ions.
- **Allow passages of:**
  1. Fat soluble substances.
  2. Nonpolar substances.



B- Cholesterol:

- They are incorporated within the lipid bilayer.
- **Functions of Cholesterol:**
  1. Stability of the membrane.
  2. Regulation of membrane fluidity in body temperature.



2- Protein Molecules

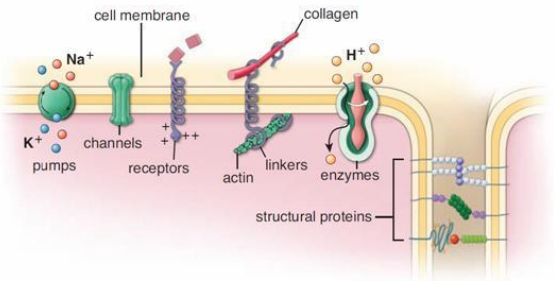
- **Two Types:**

A-Integral Membrane Proteins:

- They are embedded within the lipid bilayer.
- Most of these proteins traverse the whole thickness of the membrane and are called ***transmembrane proteins*** while others are ***partially embedded*** within the membrane.

- **There are six functional forms of integral membrane proteins:**

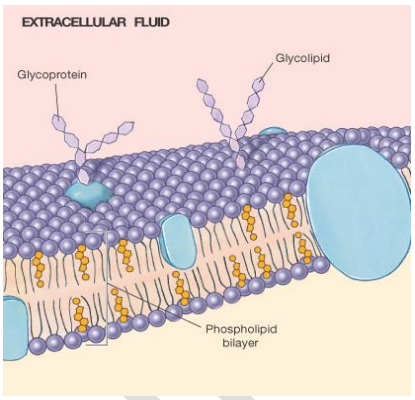
1. ***Pumps***: transport ions (Na+, K+) actively across the membrane.
2. ***Channels***: transport substances passively.
3. ***Receptors***: allow binding of specific molecules e.g., hormone.
4. ***Enzymes***: ATP synthase of the inner mitochondrial membrane and some types of digestive enzymes in the small intestine.
5. ***Linkers***: anchor the intracellular cytoskeleton to the extracellular matrix.
6. ***Structural proteins***: form junctions between neighboring cells.



B-Peripheral Membrane Proteins:

- They are not embedded into lipid bilayer, but they are *loosely associated* with membrane.
- They are usually located on the cytoplasmic surface of the membrane.
- **Function**: form a link between the cell membrane and the cytoplasmic components.

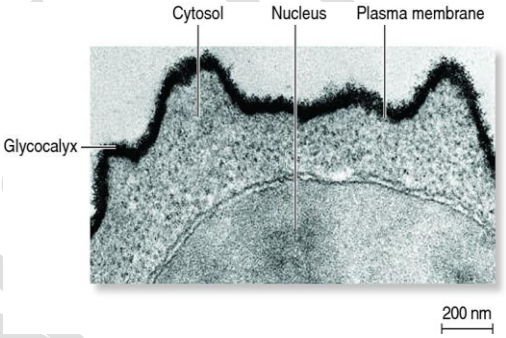
3- Carbohydrate Molecules



- They are present as glycoproteins and glycolipids of the cell membrane.
- They are oriented towards the outside of the membrane forming the *cell coat* or *glycocalyx*.
- The cell coat is represented by the "*fuzzy*" material on the outer surface of the membrane.

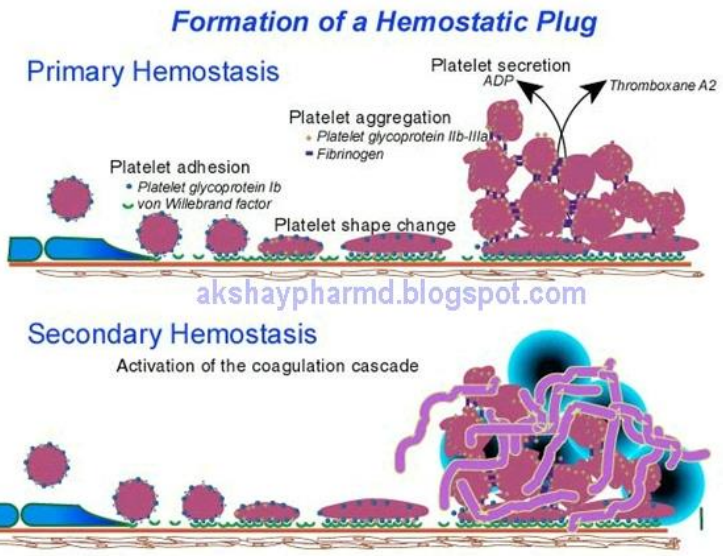
Functions of cell coat:

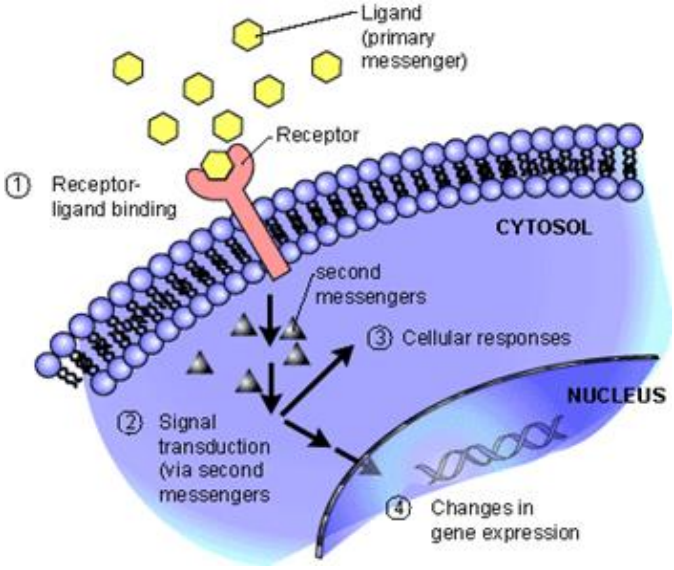
1. *Cellular recognition* e.g. the glycocalyx on the surface of red blood cells determines the four blood groups.
2. *Cell-cell adhesion*.
3. *Receptor:* for ligands by the glycoproteins of the cell membrane.



The ABO Blood System

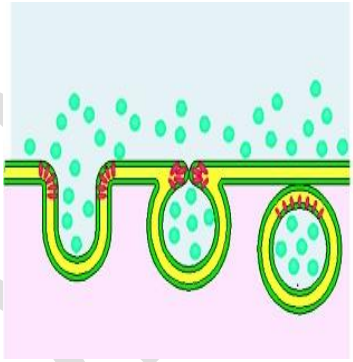
Blood Type (genotype)	Type A (AA, AO)	Type B (BB, BO)	Type AB (AB)	Type O (OO)
Red Blood Cell Surface Proteins (phenotype)	A agglutinogens only	B agglutinogens only	A and B agglutinogens	No agglutinogens





Vesicular Transport Across the Cell Membrane

•Mass transfer of materials through the cell membrane occurs by formation of *vesicles*.
•**It involves 2 processes:** 1- Endocytosis. 2- Exocytosis.

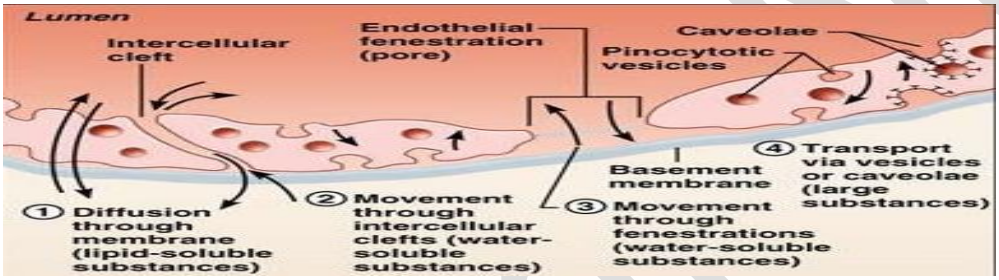


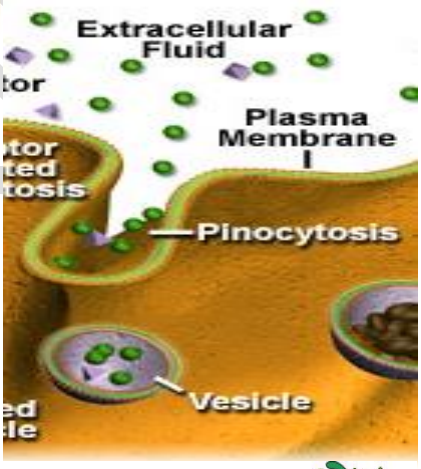
1-Endocytosis

- **Definition:** the uptake of material from the extracellular space.
- It is an *active process* that involves invagination of the membrane to form a vesicle.
- **3 mechanisms of endocytosis are present in the cell:**

A-Pinocytosis:

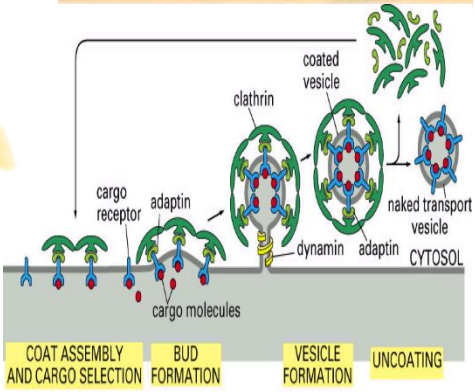
- **Definition:** *a non-selective process*, occurs in nearly all cell types for uptake of fluid containing ions and small protein molecules.
- **Vesicle:** pinocytotic vesicles are small and have smooth surface.
- **Site:** most evident in the endothelium of blood vessels.





B-Receptor- mediated endocytosis:

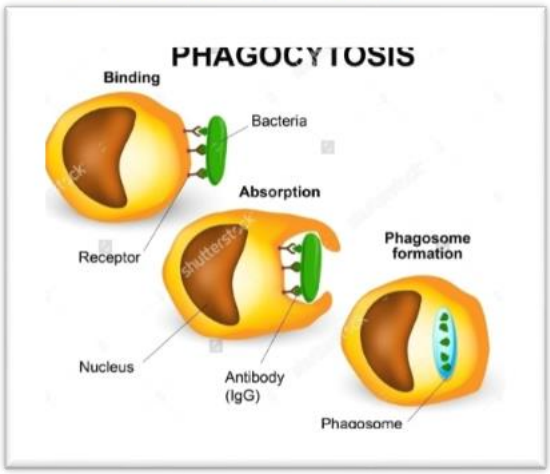
- **Definition:** *a highly selective* process resulting in uptake of specific substances by a specific cell that has *receptors* for these substances e.g. protein hormones.
- These receptors are concentrated in specialized regions of the plasma membrane called *coated pits* (coated by clathrin).



1. When a substance binds to its receptor, clathrin-coated pits invaginate and give rise to *clathrin-coated vesicles* containing this specific substance.
2. Clathrin is lost and recycled leaving *uncoated vesicles*.

C-Phagocytosis:

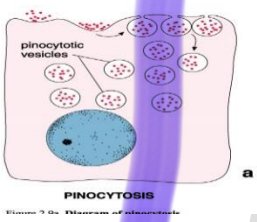
- **Definition:** ingestion of large solid particles, such as bacteria and cell debris, it is *a receptor-mediated* endocytosis; *however*, it does not involve formation of coated pits or vesicles.
- **Sites:** phagocytes e.g. macrophages& neutrophils.

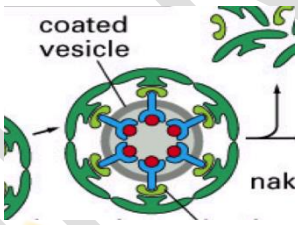


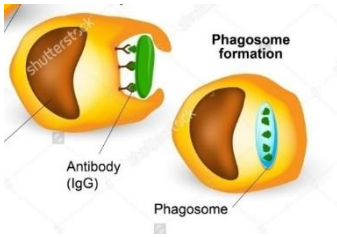
1. Binding of the receptor and foreign body results in extension

of *pseudopodia* that engulf the particle.
2. Fusion of the membrane to internalize the particle into the cytoplasm forming a *phagosome.*
3. The contents of the phagosome are then digested through *lysosome*.

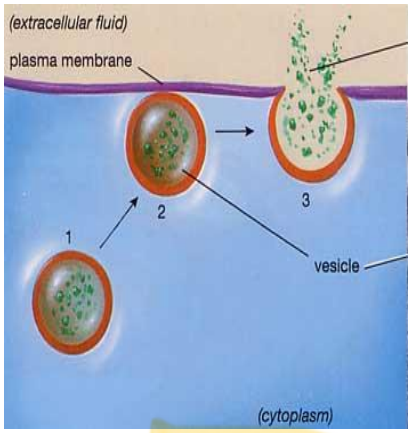
Types of endocytosis	Pinocytosis	Receptor mediated endocytosis	Phagocytosis
1- Endocytosed material	Fluid containing ions & small molecules.	Specific substances (ligand) e.g. hormone.	Large solid particles e.g. bacteria.
2- Receptors for endocytosed material	Nonselective.	Present.	Present.
3- Shape of the vesicle	Small& smooth.	Coated with clathrin.	No coated vesicle but the membrane fused to form phagosomes.
4- Type of cells	Nearly all cell types especially endothelium of blood vessels.	Specific cell that has receptor for specific substance.	Phagocytic cells.







2- Exocytosis



- **Definition:** the release of cell products into the extracellular space.
- During this process, a vesicle moves from the cytoplasm to the cell membrane, fuses with it and discharges its content.
- **There are 2 types of exocytosis:**

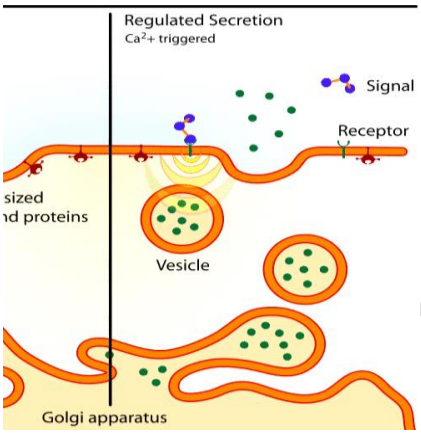
A-Regulated secretion (stimulus- dependent):

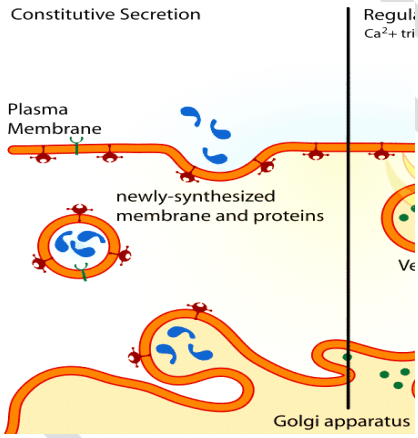
1. The secretory products become *stored* forming *secretory granules*.
2. As a result of a *stimulus* (hormonal or neural stimulus), these vesicles move to the surface and fuse with the cell membrane to pour their contents outside the cell. e.g., occurs during release of the digestive enzymes by the pancreas.

B-Constitutive secretion:

- The secretory products leave the cell *immediately* after their synthesis. These cells lack secretory granules.
- The secretion is released continuously through *secretory vesicles*.
- E.g. occurs during release of antibodies by plasma cells.

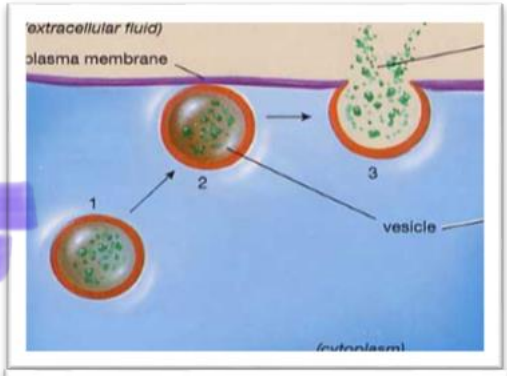
Types of exocytosis	Regulated secretion	Constitutive secretion
1- stimulus	Stimulus dependent.	No stimulus. They released continuously.
2- Secretory product	Concentrated & stored inside secretory granules.	Leave the cell membrane immediately after their synthesis. No secretory granules.
3- Example of the released secretion	Digestive enzymes from pancreatic cell.	Antibodies from plasma cell, fibers secreted from fibroblast.

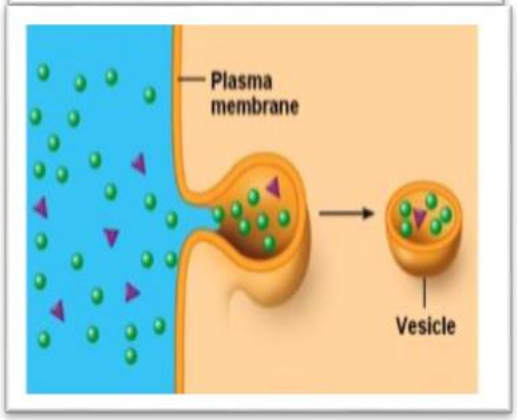




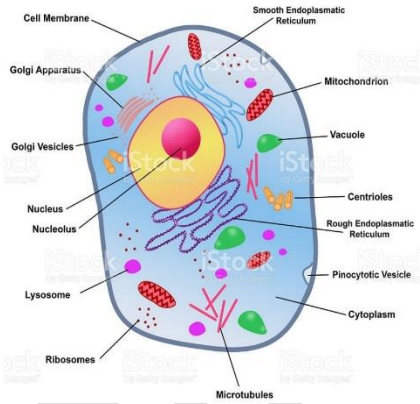
Membrane Recycling

- During the vesicular transport, the cell membrane is maintained; the excess membrane added to the cell membrane by ***exocytosis*** is constantly recycled again into the cytoplasmic compartments by ***endocytosis***.





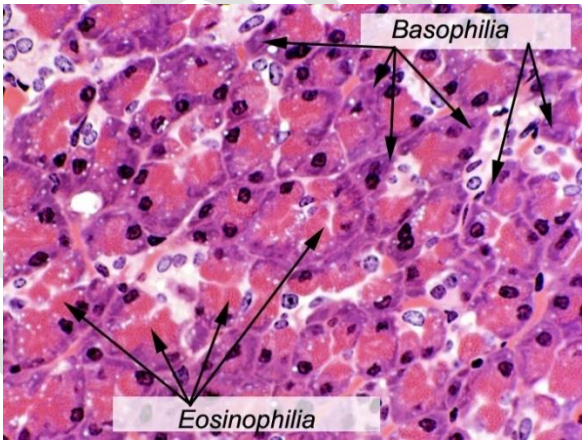
Cell Organelles



- **Definition**: metabolically active structures carrying out specific essential functions.
- **Types**:
  1. **Membranous organelles:** nucleus, endoplasmic reticulum, Golgi apparatus, transport vesicles, endosomes, lysosomes, mitochondria, and peroxisomes.
  2. **Non-membranous organelles:** ribosomes, centrosome, and the cytoskeleton.

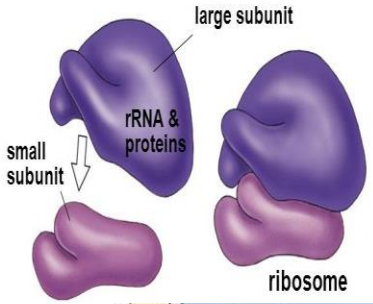
N.B: Haematoxylin and Eosin (H&E):

- **Haematoxylin** is a basic violet stain.
- **Eosin** is an acidic pink stain.
- **Basophilic structure**= A structure that has affinity to stain with basic dyes = acidic in nature…… So it stains violet with haematoxylin.
- **Acidophilic or eosinophilic structure**= A structure that has affinity to stain with acidic dyes = basic in nature……So it stains pink with eosin.

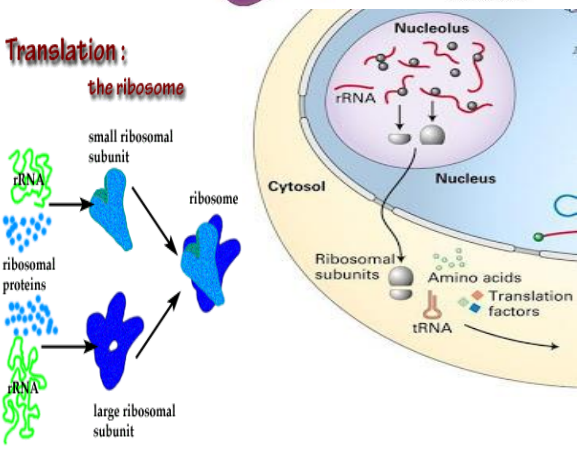


1-Ribosomes

- **Definition:** granules of *nucleoproteins* (ribosomal RNA (rRNA) + proteins).
- **Site:** They are present in all cells *especially* in protein synthesizing cells.
- **Structure:** *two subunits;* small subunit & large subunit.
- **Synthesis:**

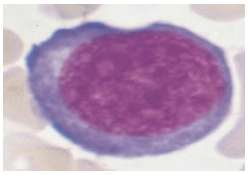


1. The rRNAs are synthesized inside *the nucleolus*.
2. Ribosomal-associated proteins are synthesized in *the cytoplasm*.
3. Ribosomal subunits then leave the nucleus, via the nuclear pores, to enter the cytoplasm.



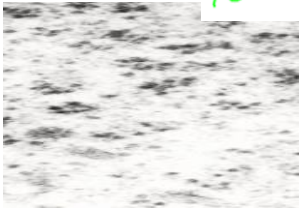
The small and large subunits are present in the cytosol individually and do not form a ribosome until protein synthesis begins.

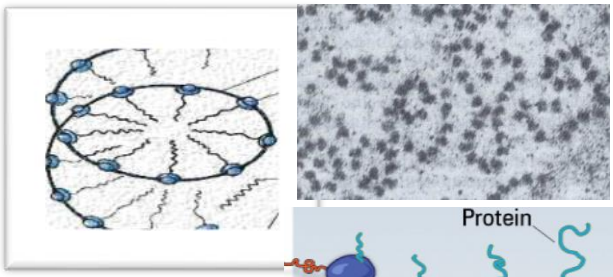
- **LM:**

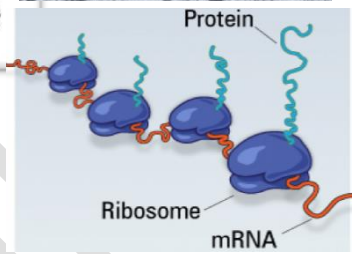


When present in large amounts they cause *cytoplasmic basophilia.*

- **EM:** Ribosomes are small electron dense granules.







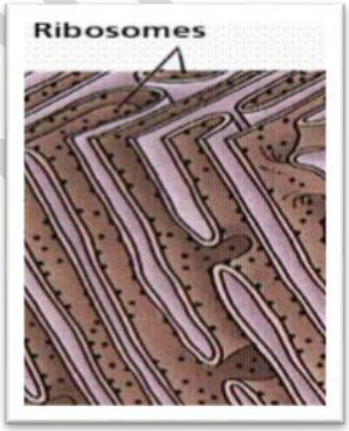
- **Types:**

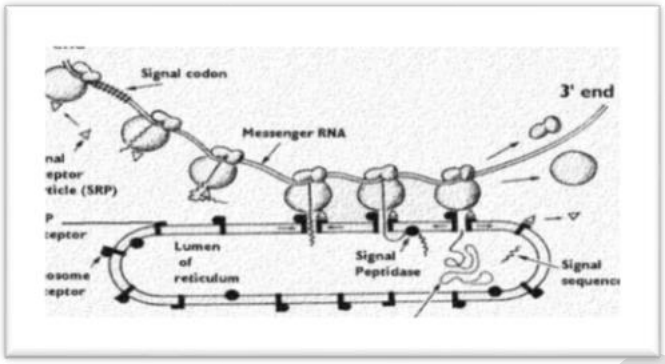
A-Free ribosomes:

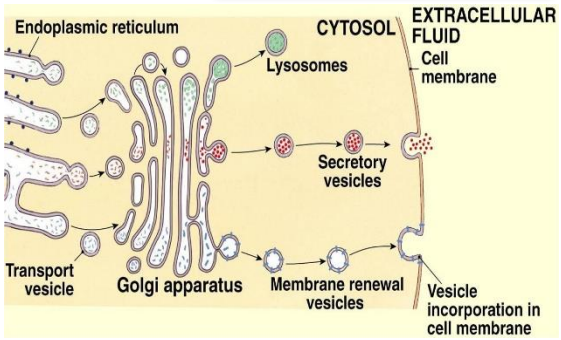
1- **Solitary particles:** scattered in the cytoplasm.
Function: act as ***a reserve***.

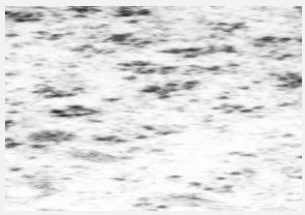
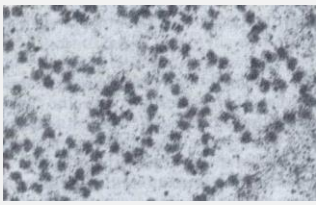
2- **Aggregated (polysomes):** clusters of 10 or more connected by single strand of mRNA.
Function of polysomes: responsible for ***synthesis of cytosolic protein*** e.g. in dividing cells and growing cells, synthesis of hemoglobin in developing red blood cells and contractile protein in muscle cells.

B- Attached ribosomes: these are polysomes that become attached to the outer membrane of the endoplasmic reticulum.





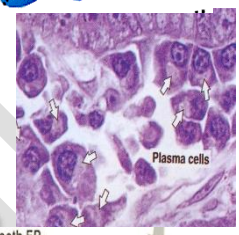


Types of ribosomes	Free solitary ribosomes	Free aggregated ribosomes (polysomes)	Attached ribosomes
1- LM		Not seen but in large amount give cytoplasmic basophilia.	Not seen but in large amount give cytoplasmic basophilia.
2- EM	Small electron dense particles.	10 or more ribosomes connected by a single strand of mRNA.	Small electron dense particles attached to rER.
3- Function	Reserve. 	Synthesis of cytosolic proteins (used within the cell) 	Synthesis of secretory proteins, lysosomal enzymes& membrane proteins. 

2-ENDOPLASMIC RETICULUM

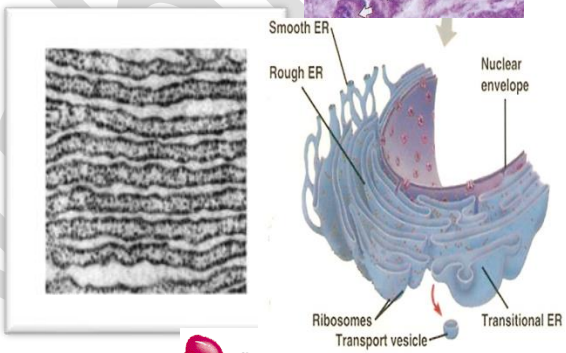
- The endoplasmic reticulum forms the most extensive membrane system in the cytoplasm.
- *The ER has two types:*
  - Rough endoplasmic reticulum (rER).
  - Smooth endoplasmic reticulum (sER).
  - ***Both types form a single membrane system.***

1-Rough Endoplasmic Reticulum (rER):



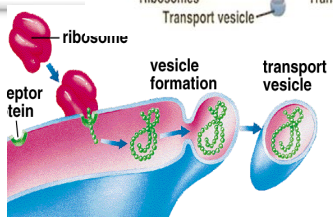
LM: When present in large amounts they cause *cytoplasmic basophilia* due to their attached ribosomes.

EM:

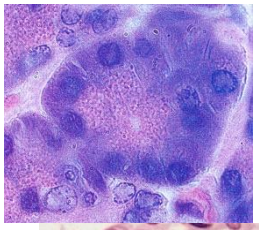


1. It consists of interconnected parallel flattened sacs called *cisternae*.
2. Its outer surface is studded *with ribosomes.*
3. It is continuous with the outer membrane of the nuclear envelope.
4. The lumen contains flocculent material that represents newly formed protein.

FUNCTIONS:

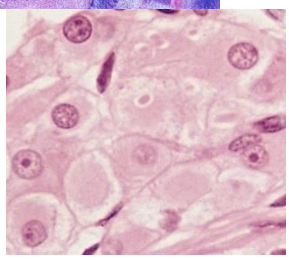


1. *Synthesis of* secretory proteins, lysosomal enzymes and proteins inserted into the cytoplasmic membranes.
2. *Post-translational modification* of the newly-formed protein e.g.folding, sulfation and initial glycosylation.
3. *Transport* the newly synthesized protein to the Golgi body by transport vesicles.



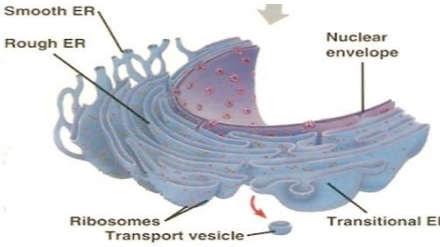
SITES: Protein synthesizing & secreting cells e.g. liver cells, pancreatic acini, fibroblasts and plasma cells.

2-Smooth Endoplasmic Reticulum (sER)

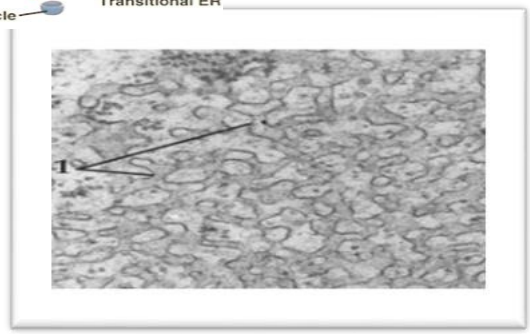


LM: Cells with large amounts of sER exhibit *cytoplasmic eosinophilia*.

EM:



1. It consists of close network of *interconnected branching tubules and vesicles*.
2. The membranes have smooth surface.
3. The membranes of the sER are continuous with that of rER.



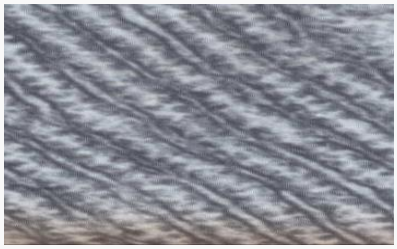
FUNCTIONS:

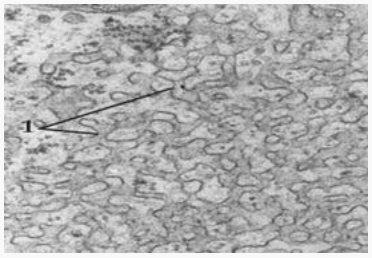
1. Synthesis of *membrane lipids*; the phospholipids and cholesterol.
2. Synthesis of *steroid hormones*.
3. Synthesis of *glycogen* in liver.
4. *Detoxification* of toxic substances e.g. alcohol and drugs.

5. Regulation of ***calcium ions*** during muscle contraction.

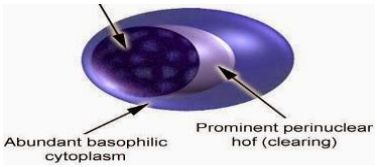
SITES: steroid-secreting cells (in the adrenal cortex, testis and ovary), liver cells & muscles.

Types of endoplasmic reticulum	Rough endoplasmic reticulum	Smooth endoplasmic reticulum
1- LM	Not seen but in large amount give cytoplasmic basophilia.	Not seen but in large amount give cytoplasmic acidophilia.
2- EM	Parallel, flattened interconnected tubules. Studded with ribosomes.	Interconnected branching tubules and vesicles. No ribosomes.
3- Functions	1- Synthesis of secretory proteins, lysosomal enzymes& membrane proteins. 2- Post translational modification of protein. 3- Transport protein to Golgi.	1- Synthesis of lipid & cholesterol of the cell membrane. 2- Synthesis of steroid hormones. 3- Synthesis of glycogen. 4- Detoxification of toxic substances. 5- Storage of calcium in muscles.
4- Sites	Protein secreting cells e.g. liver , fibroblasts.	Steroid secreting cells, liver & muscles.



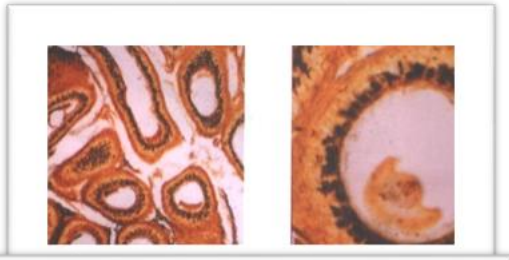


3-Golgi apparatus



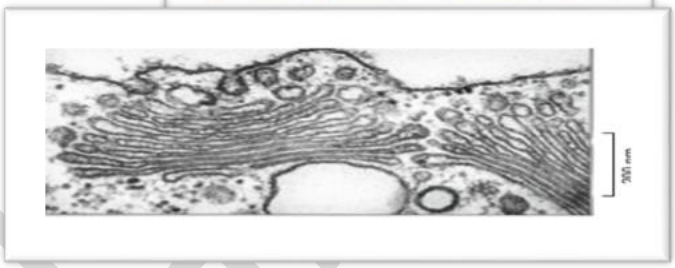
LM:

1. It is *not stained* with H&E in routine histological sections.
2. H&E-stained sections of the cells synthesizing protein, its site could be seen as *negative Golgi image* e.g. plasma cells.
3. It can be seen in histological sections stained with *silver stain*.



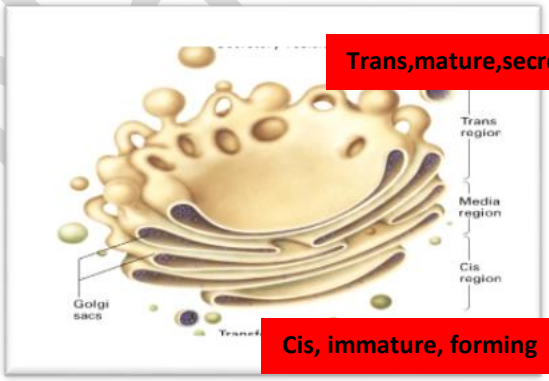
EM:

1. It consists of saccules or cisternae called the ***Golgi stacks***.
2. Each stack consists of 4- 6 ***cisternae*** (flattened, curved, membrane-bounded, slightly expanded at the ends).
3. The Golgi stack is ***cup-shaped*** with a convex surface and a concave surface:
   a) ***The cis face*** (***forming face; immature face)***:



   - Convex in shape.
   - Lies near to the rER.
   - It is the site where <u>the transport vesicles</u> containing the newly formed proteins from rER enter the Golgi for further processing.

   b) ***The trans face*** (***secretory face; mature face):***

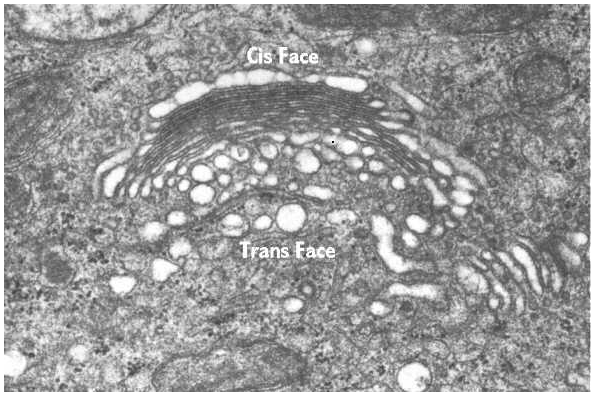


Trans,mature,secretory

Cis, immature, forming

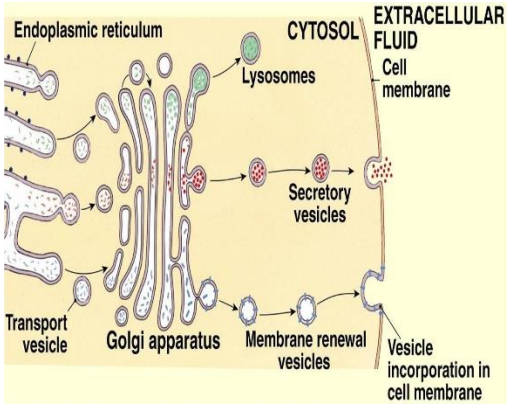
   - Concave in shape.
   - It is the site where the modified protein is packaged and released from the Golgi in <u>large secretory vesicles</u>.

   c) ***The medial compartment:*** **Between the cis & trans compartments.**



Functions:

1. *Post-translational modifications* of proteins e.g. addition of sugars.
2. *Packaging* of different proteins in membrane bounded vesicles.
3. *Sorting and targeting of vesicles* to the right destination:
   - Formation of lysosomes.
   - Formation of secretory granules for exocytosis.
   - Membrane recycling.



Sites: Protein synthesizing and secretory cells.

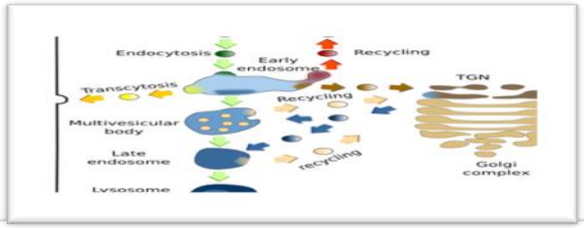
N.B: Cytoplasmic Organelles that participate in the process of Protein synthesis:

1- Ribosomes (factories)

2- Rough endoplasmic reticulum (modification& transport)

3- Golgi apparatus (chemical modification,package,sorting& targeting)

4-Endosomes

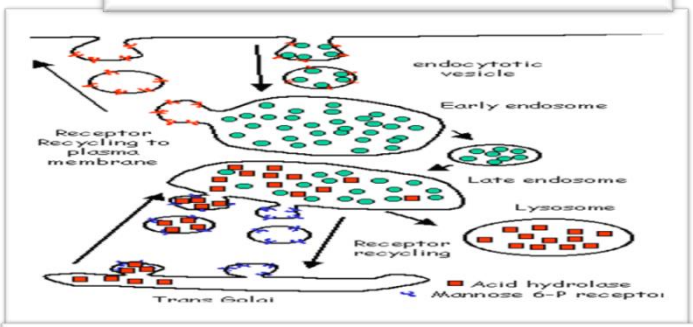


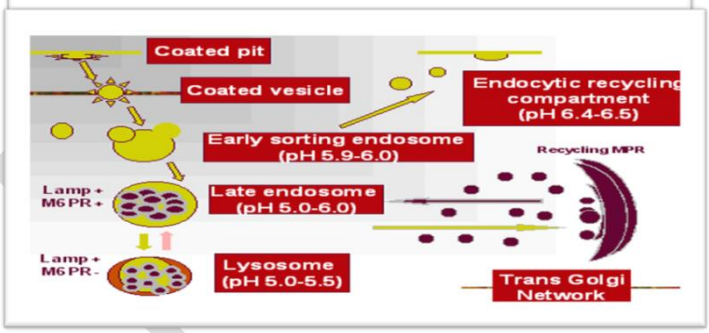
Definition: are system of vesicles and tubules involved in the endocytotic pathway.

Types:

A-Early endosomes:

- **Site**: at *the periphery of the cell* as a part in the pathway of the receptor-mediated endocytosis.
- **Content**: the receptors-ligands complex.
- The membrane of the endosomes pumps H^+ ions into its interior→ lowers the pH of endosomes to less than 6→ *uncoupling of the receptors and the ligands.*
- The receptors recycle to the cell membrane and the ligands move to the late endosomes.





B-Late endosomes:

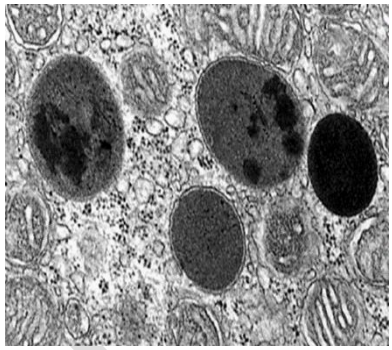
- **Site**: *deep* within the cytoplasm near the Golgi complex.
- **They receive**:

1. *the ligands* from early endosomes.
2. *clathrin- coated vesicles* containing lysosomal enzymes from Golgi complex.

- **PH**: 5.5. (The enzymes become active at the acidic pH of the late endosome).
- ***The lysosomal enzymes in the late endosome begin to degrade the ligands accompanied by further decrease in the internal pH which then "mature" to form lysosomes.***

Types of endosomes	Early endosome	Late endosome
1-Site	Periphery of cytoplasm.	Deep in cytoplasm , near Golgi.
2- Content	Receptor ligand complex.	1- Ligands from early endosome. 2- Lysosomal enzymes from Golgi.
3-Function	Uncoupling of the receptor from ligand.	Lysosomal enzymes begin to degrade ligands, then the late endosome matures to lysosome.
4- pH	Less than 6.	5.5.

5-Lysosomes

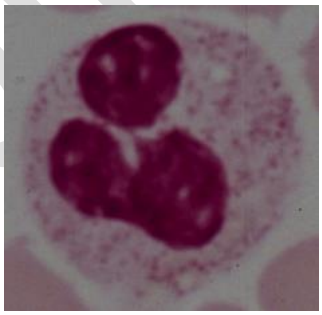


Definition: membrane-bounded organelle containing about 40 types of *acid hydrolytic digestive enzymes* (proteases, nucleases, phosphatases, and lipases).

Function: They are responsible for *intracellular digestion* of different materials.

Synthesis: by a *gradual maturation process* as by fusion of the clathrin- coated vesicles coming from Golgi complex with late endosomes.

Lysosome has a *surrounding membrane with unique phospholipids & specialized glycoproteins line the lysosomal membrane from inside* that prevents:



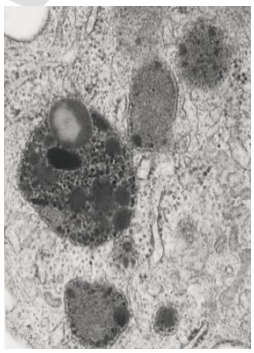
1- the leak out of the enzymes to the cytoplasm.

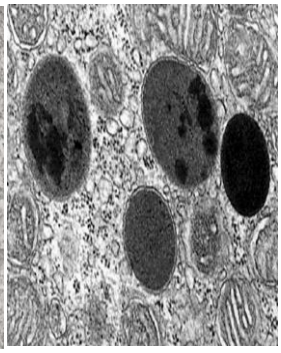
2- protects the membrane from hydrolysis by its own enzymes.

- If a lysosome leaks its contents, the released enzymes would be inactive because of neutral pH of the cytoplasm.

LM:

They can be recognized by several histochemical methods used to demonstrate the lysosomal enzymes.



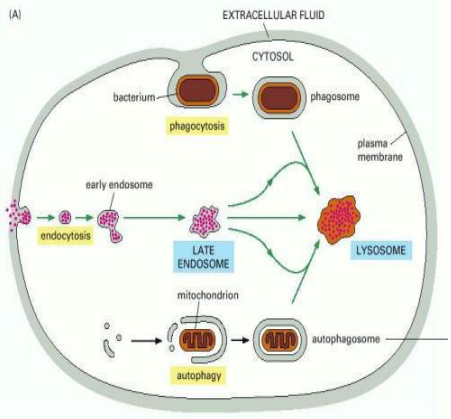


EM:

Lysosomes are *heterogeneous* in shape and the appearance of their interior. Some are electron dense, others show electron lucent areas.

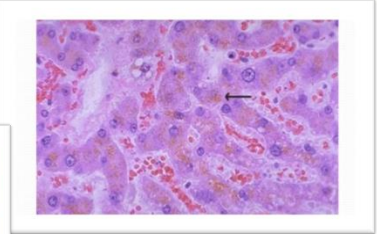
Site: are abundant in phagocytic cells.

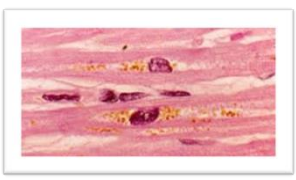
Pathways for intracellular digestion by lysosomes:

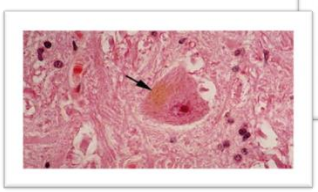


1. **Extracellular small particles:** internalized by pinocytosis and receptor-mediated *endocytosis*→ *early endosome*→ *late endosome* where the endocytosed materials are degraded by the lysosomal hydrolases.
2. **Extracellular large particles:** are engulfed in the process of *phagocytosis*→ forms a *phagosome*→ fuses with a late endosome.
3. **Intracellular particles:** are removed by a process called *autophagy*→ the enclosure of this organelle by membranes from sER→ forms an *autophagosome*→ fuses with a late endosome.

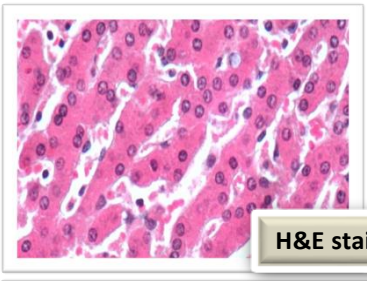
- The hydrolytic enzymes digest most of the content of the lysosomes. Any indigestible substances remain in lysosomes forming ***residual bodies***.
- In long-lived cells, accumulated residual bodies indicate cellular aging and are called ***lipofuscin pigments***.







6-Mitochondria

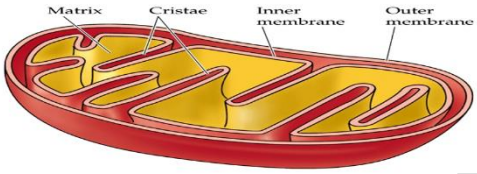

H&E stain

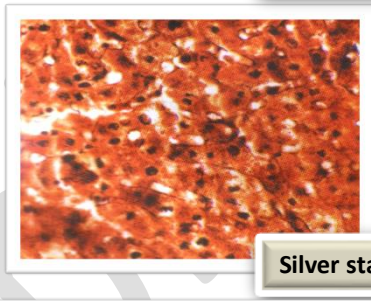
Function: Powerhouses of the cell as they are the sites of adenosine triphosphate (ATP) production.

Sites: All cells EXCEPT terminal keratocytes & RBCs.

Structure:

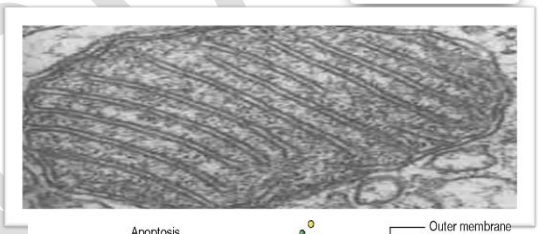
LM: When present in large numbers contribute to *the cytoplasmic eosinophilia*.



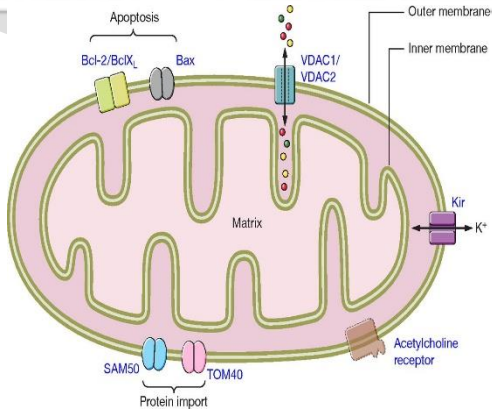

Silver stain

EM:

1. Membrane-bounded organelles.
2. Surrounded by *two membranes: outer and inner*, which define two mitochondrial compartments:
   - The intermembranous space: between the two membranes.
   - The matrix space: enclosed by the inner membrane.



1-The outer mitochondrial membrane:



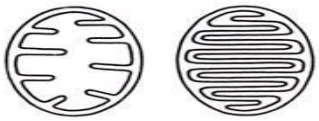
- It is *smooth* and *porous*.
- Function: allows passage of small molecules due to the presence of specific transmembrane proteins called *porins*.

2-The inner mitochondrial membrane:

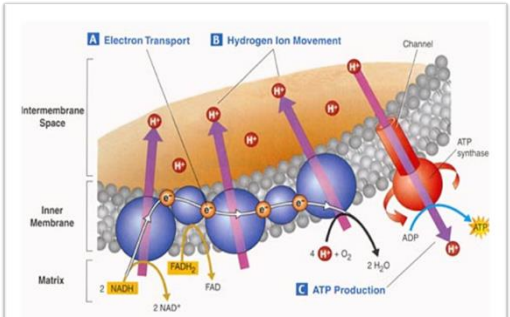
1- Folded into *cristae* which increase its surface area; the number of cristae is greater in cells of greater demand for ATP.

- Types of cristae:

Shelf/lamellar-like cristae Tubular cristae

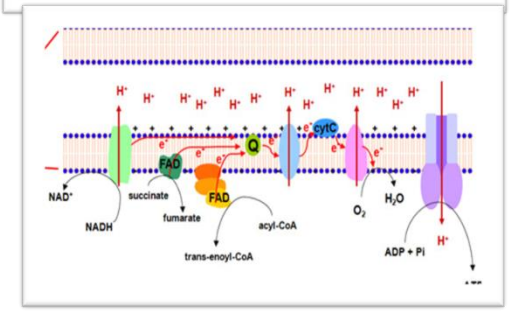


- lamellar cristae : most of cells.
- tubular cristae: steroid secreting cells.



2- *Impermeable* to ions and small molecules due to presence of phospholipid called *cardiolipin*.

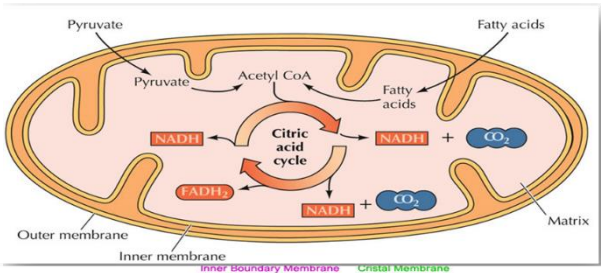
Function:contains the enzymes of the electron transport system (respiratory chain enzymes) and the ATP synthase (known as elementary particles attached to the cristae and their heads are projecting toward the matrix like a lollypop).



3-Intermembranous space:

Contains substances *diffusing* from the cytoplasm through the outer membrane and ions *pumped out* of the matrix space through the inner membrane.

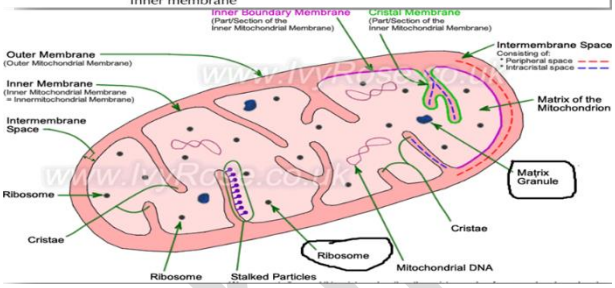
4-Matrix space:



Surrounded by the inner mitochondrial membrane.

Functions:

1. *Enzymes* involved in mitochondrial functions as citric acid cycle.
2. Mitochondrial *DNA* and few *ribosomes*.
3. *Matrix granules:* store calcium ions, play a role in mitochondrial regulation of Ca^{2+} intracellular concentration.



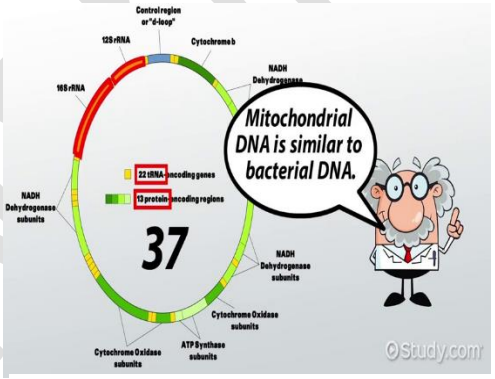
The genetic system of mitochondria:

- *The mitochondrial DNA:*

1- a circular molecule.

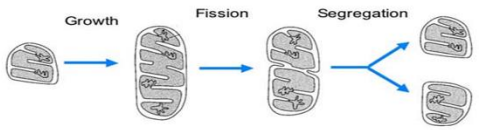
2- limited coding capacity.

3- represents 1% of the total DNA of the cell.



Function: Mitochondria can synthesize some of their structural proteins by their own RNAs.

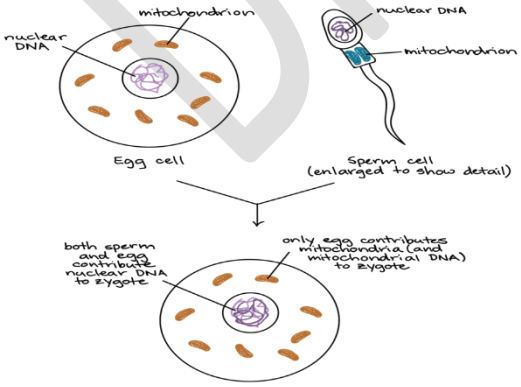
- *Most of the mitochondrial proteins are encoded by the nuclear DNA and are synthesized in the cytoplasm and imported into mitochondria.*
- Mitochondria are self-replicating organelles.

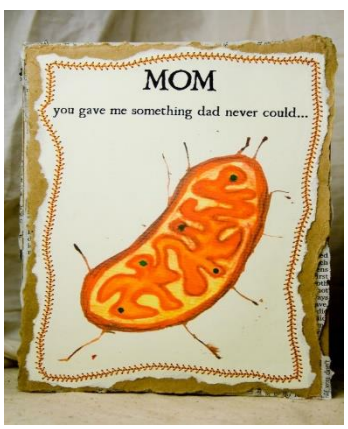


How do mitochondria adapt to its function? (E/M)

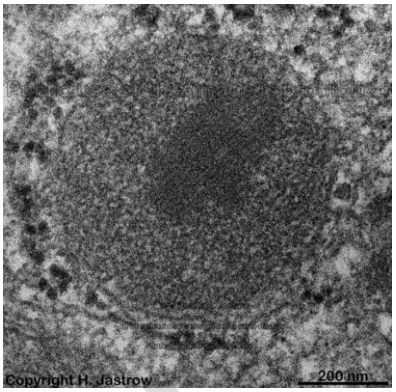
1. **Outer membrane:** smooth &porous contains mitochondrial porins allow easy passage of small molecules.
2. **Inner membrane** is folded into numerous cristae→ increase surface area for energy production.
3. **Inner membrane** contains cardiolipin→ make it highly impermeable to ions & small molecules.
4. **Matrix space:** contains enzymes for citric acid cycle, mito DNA & ribosomes→ synthesize some of their structural proteins, also contains matrix granules→ store Ca thus play an important role in regulation of intracellular Ca concentration.

What is your source of mitochondria?





7-Peroxisome



Definition: membrane-bounded organelles that contain oxidative enzymes.

- Peroxisomes possess ***no genetic material*** of their own.

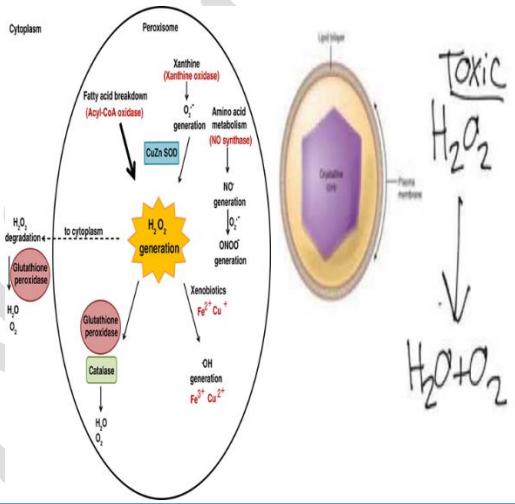
A-Structure of Peroxisome:

LM: They are not seen by H&E stain.

EM:

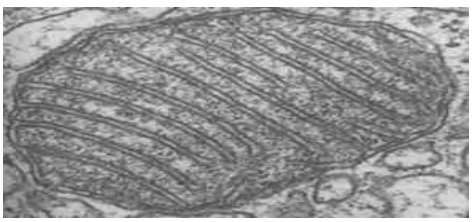
1. Small, spherical bodies with fine granular electron dense content.
2. Surrounded by a single membrane.

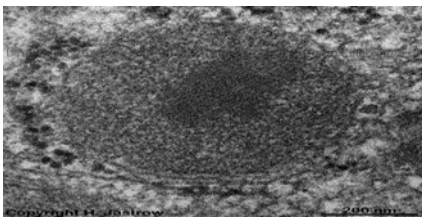
B-Functions of peroxisomes:



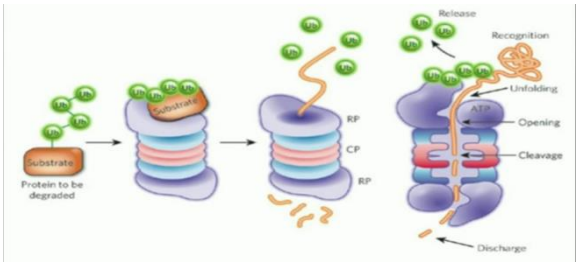
1. *β-oxidation of long chain fatty acids to release energy*. However, they differ from mitochondria in that they are unable to store this energy in the form of ATP. This energy is released as *heat* to maintain body temperature.
2. *Generation of hydrogen peroxide*, which detoxifies toxic agents.
3. Contain *catalase enzyme* that converts the excess hydrogen peroxide into water, thus protecting the cell.
4. *Detoxification of alcohol* in cooperation with the smooth endoplasmic reticulum in the liver.

	Mitochondria	Peroxisome
1- LM	-Not seen by H&E except in large amount cause cytoplasmic acidophilia. -By special stain (silver stain) appear as brownish granules.	Not seen.
2- EM	Double membrane: outer is smooth, and inner is folded into cristae enclosed matrix space.	Single membrane enclosed fine granular contents.
3- Function	Production of energy & store it in the form of ATP.	1- Produce energy & released it in the form of heat (unable to store it). 2- Produce hydrogen peroxide. 3- convert excess hydrogen peroxide into water. 4- Detoxification of toxic substances.
4- sites	All body cells except red blood cells & keratinocytes.	Many cells especially liver.
5- Genetic material	Present	Absent





8-Proteasome

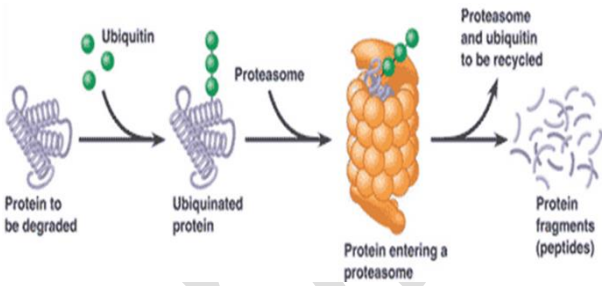


Definition & Function: small organelles responsible for proteolysis of *malformed endogenous proteins* (proteins synthesized within the cell) such as:

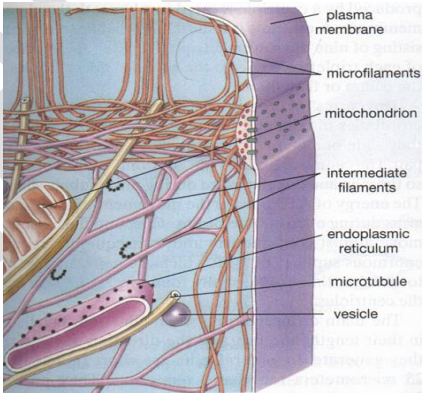
1- Excess enzymes & other proteins that become unnecessary after performing their function.

2- Proteins that have been denatured, damaged, malformed.

3- Aberrant proteins of the viruses.



9-Cytoskeleton



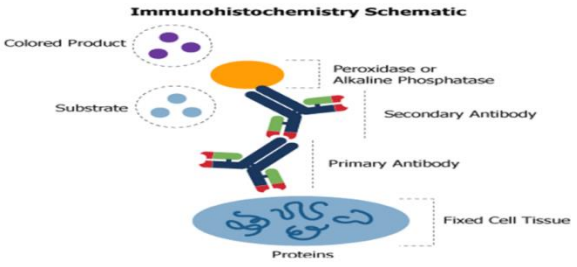
The cytoskeleton is a network of structural proteins (***non-membranous*** cell organelles).

Types of cytoskeletons:

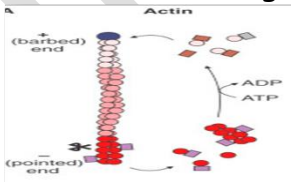
3 types, depending on their thickness& their structural proteins:

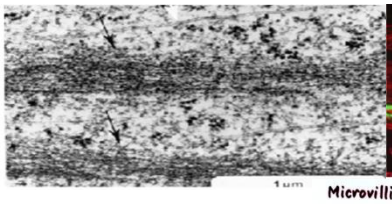
1-Microfilaments. 2-Microtubules. 3-Intermediate filaments.

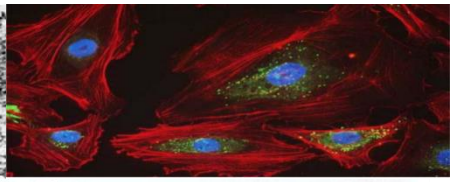
1-Microfilaments (actin filaments):



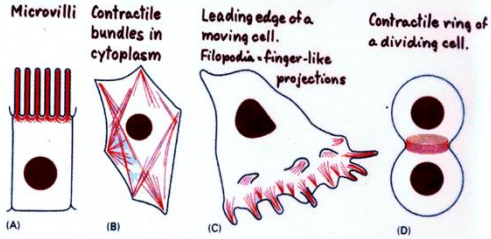
- **Diameter:** 7 nm.
- **LM:** can be visualized by using immunohistochemical staining.
- **EM:** thin electron dense filaments.
- **Structural proteins:** monomers of *G-actin* (globular actin) polymerize to form *F-actin* (filamentous *actin*) arranged as a double helix.
- They are dynamic structures that can elongate & shorten.





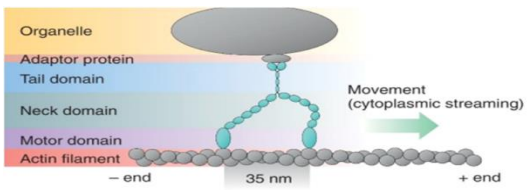


Functions of microfilaments:



A- Cell motility for:

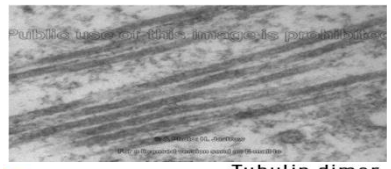
- Cell migration.
- Cytoplasmic streaming: during movement of organelles and transport of vesicles.
- Cytokinesis: formation of contractile ring during cell division.
- Muscle contraction associated with myosin.

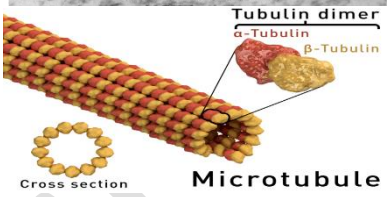


B-Structural role:

- Maintenance of the cell shape.
- Formation the core of microvilli.

2-Microtubules:

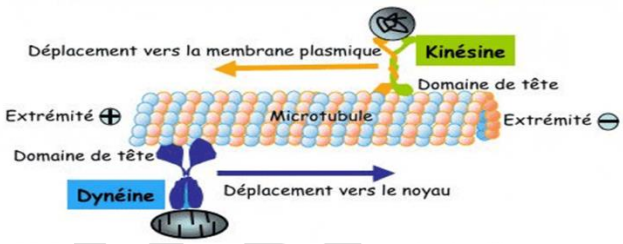




- **Diameter:** 25 nm.
- **LM picture:** by using immunohistochemical staining.
- **EM picture:** fine tubules.
- **Structural proteins:**

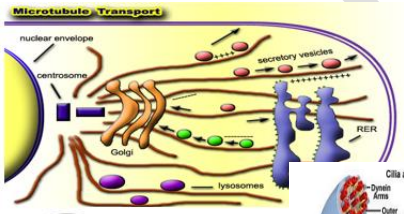
A. a globular protein dimer called *tubulin* (each is composed of alpha and beta subunits).
B. Chains of tubulin dimers form a *protofilament*.
C. The wall of a microtubule is made up of 13 protofilaments that run longitudinally.

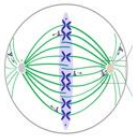
- **Motor proteins associated with microtubules: Kinesin** & **dynein**; they use ATP to provide energy for movement of vesicles and organelles along the microtubules.
- **Microtubules are dynamic structures; can elongate & shorten**

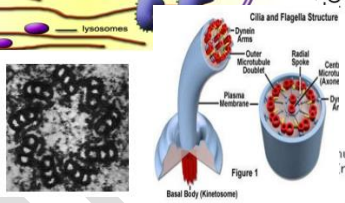


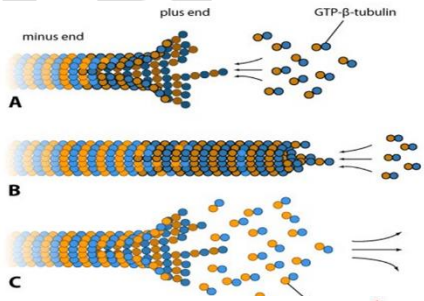
Functions of microtubules:

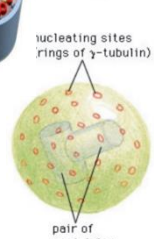
1. *Transport:* of organelles & vesicles in the cytoplasm.
2. *Structural role:*
   - Formation of the mitotic spindle.
   - Formation of centrioles, cilia & flagella.

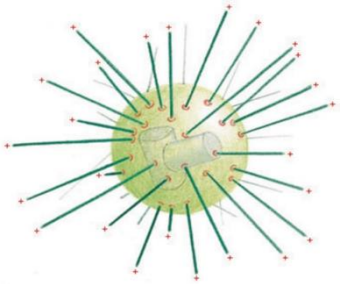








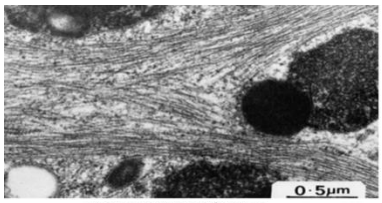


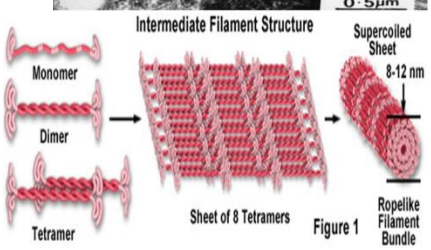


The microtubule organizing centers:

1. *Centriole* which forms the mitotic spindle.
2. *The basal bodies* of cilia and flagella.

3- Intermediate filaments:

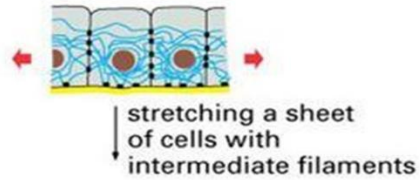


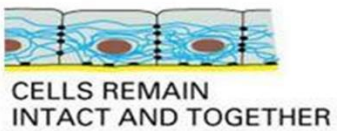


- **Diameter:**10 nm
- **LM:** by using immunohistochemical staining.
- **EM:** electron dense filaments thicker than actin filaments.
- **Structural proteins:** like woven ropes.

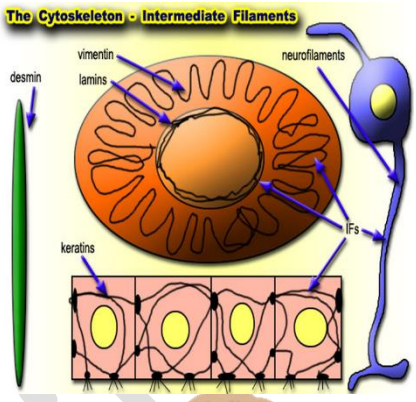
Function of intermediate filaments:

They are the ***most stable*** (not dynamic) types of the cytoskeletons thus they play a structural role .





Classification Of Intermediate Filaments:



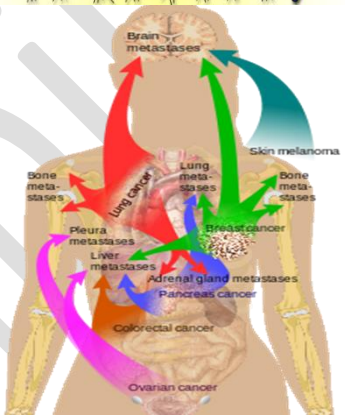
- According to their protein composition and their cellular distribution into:

A- Cytoplasmic:

1. **Keratin:** epithelial cells.
2. **Vimentin:** in the cells of mesenchymal origin e.g., fibroblasts.
3. **Desmin:** muscle cells.
4. **Glial fibrillary acidic protein:** neuroglia.
5. **Neurofilaments:** nerve cells.

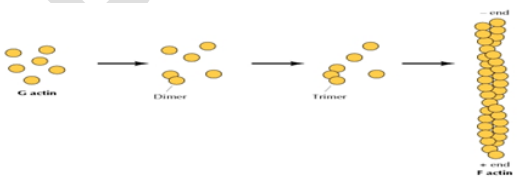
B- Nuclear:

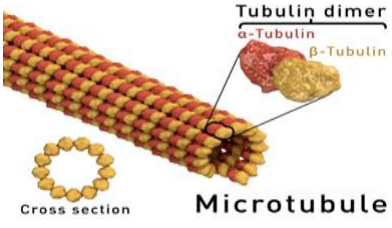
- **Lamins:** lining the inner nuclear envelope.

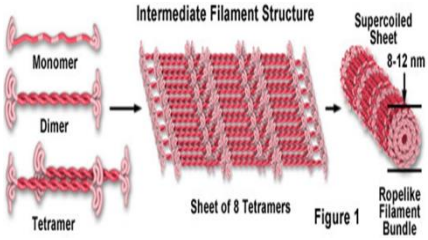


The intermediate filaments (except for the lamins) are located in specific tissue types; they can be used to determine the origin of cancer by immunohistochemical staining.

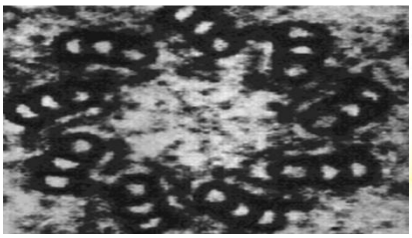
Cytoskeleton	Microfilaments	Microtubules	Intermediate filaments
1- diameter	7 nm.	25 nm.	10 nm.
2- LM	Seen only by immunohistochemistry.	Seen only by immunohistochemistry	Seen only by immunohistochemistry
3- EM	Thin electron dense filaments.	Fine tubules.	Thicker electron dense filaments.
4- Structural proteins	Monomers of G actin polymerize to form F actin.	Tubulin dimer polymerize to protofilaments. 13 protofilaments form a microtubule,	Woven ropes.
5- Functions	Dynamic 1- Muscle contraction. 2- Contractile ring in cell division. 3- Pseudopodia in migration. 4- Microvilli. 5- Cytoplasmic streaming.	Dynamic. 1- Transport of organelles & vesicles. 2- Formation of centrioles, cilia & flagella.	Not dynamic. Structural support.

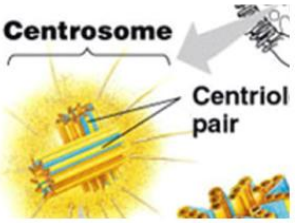






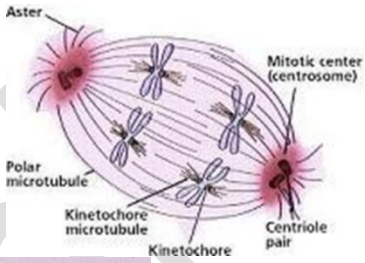
Centrosome





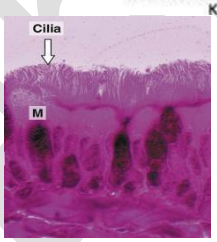
- **Definition:** a non-membranous organelle.
- **EM:**

1. It is formed of ***2 centrioles,*** perpendicular to each other.
2. Each centriole is composed of ***9 triplets of microtubules*** (a sum of 27 microtubules).
3. Each triplet is composed of three microtubules (one complete; formed of 13 protofilaments and 2 incomplete; each is formed of 10 protofilaments).

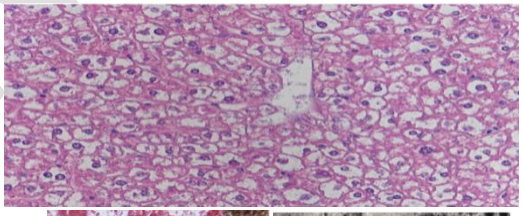


Functions of centrosome:

1. It is the microtubule- organizing center.
2. Formation of mitotic spindles.
3. Formation of cilia & flagella.

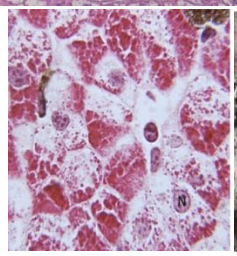


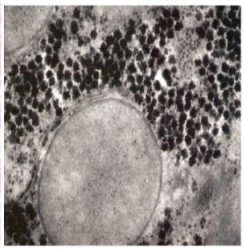
Cytoplasmic inclusions



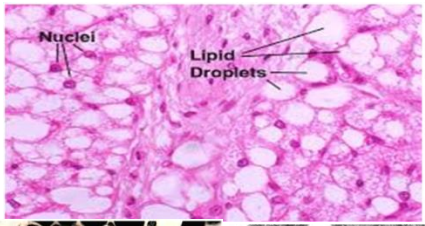
1- Stored Food:

A-Glycogen:





- Storage form of carbohydrates.
- **Function:** source of energy.
- **Sites:** mainly in liver & muscle cells.
- **LM:**
  - **H&E:** not visualized as they dissolve during preparation of the specimen leaving a **pale vacuolated cytoplasm.**
  - **Periodic acid Schiff:** appears **magenta** red.
  - **Best's carmine:** appears **bright** red.
- **EM:** dense granules, larger than ribosomes. In cytoplasm of hepatocytes, glycogen appears as rosette-shaped aggregates

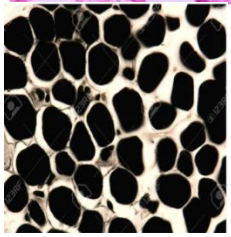


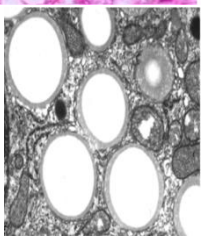
B-Lipids:

- **Function:**

1. Source of energy.
2. Synthesis of membranes & steroid hormones.

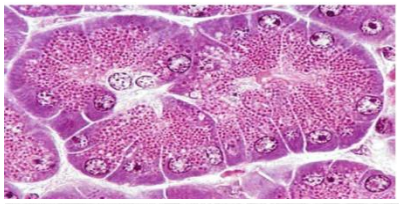
Sites: stored in the adipocytes; many other cell types contain few small lipid droplets.

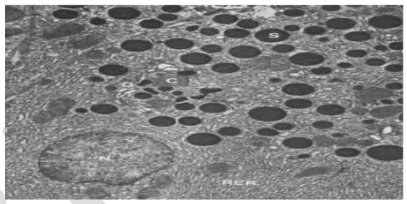




- **LM:**
  - **H&E:** not visualized because they dissolve during preparation of the specimen leaving a **pale vacuolated cytoplasm.**
  - **Osmium tetroxide:** appear black.
- **EM:** grey ***non- membrane*** bounded small droplets or large globules.

C-Proteins:

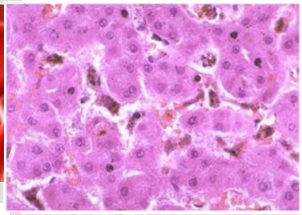




- **Site:** in protein- synthesizing cells e.g. salivary gland and pancreas.
- **LM:** eosinophilic zymogen granules.
- **EM:** homogenous electron dense membrane-bounded *secretory granules.*

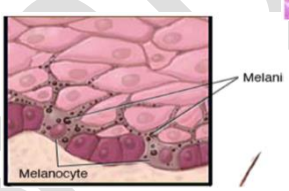
2- Pigments:

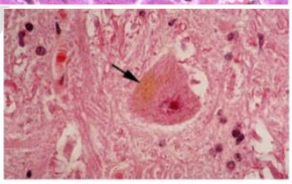
A-Endogenous pigments:



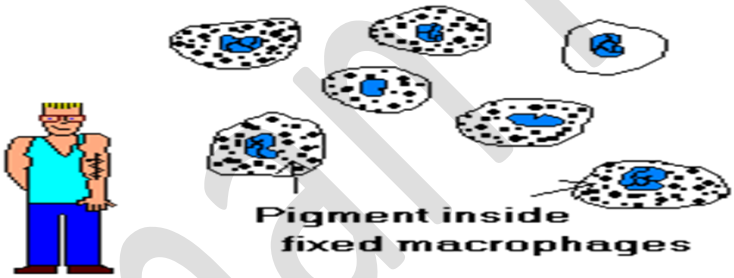
1. ***Hemoglobin:*** *in* red blood cells.
2. ***Hemosiderin:*** brownish granules in phagocytic cells of liver and spleen following phagocytosis of old RBCs.
3. ***Melanin pigment:*** brown to black granules.
4. ***Lipofuscin pigment:*** yellow-brown pigment present in cells with long life span.

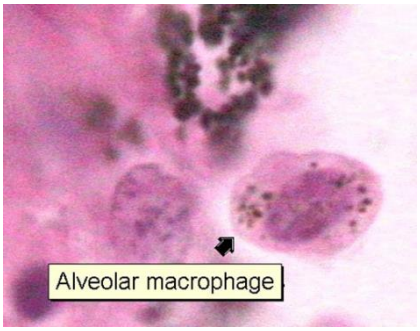
B- Exogenous pigments:



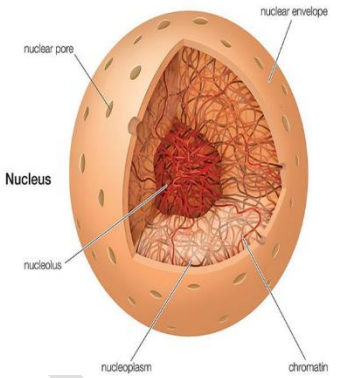


1. **Tattooing:** colored pigments are injected into the deep layers of the skin.
2. **Dust & smokes:** in lung of smokers and people living in polluted areas.





Nucleus

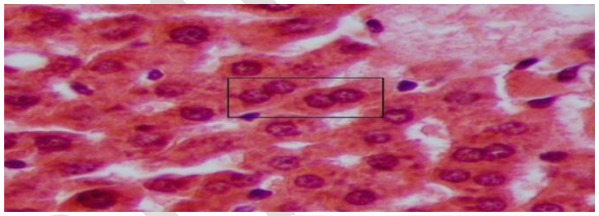


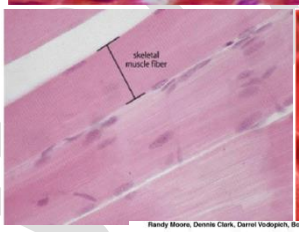
- It is the largest membranous organelle of the cell.
- **Functions**:

1. It contains the chromosomes.
2. Contains the machinery for DNA replication& RNA transcription.

- **Number**:

1. ***Single***: most of the cells.
2. ***Binucleated***: liver cells.
3. ***Multinucleated***: skeletal muscle fibers.
4. ***Absent***: RBCs.



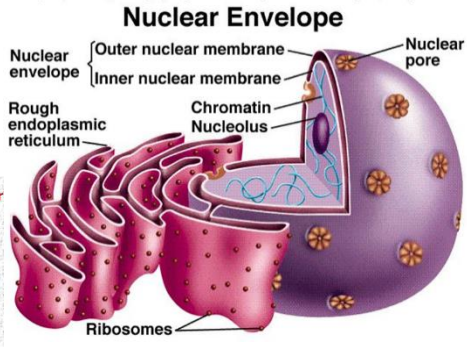


Components of the Nucleus:

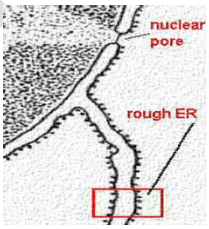
1. The nuclear envelope.
2. The chromatin.
3. The nucleolus.
4. The nucleoplasm (nuclear matrix; sap).

I-The Nuclear Envelope:

1. It consists of two parallel membranes; ***outer & inner*** **separated by the** ***perinuclear cisterna***.
2. It is perforated by the ***nuclear pores*** which provide a channel between the nucleus and cytoplasm.

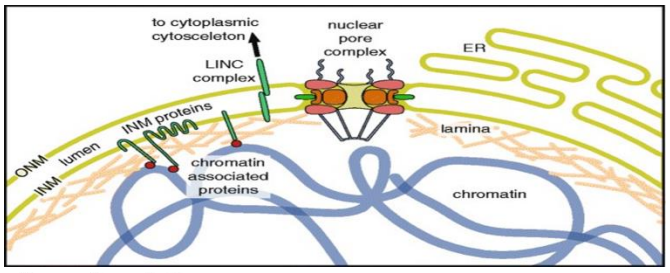


1-The outer membrane:



- It is continuous with the rough endoplasmic reticulum. It is covered with ***ribosomes*** on its outer surface.
- **Function**: The ribosomes synthesize the transmembrane proteins of the nuclear membranes.

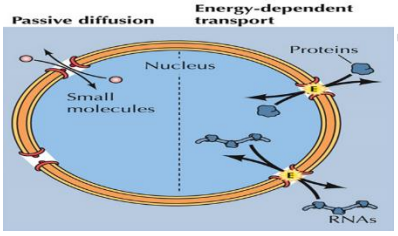
2-The inner membrane:

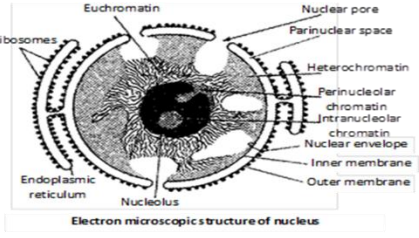


- It is supported at its inner surface by the lamins.
- **Functions of the lamin:**

1. Supports the nuclear envelope.
2. Influences chromosome distribution and function.

3-The nuclear pores:

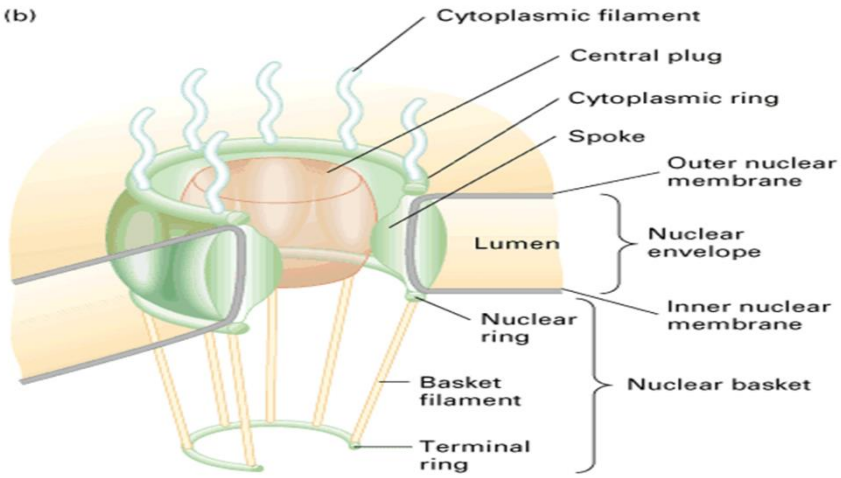




Electron microscopic structure of nucleus

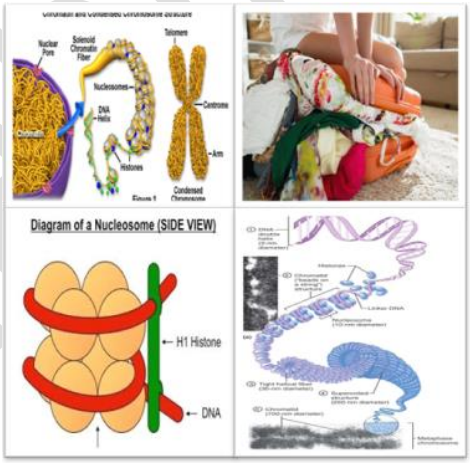
- **Definition**: They are perforations in the nuclear envelope where the outer and inner nuclear membranes fuse.
- **Distribution**: not uniformly distributed.
- **Number**: vary according to the cell activity.
- **Function**: provide a bidirectional channel through which the nucleus and cytoplasm communicate.

Nuclear Pore Complex →



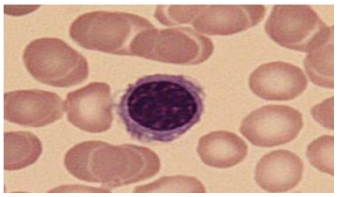
II-The Chromatin:

- It is formed of DNA + histone proteins.
- DNA is extensively packaged in chromatin as:



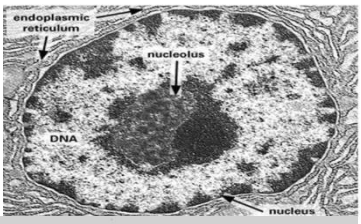
1. A segment of the DNA is wrapped two times around eight histone proteins to form a ***nucleosome***. Each nucleosome is separated from the next by a region of linker DNA.
2. Repeating nucleosomes with intervening DNA (linker DNA) form a ***10nm fiber*** (beads on a string).
3. This chain of nucleosomes is packed to form a ***30nm fiber***.
4. Higher orders of packaging gives the compact structure ***700nm*** seen in the metaphase of the dividing cell known as the chromatid of a chromosome.

Types of chromatins:



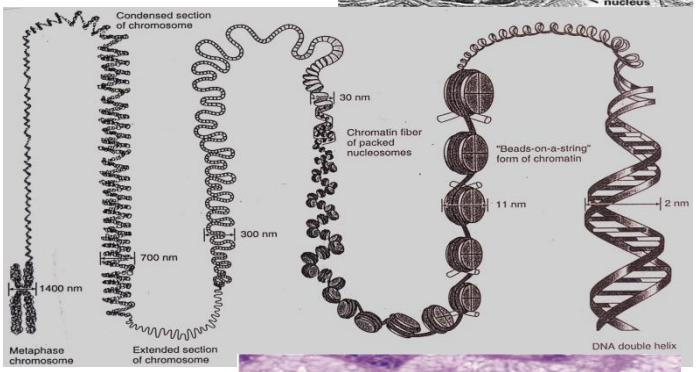
1- Heterochromatin (condensed chromatin; the inactive chromatin):

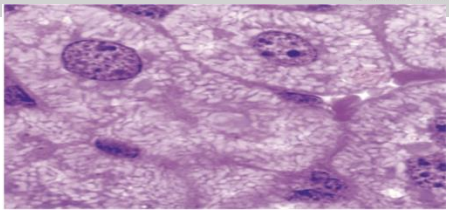
- **LM:** appears as dense basophilic clumps.
- **EM:** appears as condensed filaments or granules distributed in the following sites:
  - **Nucleolar-associated heterochromatin**: around the nucleolus.
  - **Peripheral heterochromatin:** at the inner nuclear membrane(associated with the nuclear lamin).
  - **Heterochromatin islands:** swimming in the nuclear sap.
- **Function:** transform into euchromatin when needed.



2- Euchromatin (extended chromatin; the active chromatin)

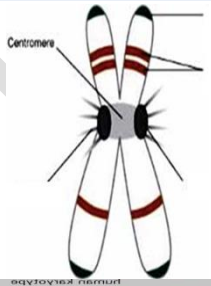
- **LM:** appears as lightly stained basophilic areas.
- **EM:** appears as dispersed filaments or granules.
- **Function:** It is stretched so, the genetic information in the DNA can be transcribed.
- The proportion between euchromatin and heterochromatin differs from one cell to another according to **its activity**.





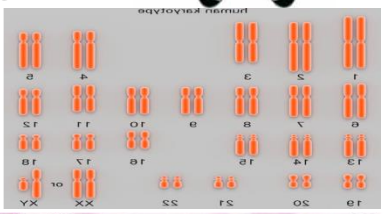
Types of chromatin	Heterochromatin	Euchromatin
1- LM	Dense basophilic clumps.	Lightly stained basophilic areas.
2- EM	Electron dense filaments or granules distributed in: 1- around nucleolus. 2- associated with inner nuclear membrane. 3- swimming in nuclear sap.	Dispersed fine filaments or granules.
3- Function	Inactive part acts as a reserve (transformed into euchromatin when needed).	Active part (transcribed into RNA).
4- Site	Inactive cells.	Active cells e.g., dividing cells.

Chromosome:

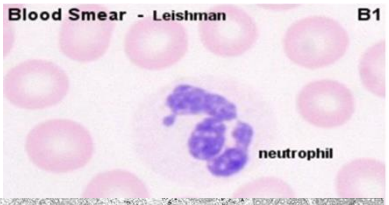


- **During cell division:** chromatin is condensed into the ***chromosomes***; formed from two ***chromatids*** held together at the ***centromere***. Each chromatid is formed of a ***single*** DNA molecule.

Karyotyping:

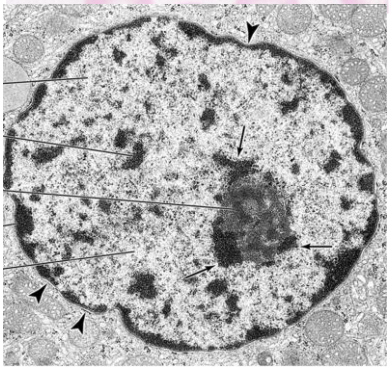


- The ***somatic cell*** contains 46 chromosomes.
- **Karyotyping:** is the arrangement of the chromosomes during metaphase into groups of homologous pairs (22 homologous pairs of ***autosomes*** and one pair of ***sex*** chromosomes).
- In females (44 autosomes +XX): one X chromosome is heterochromatic (***Barr body***), it can be identified in neutrophils, attached to the nucleus in the form of a drumstick mass.



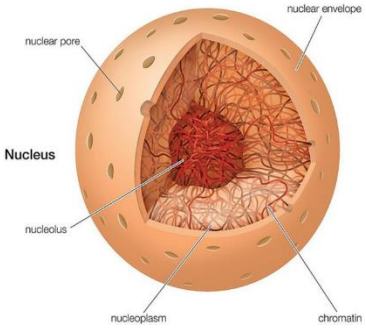
III-The Nucleolus:

- **Definition:** It is a spherical body with no surrounding membrane.
- **Number:** single or multiple.
- **Function:** it is the site of formation of ribosomal RNA.

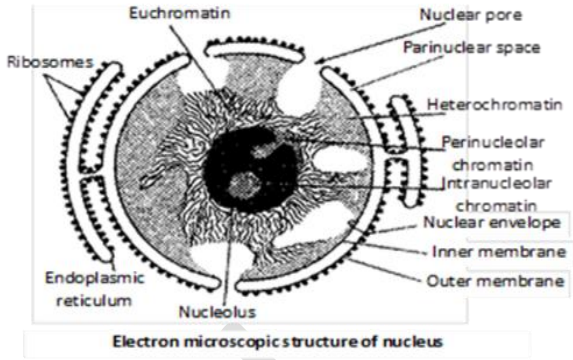


IV-The Nucleoplasm (nuclear matrix; sap):

- **Definition**: It is a colloidal protein solution
- **Function:** provides a medium for the rapid diffusion of metabolites.



Nuclear Pore Complex



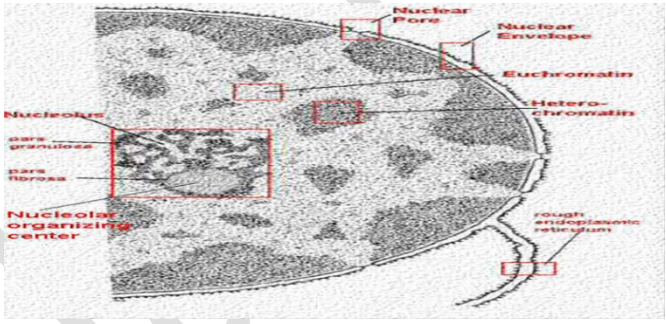
Electron microscopic structure of nucleus

Nuclear Pores:

- **Definition**: They are perforations in the nuclear envelope where the outer and inner nuclear membranes fuse.
- **Distribution**: not uniformly distributed.
- **Number**: vary according to the cell activity.
- **Function**: provide a bidirectional channel through which the nucleus and cytoplasm communicate.

Nuclear Pore Complex:

- **Definition:** non membranous structures(glycoproteins) surround the nuclear pore & embedded in its rim.
- **Structure:**

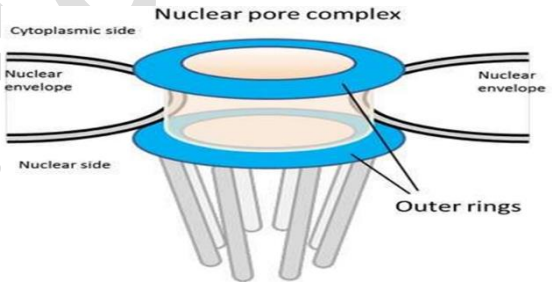


A. 3 rings of proteins(nucleoporins) arranged one on top of each other.
B. A nuclear basket.

❑ **3 rings are:**

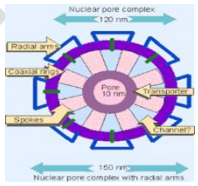
A- Cytoplasmic ring:

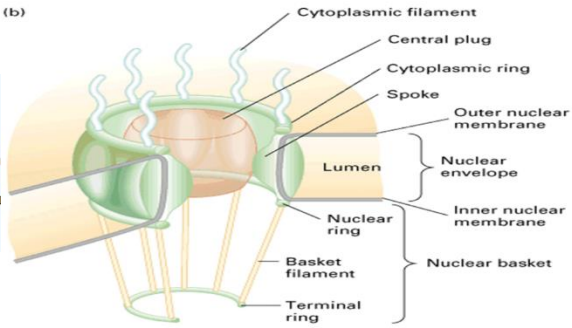
- **Site:** on the rim of the cytoplasmic aspect of the nuclear pore.
- **Structure:** formed of 8 similar protein subunits.
- It possesses *cytoplasmic filaments* that extend into the cytoplasm.



B- The spoke ring (middle ring):

- **Structure:** formed of 8 transmembrane proteins that project into the lumen of the nuclear pore as well as into the perinuclear cisternae.
- **Function:** anchor the components of the nuclear pore complex into the rim of the nuclear pore.

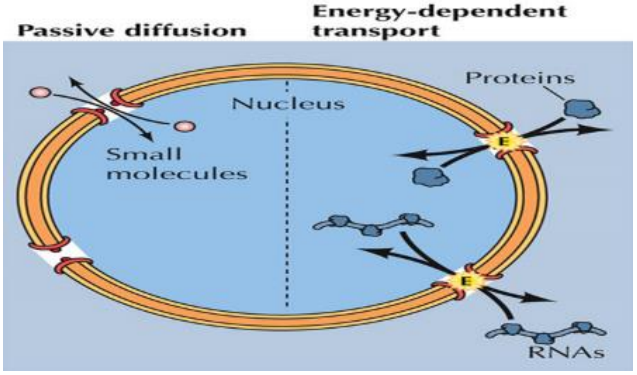




C- The nuclear ring:

- **Site:** on the rim of the nucleoplasmic aspect.
- **Structure:** formed of 8 similar units, from which arise a filamentous basket -like structure (***nuclear basket***) protruding into the nucleoplasm& terminating in ***the terminal ring***.

Transport across the nuclear pore complex:



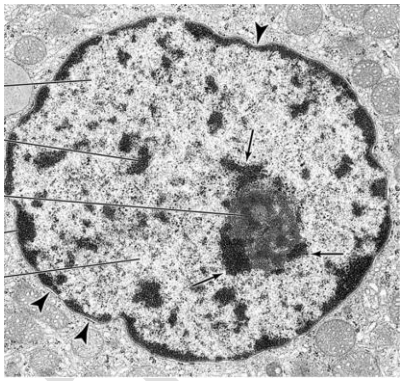
1- Small molecules (less than 9 nm in diameter):

✓ Diffuse passively across the nuclear pore.
✓ Bidirectional.

2- Macromolecules (from 9-50 nm as proteins; histone, lamin, RNA proteins):

✓ Transported actively.
✓ In one direction.

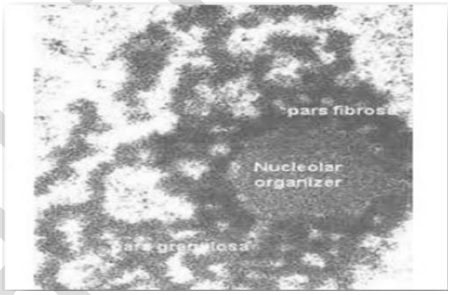
The Nucleolus



- **Definition:** It is a spherical body with no surrounding membrane.
- **Number:** single or multiple.
- **Function:** it is the site of formation of ribosomal RNA.

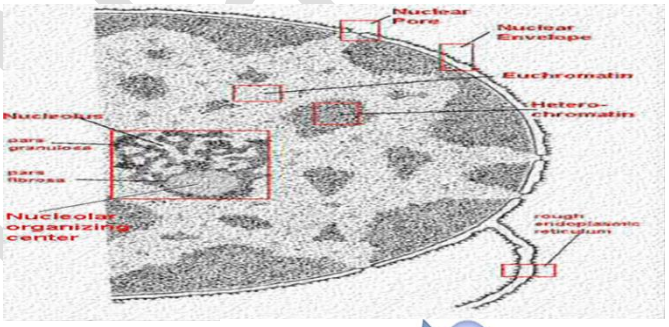
Components of the nucleolus:

1- **Fibrillar center (nucleolar organizing center):**
- Pale areas.
- Represent large loop of inactive DNA containing: rRNA genes+ RNA polymerase &transcription factors.



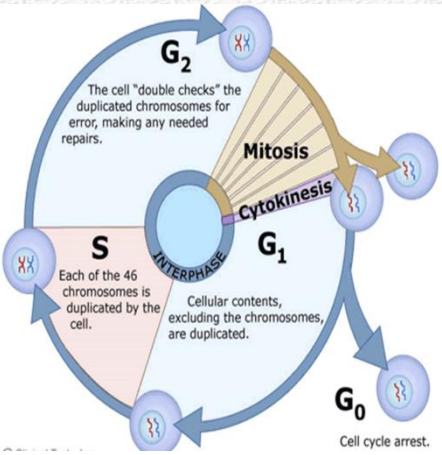
2- **Pars fibrosa:**
- Dense regions.
- Represent actively transcribed ribosomal genes+ RNA.

3- **Pars granulosa:** represent the mature ribosomal subunits.
4- **Nucleolar matrix.**



Cell Cycle & Cell Division

The Cell Cycle:



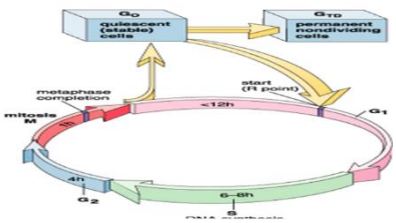
- Definition: it is the alternation between interphase and mitosis.

I-Interphase: a longer period:

1- The cell increases in size.
2- Performs its normal functions.
3- Replicates its DNA for preparing itself for division.

II-Mitosis: a shorter period during which parent cell gives 2 daughter cells each containing the same number of chromosomes (identical to the parent cell =46 chromosomes).

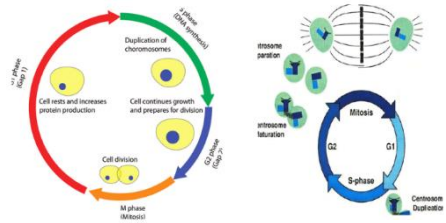
I-Interphase(الطور البينى):



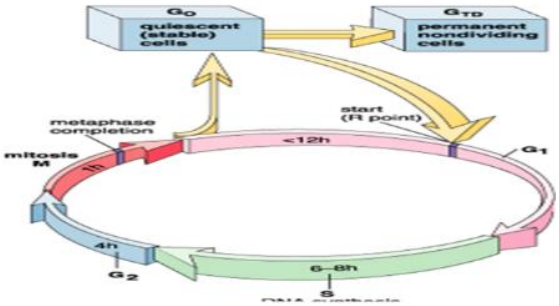
First gap phase (G_1 phase):

It is *the longest period* of the cell cycle between the end of mitosis and the beginning of DNA replication:

1. The RNA and protein synthesis occurs.
2. The cell attains its full size.
3. The cell performs its function.

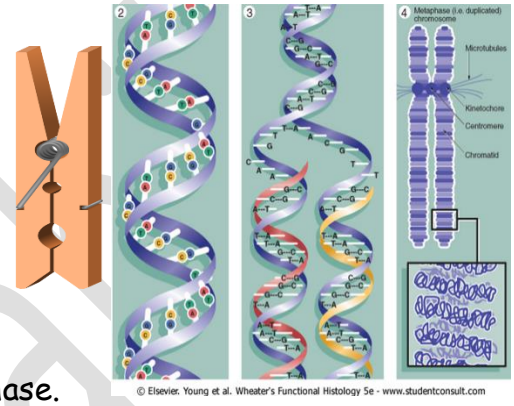


4. Duplication of centrosomes occurs near the transition between G_1 and S phase.



The GO phase:

- **Definition**: Differentiation of the cell to carry out specialized function and no longer divide (outside *the cycle*).
- GO may be *permanent* or *temporary*.

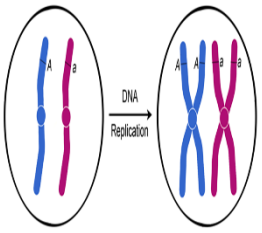


DNA synthesis phase (S phase):

•Replication of DNA, thus the amount of DNA is doubled but *not the total chromosomal number*.

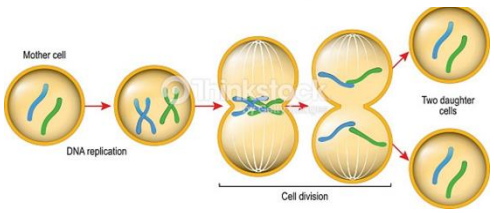
Types of chromosomes:

•**S-Chromosomes** made of one DNA molecule (interphase chromosomes = chromatin or chromatids).
•**d-Chromosomes** (mitotic chromosomes):are formed during the S phase. Each d-chromosome is formed of two chromatids, linked at the centromere. Each chromatid is made of a DNA molecule.

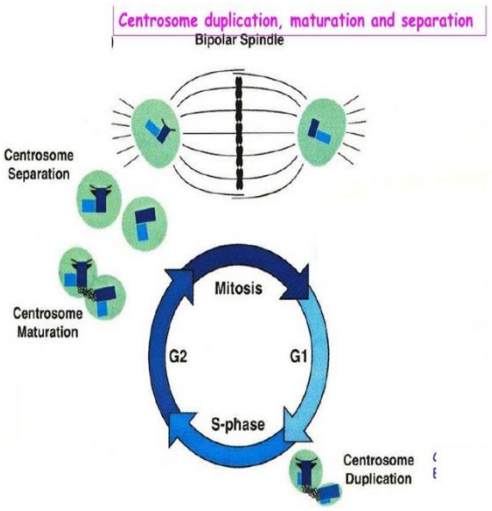


Second gap phase (G2 phase):

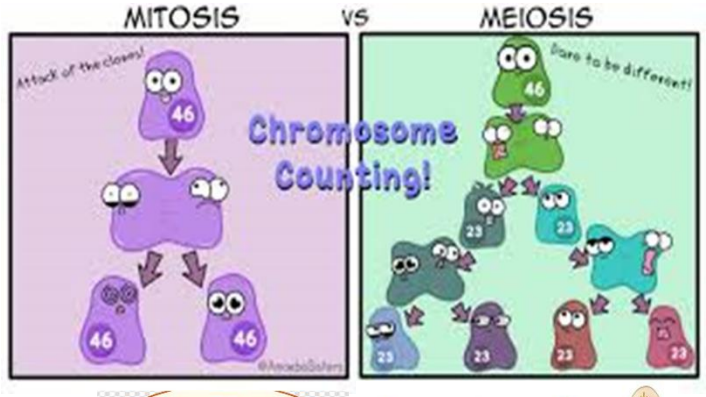
•It starts by the end of the DNA replication and lasts until the beginning of mitosis.



1. Proteins and energy essential to mitosis are stored.
2. Duplication of the centrosome is ***completed***.



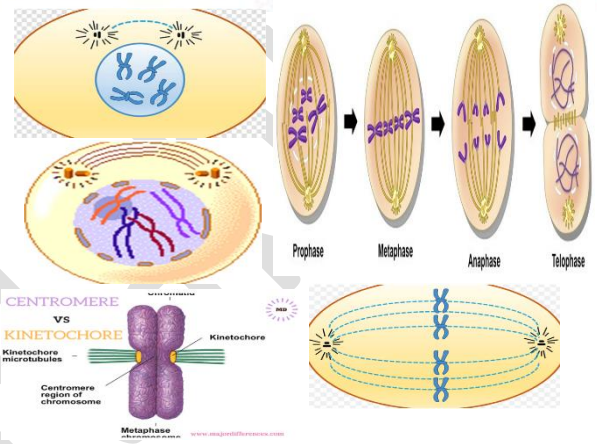
Cell Division:



Mitosis

- **Definition:** division of the somatic cell into two daughter cells identical to the mother cell.
- **Function:**

1. Growth & development of the organism.
2. Renewal & repair of cells.

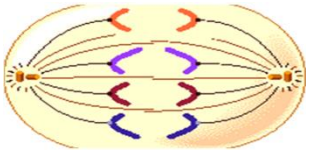


I-Prophase (الطور التمهيدي) :

1. The ***nucleolus*** disappears.
2. Condensation of ***chromatin*** gives rise to 46 rod-shaped short d-chromosomes.
3. Each pair of ***centrioles*** migrates to opposite pole of the cell forming the mitotic spindles.
4. The ***nuclear envelope*** breaks up into small vesicles

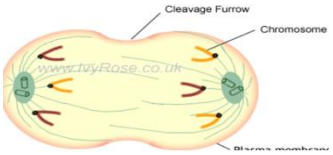
2-Metaphase (الطور الاستوائي)

1. The 46 d-chromosomes become maximally condensed.
2. The chromosomes ***aligned at the equatorial plate*** of the cell.
- Each pair of sister chromatid is attached to the mitotic spindles at ***the kinetochore***.



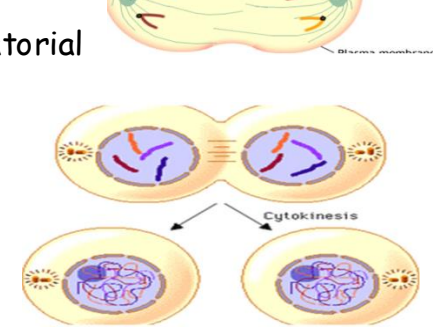
3-Anaphase (الطور الانفصالي) :

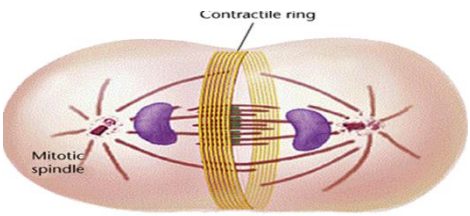
1. ***Division of the centromere*** results in the separation of the sister chromatids.
2. Each 46 chromatids migrate toward the opposite poles of the cell.
3. In late anaphase, ***a constriction (cleavage furrow)*** develops at the equatorial plate of the cell.

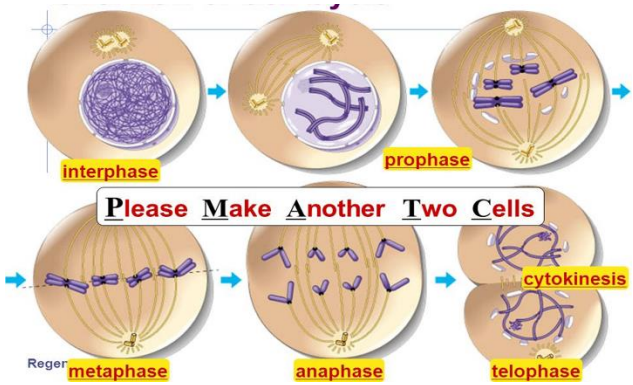


4-Telophase(الطور النهائي)

1. The ***mitotic spindle*** disappears.
2. The ***nucleolus*** reappears.
3. The ***chromosomes*** start uncoiling (46 s-chromosomes).
4. The ***nuclear envelope*** is reformed around the new sets of chromosomes.
5. Division of the ***cytoplasm*** **(cytokinesis):** the cleavage furrow becomes deeper due to the formation of a **contractile ring** of microfilaments until it divides the cytoplasm and its organelles in half resulting into two daughter cells.



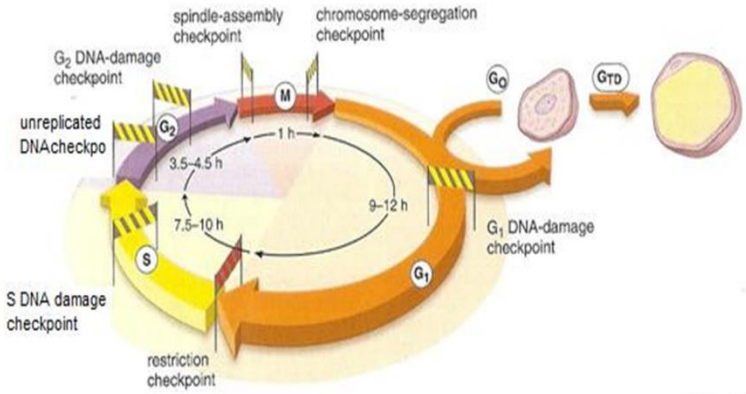




Regulation of the cell cycle:

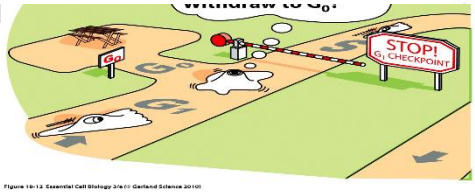
- The cell cycle is regulated by growth factors that control cell proliferation to keep its coordination with the needs of the living organism.
- Several ***checkpoints*** control the transition between the cycle stages.
- Checkpoints detect external or internal problems and stop the cycle until the problem solved.

Checkpoints of the cell cycle:



1. The restriction checkpoint:

- It occurs in the G_1 phase.
- It detects ***the cell size & its interactions with the surrounding environment***.
- Cells that do not receive appropriate growth stimuli do not progress past this point (G_1 phase) and will be die by apoptosis.
- ***It is the most important checkpoint in the cell cycle.***



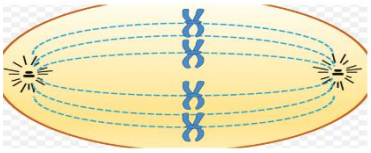
2. DNA damage checkpoints:

- It occurs in G1, S, and G2 phases.
- It blocks cell cycle progression until repair of the damaged DNA or cell apoptosis occurs.

3. The unreplicated DNA checkpoint:

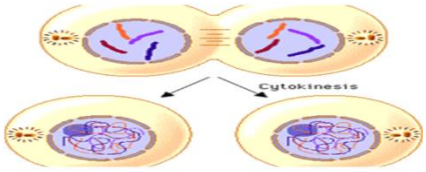
- It occurs in the G2 phase.
- It prevents progression of the cycle into the mitosis before complete synthesis of DNA.

4. The spindle-assembly checkpoint (the metaphase checkpoint):



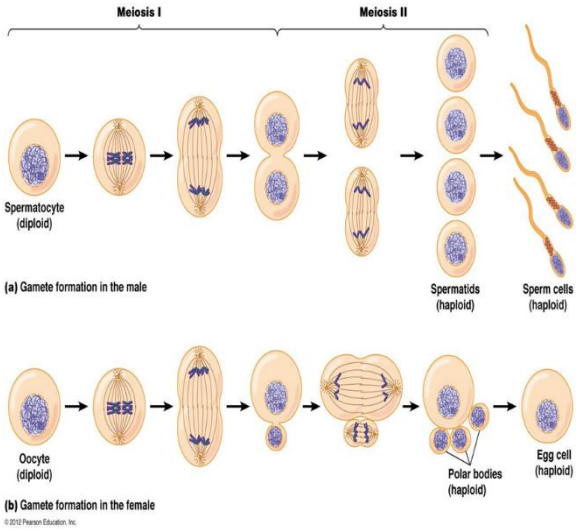
- It occurs in mitosis.
- It prevents entry into anaphase until all chromosomes have attached properly to the mitotic spindle.

5. The chromosome-segregation checkpoint:



- It occurs in telophase.
- It prevents the cytokinesis until all of the chromosomes have been correctly separated.

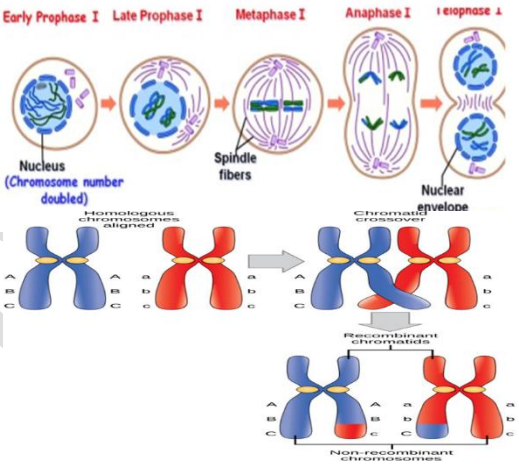
Miosis



- It occurs in ***germ cells*** and results in the formation of gametes.
- It results in formation of ***4 daughter cells*** (each contains 23 s-chromosomes=haploid number).
- It consists of two successive divisions: ***without an intervening S phase***.

I-First meiotic division (reductional division):

It is preceded by interphase with an *S phase*, in which the chromosomes are replicated (46 s chromosomes → 46 d chromosomes).



1. Prophase I:

A. ***Pairing of the homologous chromosomes*** occurs forming **tetrads(bivalent)**.
B. ***Crossing-over*** occurs between the chromatids of the homologous chromosomes so that each homologous chromosome is no longer solely paternal or maternal but a mixture of both.
C. The nucleolus and the nuclear envelope disappear, and the mitotic spindle is formed.

2. Metaphase I:

The ***paired chromosomes*** arrange themselves at the equatorial plate of the cell.

3. Anaphase I:

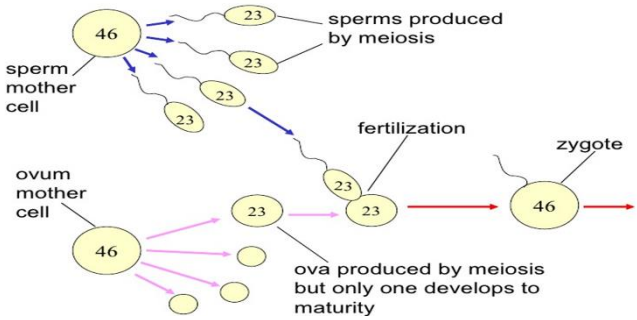
The centromeres ***do not divide***, instead, each chromosome of homologous pairs moves separately towards the opposite poles of the cell.

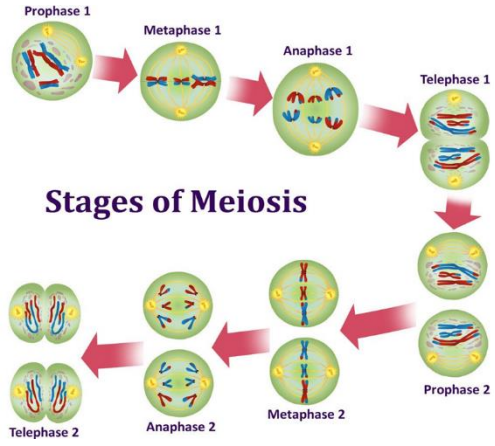
4. Telophase I:

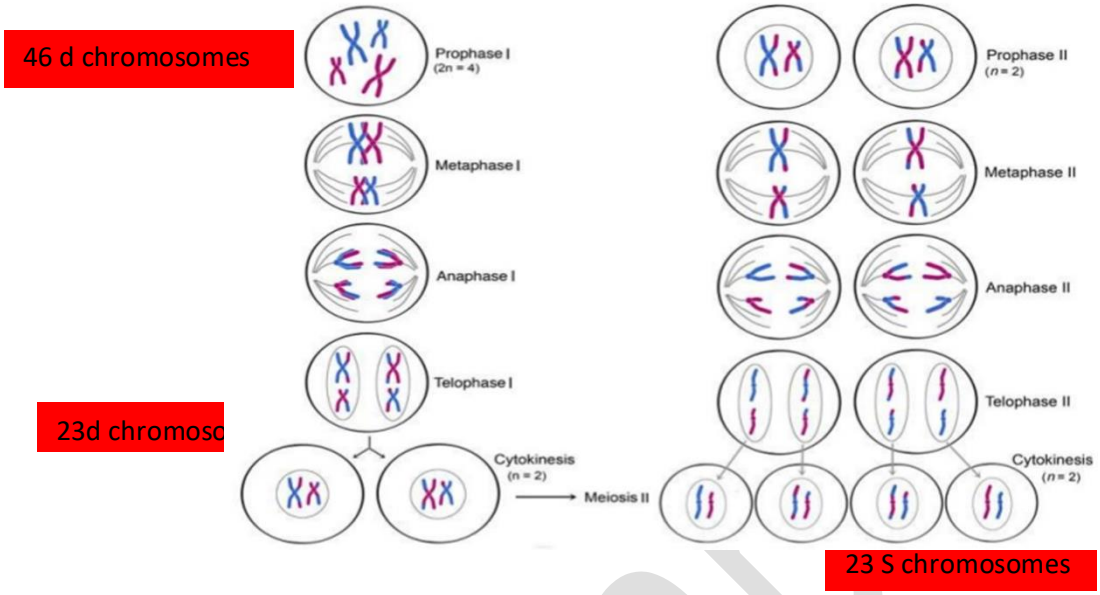
Cytokinesis occurs results in two daughter cells each containing the haploid number(23d-chromosomes).

II-Second meiotic division (equatorial division):

- It is similar to mitosis but, it is ***not preceded by S phase***.
- It results in formation of ***4 daughter cells***, each contains 23 s-chromosomes (haploid number).







	Mitosis	Meiosis
1-Types of cells	Somatic cells	Germ cells of testis & ovaries
2- No of division	Single division	2 successive divisions: Meiosis I & Meiosis II.
3- Interphase	Preceded by interphase with S phase	Meiosis I preceded by interphase with S phase, Meiosis II not preceded by S phase.
3- Prophase	No crossing over	Meiosis I: Crossing over occurs
4-Metaphase	46 d chromosomes arranged individually at the equatorial plane of the cells.	In Meiosis I :23 bivalent arranged at the equatorial plane of the cells.
5- Anaphase	Each chromosome divides at centromere into 2 chromatids	In Meiosis I: each chromosome of a bivalent moves apart.
6- Cells produced	Two daughter cells with diploid number of chromosomes (46 S) Daughter cells are genetically identical	Four daughter cells with haploid number of chromosomes (23 S) Daughter cells are genetically variable.

Meiosis	Meiosis I	Meiosis II
1- Preceded S phase	Present (the cell enter the prophase with 46 d chromosomes).	Absent (the cell enter the prophase with 23 d chromosomes).
2- Prophase	Pairing of homologous chromosomes result in 23 tetrad. Crossing over occurs between each tetrad .	No pairing No crossing over.
3- Metaphase	23 tetrad arranged at the equatorial plane of the cells.	23 d chromosomes arranged individually at the equatorial plane of the cells.
4- Anaphase	No division of the centromere. Each **chromosome** moves independently to the opposite pole of the cell.	Centromere splits so each **chromatid** moves independently to the opposite pole of the cell.
5- Telophase	Cytokinesis results in 2 daughter cells each with 23 d chromosomes.	Cytokinesis results in 4 daughter cells each with 23 S chromosomes.

The Human Chromosome

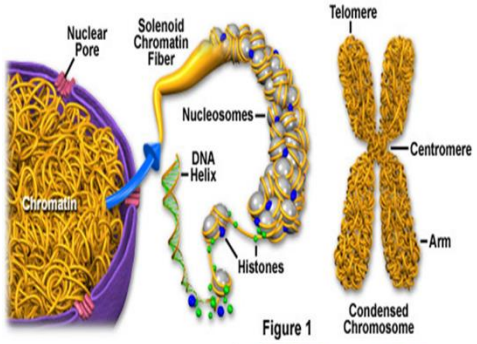
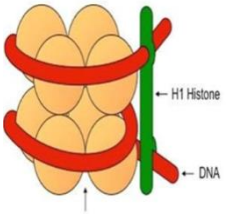
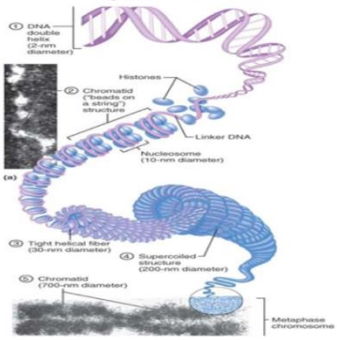


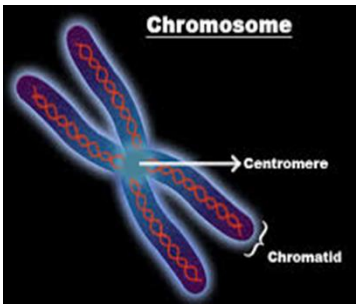
Figure 1

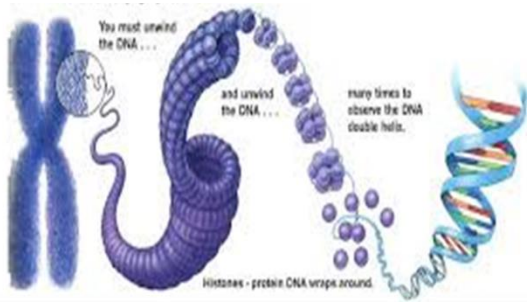
- **DEFINITION:** thread-like structures, present in the nucleus.
- **FUNCTION:** carries the genetic information in the form of genes.
- **STRUCTURE OF THE CHROMOSOME:**
- The DNA is packed in the form of chromatin (DNA + histone proteins).
- **DNA is extensively packaged in chromatin as:**



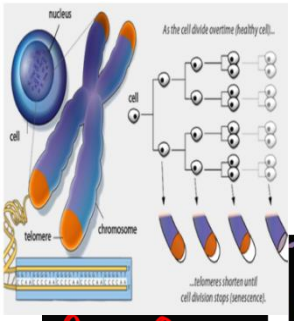


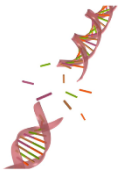
1. A segment of the DNA is wrapped two times around eight histone proteins to form a ***nucleosome***. Each nucleosome is separated from the next by a region of linker DNA.
2. Repeating nucleosomes with intervening DNA (linker DNA) form a ***10nm fiber*** (beads on a string).
3. This chain of nucleosomes is packed to form a ***30nm fiber***.
4. Higher orders of packaging give the compact structure ***700nm*** seen in the metaphase of the dividing cell known as the chromatid of a chromosome.

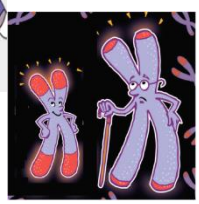


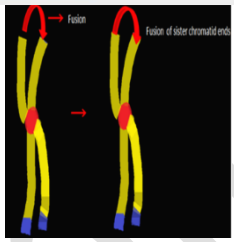


Telomere



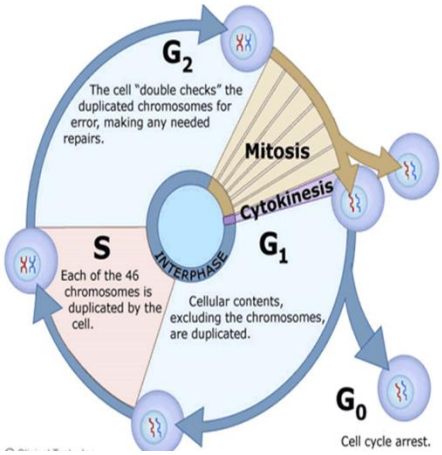


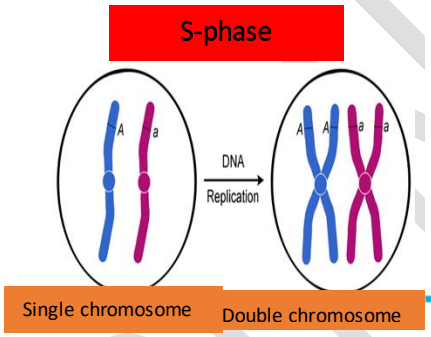


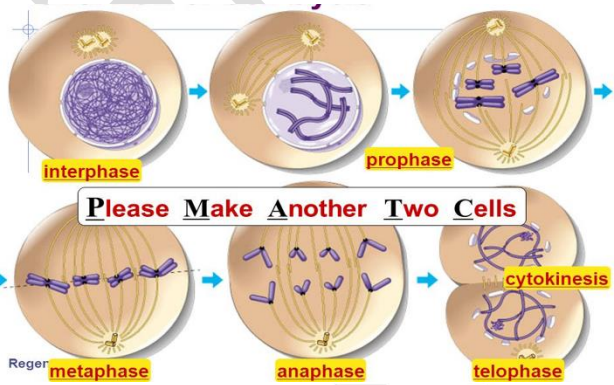


- **DEFINITION:** a segment of the DNA present at the end of the chromosomes.
- **FUNCTIONS:**

1. Prevent the end of the chromosomes from sticking together.
2. Allow proper dividing of the cells.
   - Each time the cell divides, the telomere gets shorter, until reaching a certain length, the cell stop dividing& become senescent.



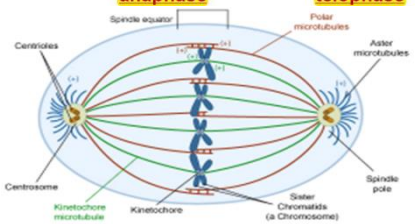




- **TYPES OF MICROTUBULES:**

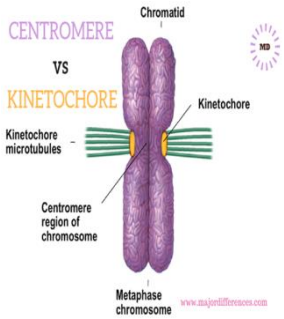
a. Astral microtubules:

- Originate from the MTOCs in the centrosome & radiate from it toward the cell membrane.
- **Function:** necessary for proper orientation of the spindle apparatus within the cell.



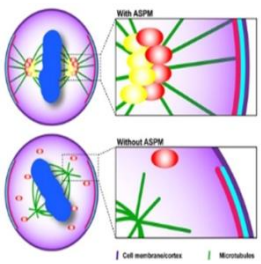
B. Polar microtubules:

- Originate from the MTOCs in the centrosome & begin to polymerize between the centromeres, overlapping each other.
- **Function:** help to push the spindle apparatus apart away from each other.

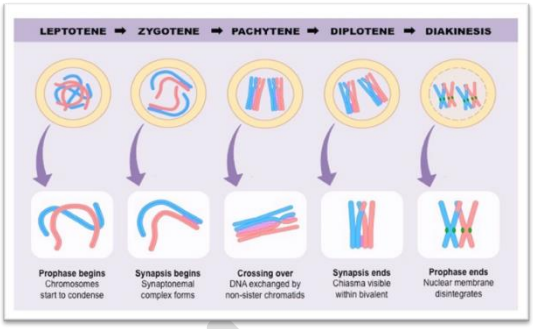


C. Kinetochore microtubules:

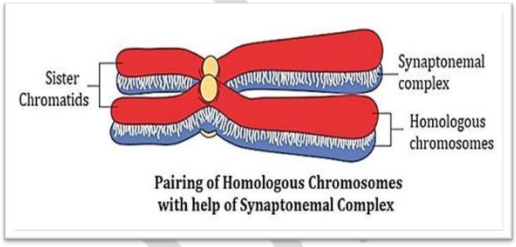
- Attach to the kinetochore on each side of the centromeres.
- **Function:** pull on the chromosomes and move them.



Meiosis, Prophase 1



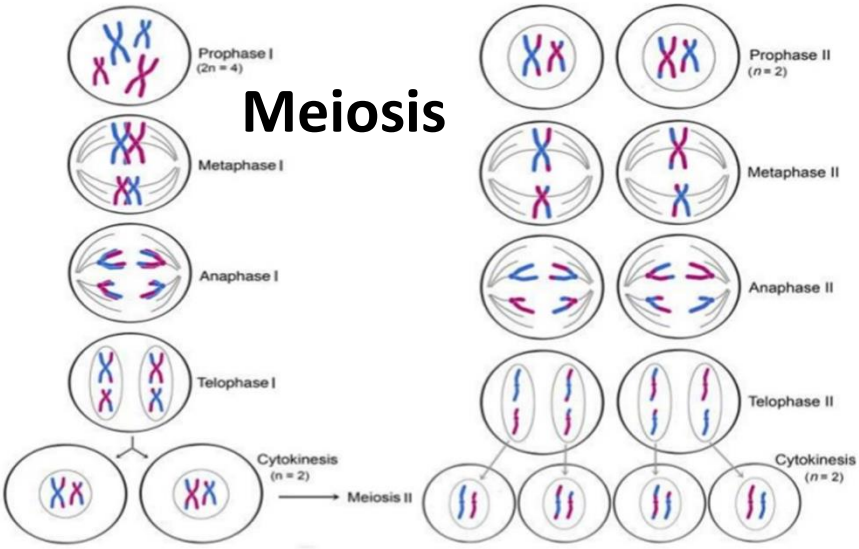
- **Leptotene** → chromosomes begin to condense appear as *long &thin threads*. Each chromosome consists of 2 chromatids joined together by a centromere.
- **Zygotene** → homologous chromosomes *pair up* forming 23 bivalents or tetrads. They begin to make connection (synapsis) by **synaptonemal complex**.
- **Pachytene** → chromosomes becoming *shorter and thicker*. **Crossing-over** occurs between the chromatids of the homologous chromosomes at sites called **chiasmata**.
- **Diplotene** →the synaptonemal complex dissolves, so the *2 homologous chromosomes* are separated from each other, but they are connected at the chiasmata. Each chromosome contains some genes inherited from the mother and other genes inherited from the father.
- **Diakinesis** → bivalents *more condensed* & the nuclear membrane and the nucleolus disappear.



Pairing of Homologous Chromosomes with help of Synaptonemal Complex

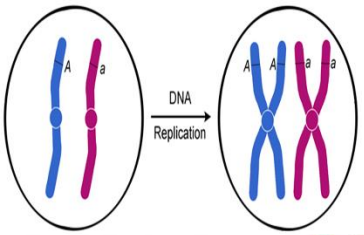
SIZE OF THE CHROMOSOME:

1) **Interphase:** long & thin.
2) **Division:**
   - **Prophase:** progressive decrease in its length accompanied by increasing its thickness.
   - **Metaphase:** very thick & quiet short (easily recognized).



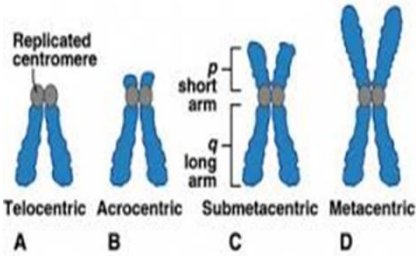
TYPES OF CHROMOSOMES:

A- According to the amount of the DNA:



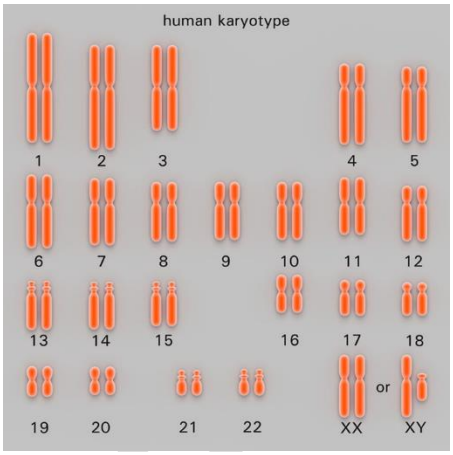
- **Single-chromosomes (s-chromosomes):** made of one DNA molecule (interphase chromosomes = chromatin or chromatids).
- **Double-chromosomes** (d- chromosomes; mitotic chromosomes):are formed during the S phase. Each d-chromosome is formed of two chromatids, linked at the centromere. Each chromatid is made of a DNA molecule.

B- According to position of centromere:



1. **Metacentric:** the centromere *in the middle.*
2. **Submetacentric:** the centromere is displaced *slightly away* from the center.
3. **Acrocentric:** the centromere is displaced *away* from the center.
4. **Telocentric:** the centromere is positioned *at the very end* of the chromosome.

C- Autosomal or sex chromosome:



1- Autosomal chromosomes:

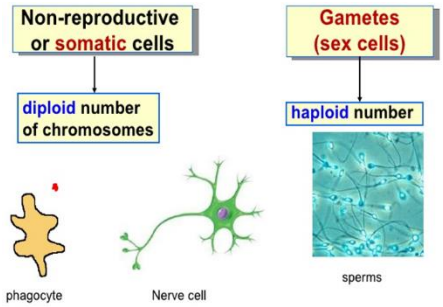
- Paired chromosomes with the same length, shape, position of the centromere & genetic information.
- Carry the genes for *somatic characteristics*.

2- Sex chromosomes:

- Paired chromosomes differ between males & females.
- Carry genes for *sex characteristics*.

X chromosome	Y chromosome
It is a sex chromosome, that occurs paired in females & single in males.	It is a sex chromosome, that is present normally single in males.
In female: one X chromosome is inherited from the mother& the other inherited from the father. In male: one X is inherited from the mother.	In male: One chromosome is inherited from the father.
Contains genes for female sex determination.	Contains genes for male sex determination.
Bigger in size. Contains about 1000 genes.	Smaller. Contains about 50-60 genes.
Represents 5 % of the entire human genome.	Represents 2 % of the entire human genome.

TYPES OF CELLS IN THE HUMAN BODY:

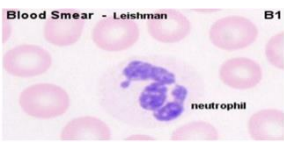


1- Somatic cells: contain 46 chromosomes (44 autosomal+ 2 sex chromosomes).

2- Germ cells (Gametes= sperm & ovum): contains 23 chromosomes (haploid number; 22 autosomal+ 1 sex chromosome).

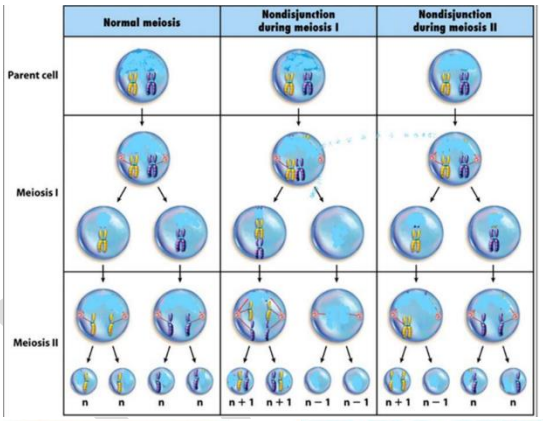
KARYOTYPING:

- The *somatic cell* contains 46 chromosomes.
- **Karyotyping:** is the arrangement of the chromosomes pf a person during metaphase into groups of homologous pairs:
  - 22 homologous pairs of *autosomal chromosomes* ; the same in length, position of centromere& genetic information,
  - One pair of *sex* chromosomes.
  - Each pair contains one chromosome originally derived from the mother& the other chromosome derived from the father.
  - In females (44 autosomes +XX): one X chromosome is heterochromatic (*Barr body*), it can be identified in neutrophils, attached to the nucleus in the form of a drumstick mass.



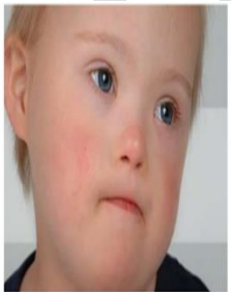
- Importance: regulates the amount of X-linked gene products being transcribed.

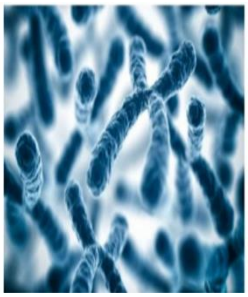
How do chromosome abnormalities happen?



- Chromosome abnormalities usually occur when there is an ***error in cell division***: in mitosis & meiosis: the correct number of chromosomes is supposed to end up in the resulting cells. However, errors in cell division can result in cells with too few or too many copies of a chromosome.
- Errors can also occur when the DNA are being ***duplicated***.
- **Factors that can increase the risk of chromosome abnormalities are:**

1- Maternal Age:

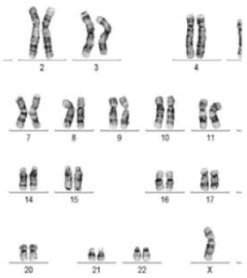




- **Older women** are at higher risk of giving birth to babies with chromosome abnormalities than younger women because they are born with all the eggs they will ever have.
- Some researchers believe that errors can crop up in the eggs' genetic material as they age.
- Because men produce new sperm throughout their lives, paternal age does not increase risk of chromosome abnormalities.

2- Environment: it is still possible that the environment may play a role in the occurrence of genetic errors.

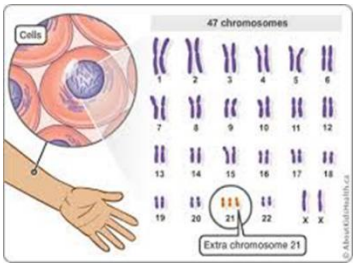
Types of chromosomal abnormalities:



1- Numerical abnormalities (aneuploidy): when a whole chromosome from a pair either ***missing*** (monosomy) or ***extra*** to the normal pair (trisomy).

2- Structural abnormalities: when part of an individual chromosome is missing, extra, switched to another chromosome, or turned upside down.

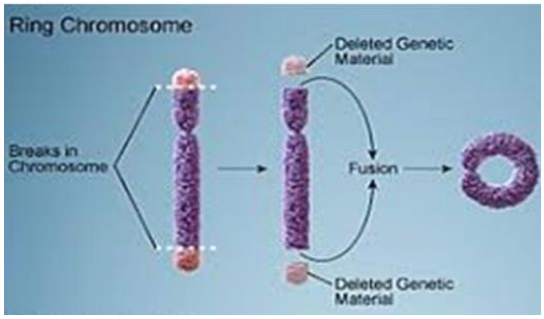
Structural abnormalities:

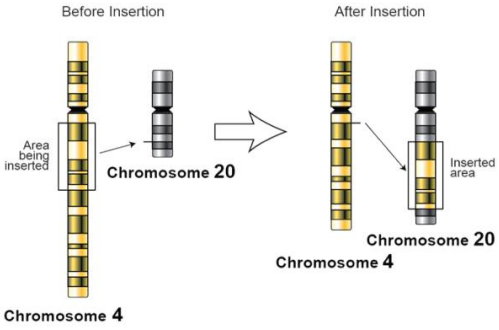


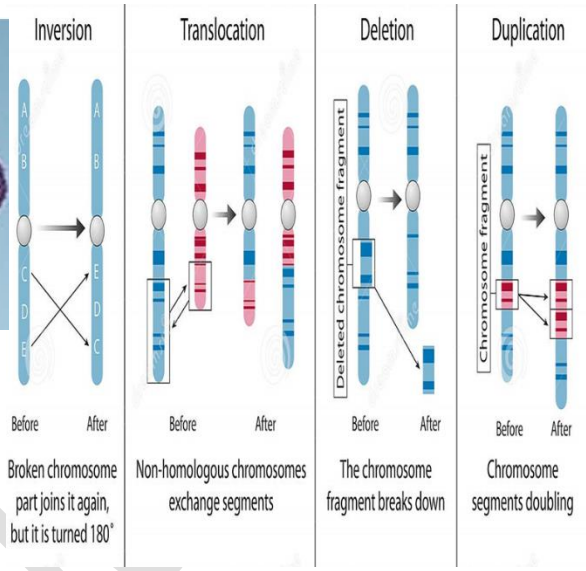
1- **Deletion:** When a chromosome ***breaks*** with loss of some genetic materials.
2- **Duplication:** When a part of the chromosome is ***duplicated*** (2 copies which means having extragenetic materials)
3- **Translocation:** When a piece of one chromosome *breaks off & attaches to another chromosome*.
4- **Inversion:** When a piece of one chromosome *breaks off & turned upside down, and reattached to the same chromosome*. As a result, the genetic material is inverted.
5- **Rings:** when a chromosome breaks in two places and *its broken ends fuse together.*
6- **Insertions:** when a segment of one chromosome *is translocated and inserted* into another non-homologous chromosome (inter-chromosomal insertion), or into a different region of the same chromosome (intra-chromosomal insertion)

- Most chromosome abnormalities occur as an *accident in the egg or sperm*. In these cases, the abnormality is present *in every cell* of the body.

- Some abnormalities, however, happen ***after conception***; then ***some cells*** have the abnormality and some do not.
- Chromosome abnormalities can be ***inherited*** from a parent or be "***de novo***" (new to the individual). This is why, when a child is found to have an abnormality, chromosome studies are often performed on the parents.





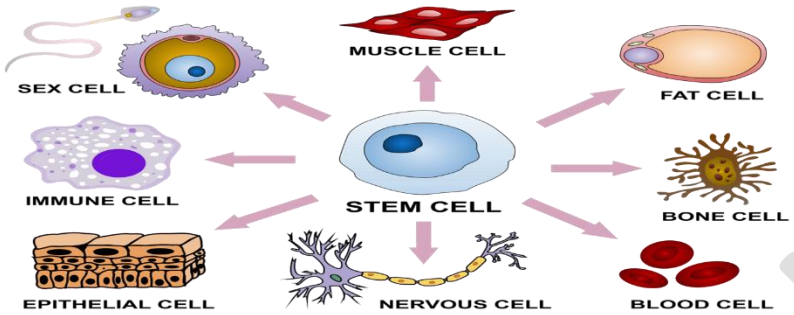


Cell Proliferation & Cell Death

→Difference between cell proliferation and cell differentiation:

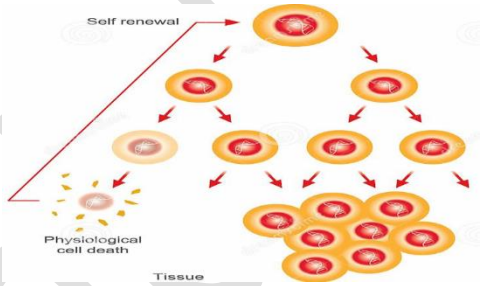
Cell differentiation

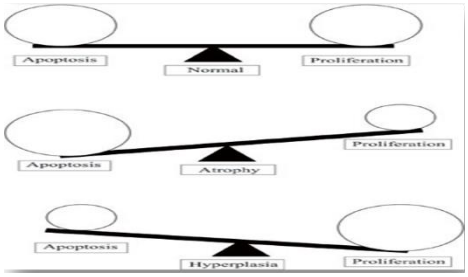
It is the process by which *unspecialized cells* acquire specialized *structural* and/or *functional* features that characterize the specialized cells.



Cell proliferation

Increase in the number of cells by division.





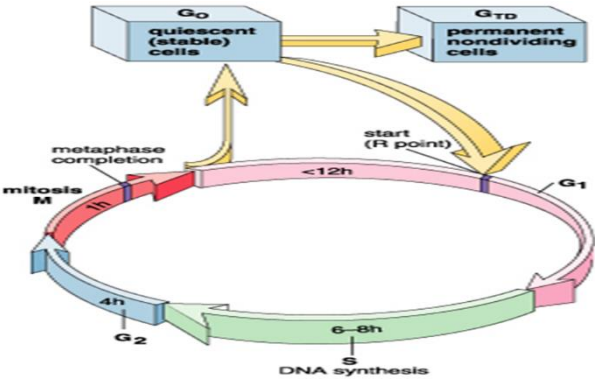
CELL PROLIFERATION & DIFFERENTIATION:

- **Early development**: *Rapid* proliferation of embryonic cells, which then differentiate to produce the many specialized types of cells that makeup the organs.
- **As cells differentiate**: The rate of proliferation *decreases*, and many cells are arrested in the GO stage.
  - ***Cell proliferation is balanced with cell death to maintain a constant number of cells.***

CLASSIFICATION OF THE BODY CELLS ACCORDING TO THEIR ABILITY OF PROLIFERATION:

1-Static cell population (non-dividing, permanent):

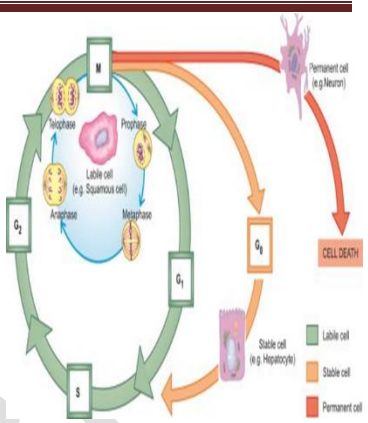
- They leave the cell cycle to perform specialized function (GO stage), e.g. cardiac muscle fibers& neurons.



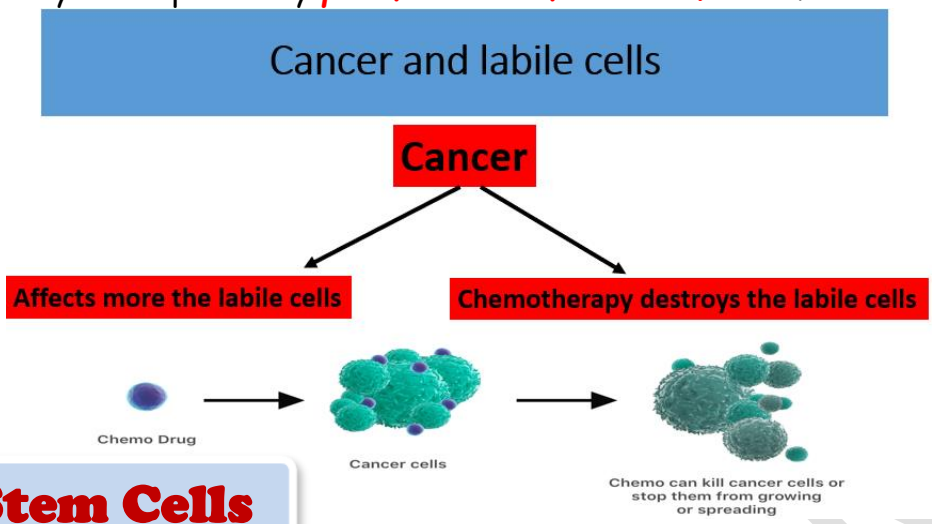
2-Stable cell population(quiescent):

- They are considered to be in Go stage, but ***they may be stimulated to divide by signals*** e.g. smooth muscle fibers and the cells of the liver.

3-Labile cell population:



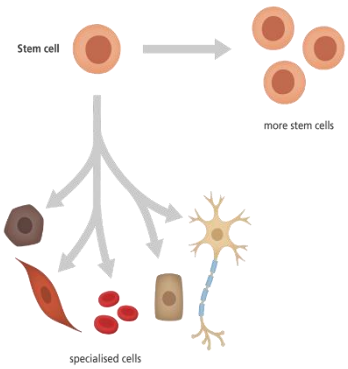
- They are ***continuously renewing*** *cells* e.g. cells have short life span as blood cells, epithelial cells of the skin &epithelial cells lining the digestive tract
- They are replaced by ***proliferation of the stem cells***.



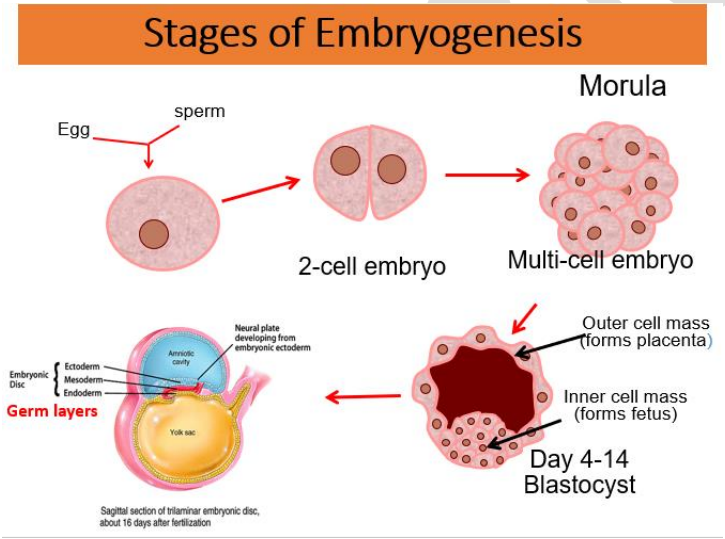
Stem Cells

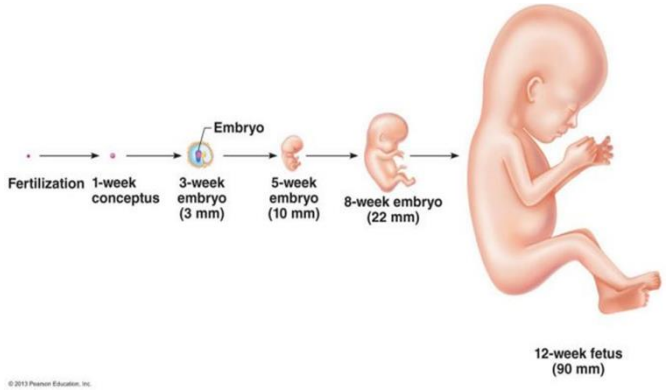
- **DEFINITION:** undifferentiated (unspecialized) cells that can proliferate & differentiate to give specialized cells.
- **STEM CELL PROPERTIES:**

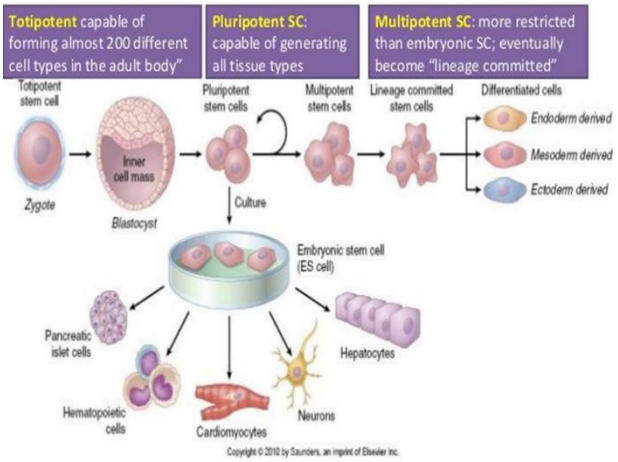
1- *Self-renewal*: the ability of the cell to go through numerous cycles of cell division while maintaining the undifferentiated state.
2- *Potency*: the capacity to differentiate into different cell types.



- **TYPES OF STEM CELLS:**







1-Totipotent stem cells:

- They have the potential to generate all types of cells and construct a ***complete organism***.
- They are derived from the cells produced by the first few divisions of the fertilized ovum ***(morula cells)***.

2-Pluripotent stem cells:

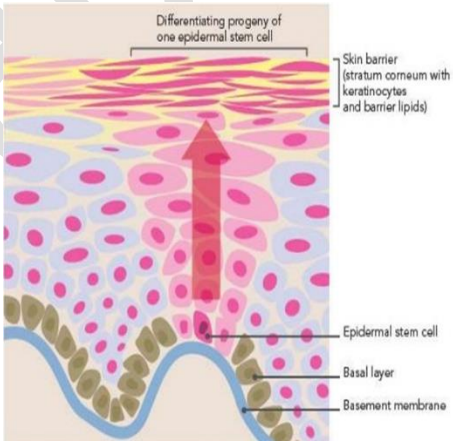
- They can differentiate into the derivatives of ***the three germ layers*** =ectoderm, endoderm, and mesoderm.
- They are derived from ***the inner cell mass*** of the blastocyst.

3-Multipotent stem cells:

- They can produce cells of a ***closely related family*** e.g. hematopoietic stem cells that can differentiate into red blood cells, white blood cells and platelets.

4-Unipotent cells:

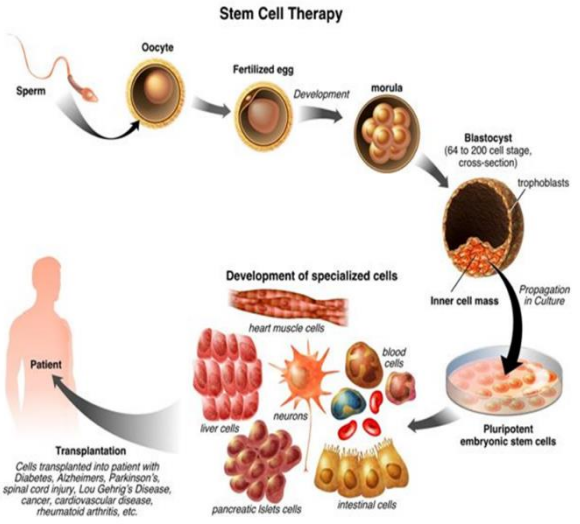
- They can produce ***a single type of*** mature cell ***but*** still have the property of self-renewal which distinguishes them from non-stem cells e.g. stem cells in the skin epidermis.



- **POTENTIAL SOURCES OF STEM CELLS FOR CLINICAL APPLICATION:**

1- Embryonic stem cells:

- They are ***pluripotent*** stem cells derived from inner cell mass of blastocyst.
- **Advantage:** They can specialize and become any type of body cells.
- **Disadvantage:** ethical restriction.

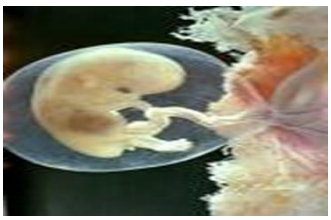


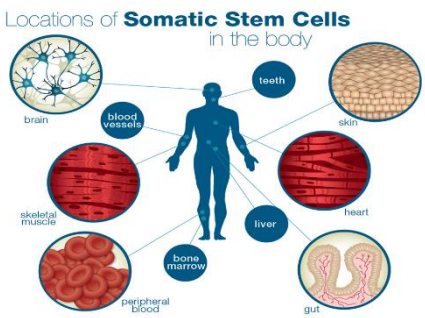
2- Adult stem cells:

Most of them are ***multipotent***.

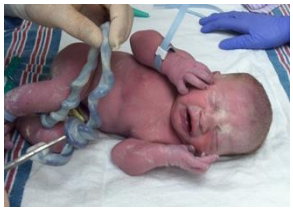
3-Amniotic fluid stem cells:

They are ***multipotent***.





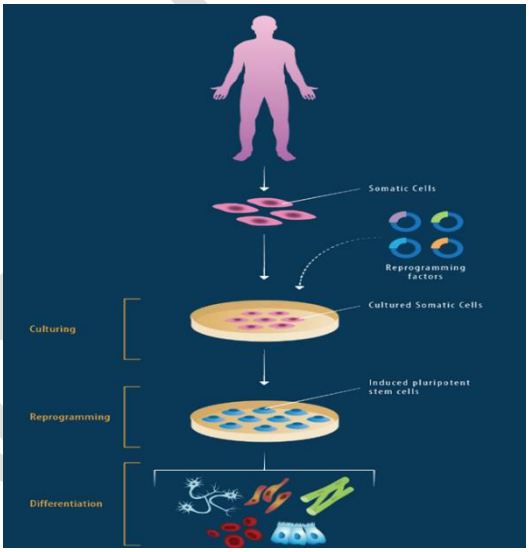
4-Umbilical cord blood stem cells:

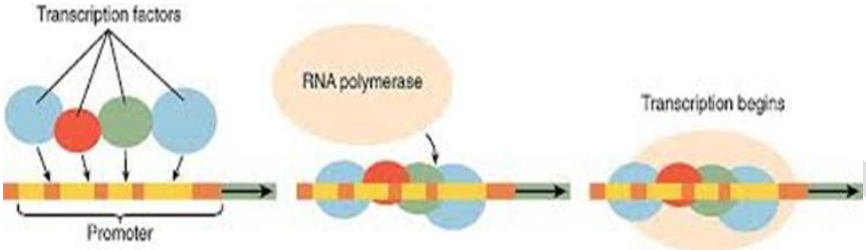


They are ***pluripotent.***

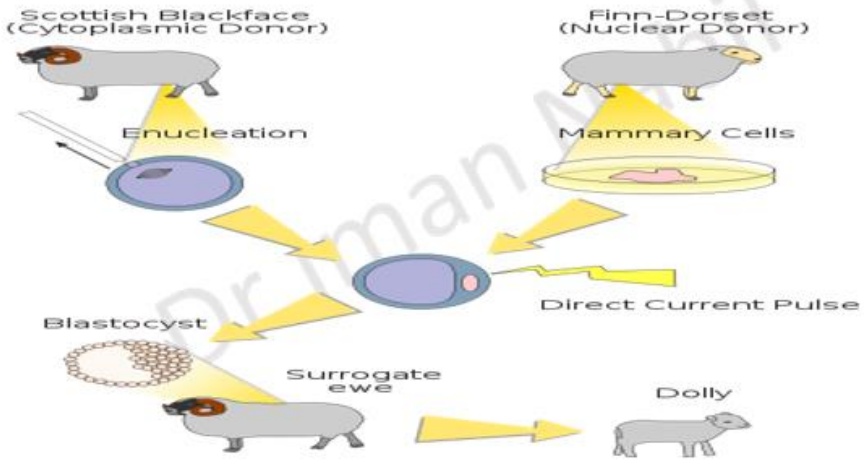
Induced Pluripotent stem cells:

Definition: Stem cells produced after alteration of the genes of *adult somatic cells* (dedifferentiation) to give them the properties of *the embryonic stem cells*.



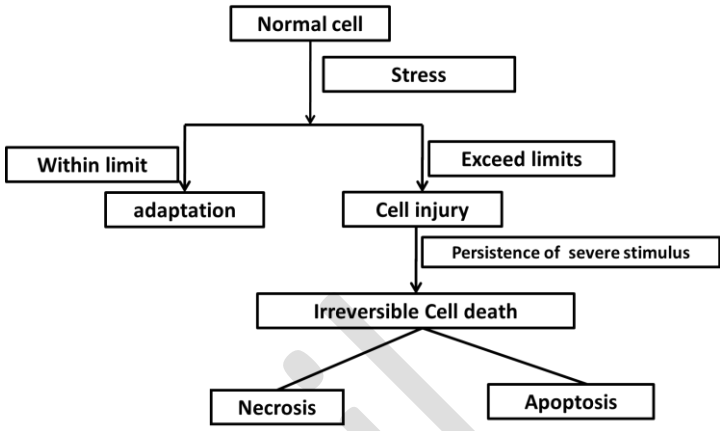


Dolly Sheep (1996-2003)



Cloning

Cell Death



Types of cell death

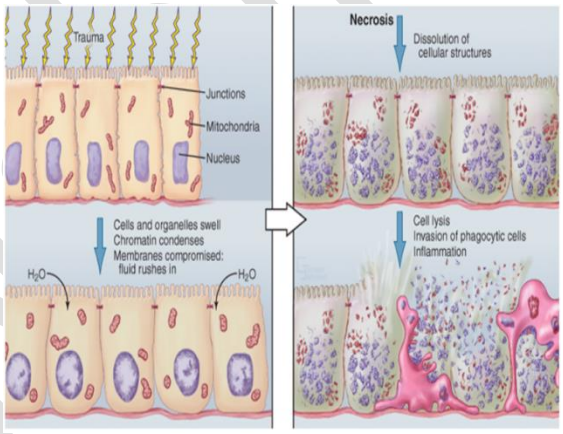
Apoptosis

Necrosis

1- Necrosis = accidental cell death:

- **Causes:** It is a *pathological process* due to e.g. hypoxia, radiation or pathogens such as viruses.
- **Morphological features:**

1- *Damage of the cell membrane* with cell swelling& rupture.
2- Breakdown of cell organelles.
3- Denaturation or coagulation of cytoplasmic proteins.
4- Inflammation with extensive damage of the surrounding tissue.



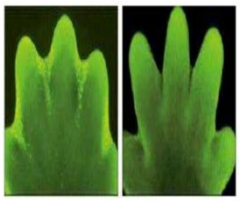
2- Apoptosis = programmed cell death:

It is a *physiological process* controlled by several genes (loss of mitochondrial function initiates several reactions that lead to cell death).

What makes a cell decide to commit suicide?

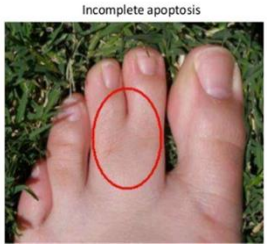
I-During embryonic development:

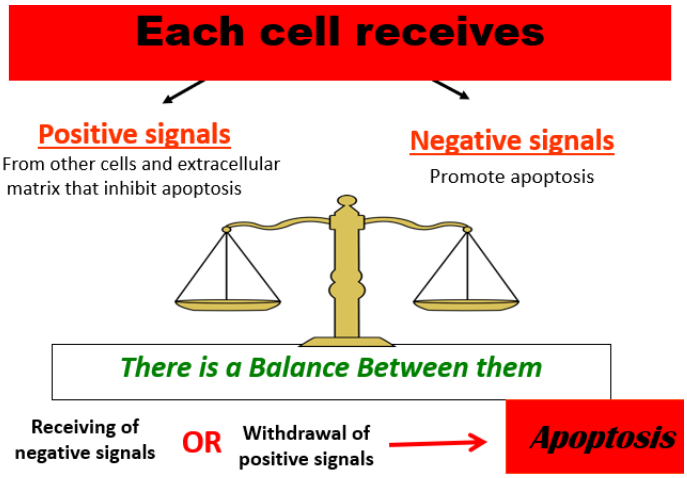
Removal of excess cells that have no function e.g. during morphogenesis and for determination of organ size.



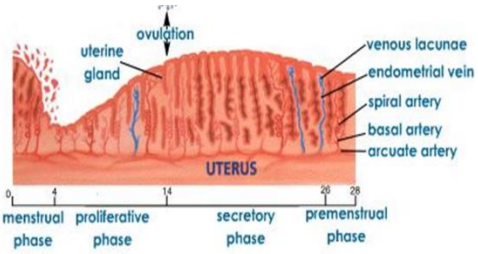
Development of toes

Incomplete apoptosis





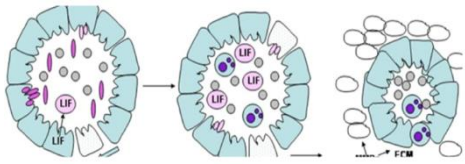
II-In adult:



1- Hormone-dependent:

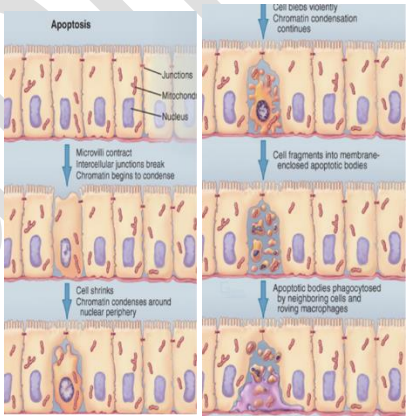
- Involution of the endometrium during the menstrual cycle.
- Regression of lactating mammary gland after weaning.
- Regression of prostate in old males

2- Elimination of cells during cell cycle when their DNA damage is not repaired.



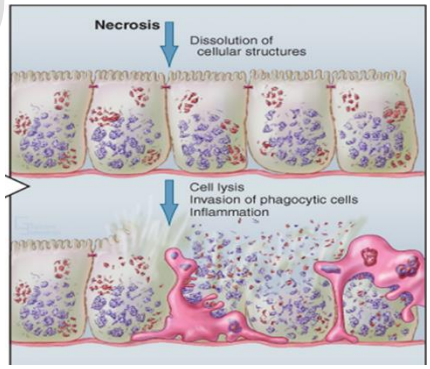
3- Maintaining a constant number of cells in proliferating cell populations, e.g. intestinal epithelium.

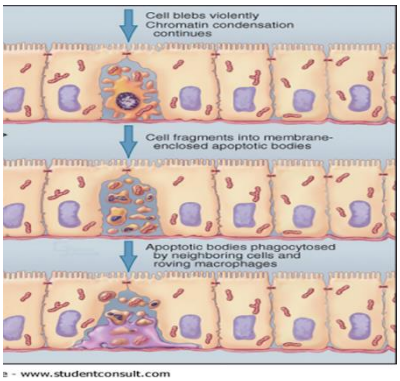
• MORPHOLOGICAL FEATURES OF APOPTOSIS:



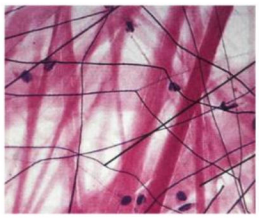
1- Loss of microvilli and intercellular junctions.
2- Shrinkage of the cell with membrane blebing.
3- Breakdown of DNA with hypercondensation of chromatin and its collapse against the nuclear periphery.
4- Change of cell membrane characters ***without loss of its integrity***.
5- Cell organelles remain apparently normal but become clumped inside the cytoplasm.
6- Fragmentation of the cell into ***apoptotic bodies*** that contain fragments of the nucleus, mitochondria, and other organelles.
7- The apoptotic bodies are removed by the phagocytic cells.

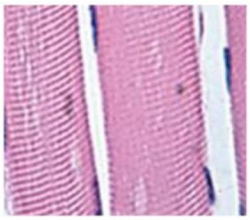
	Necrosis	Apoptosis
1- Type	Pathological.	Physiological.
2- Cell membrane	Damage with loss of its integrity.	Change of some characters without loss of its integrity.
3- Organelles	Broken down.	Intact.
4- Proteins	Denatured or coagulated.	Broken down of DNA with hypercondensation of chromatin.
5- Apoptotic bodies	Absent	Present
6- inflammation	Present	Absent

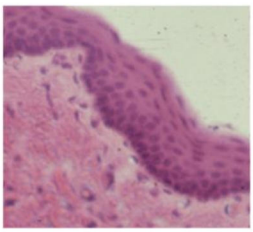


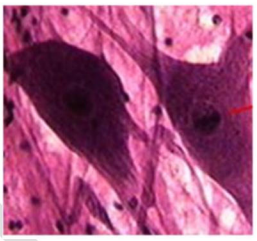


Basic tissues: A group of similar cells specialized to perform a common function. These tissues exist in associations forming body organs. They are 4:


Connective tissue

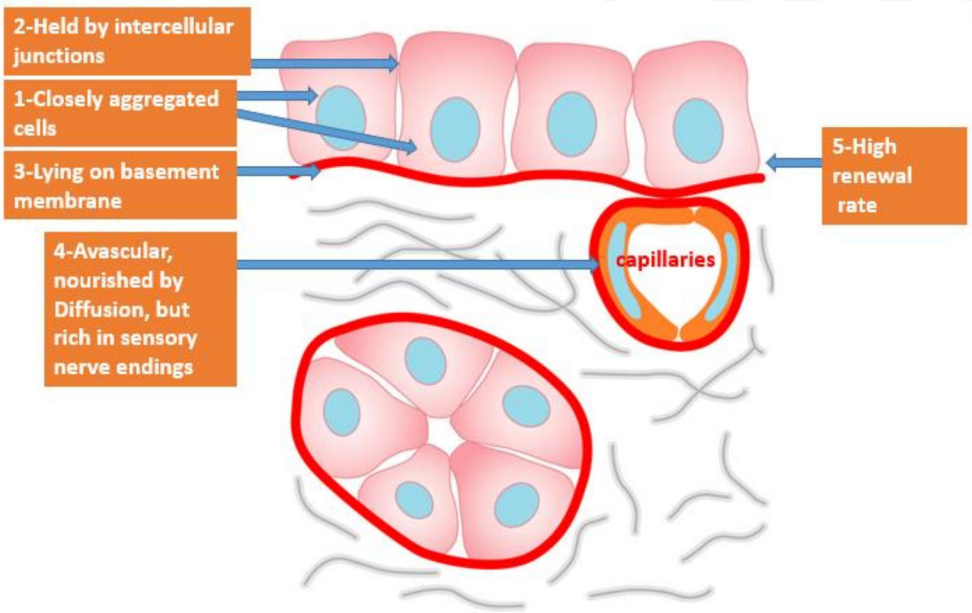

Muscular tissue


Epithelial tissue

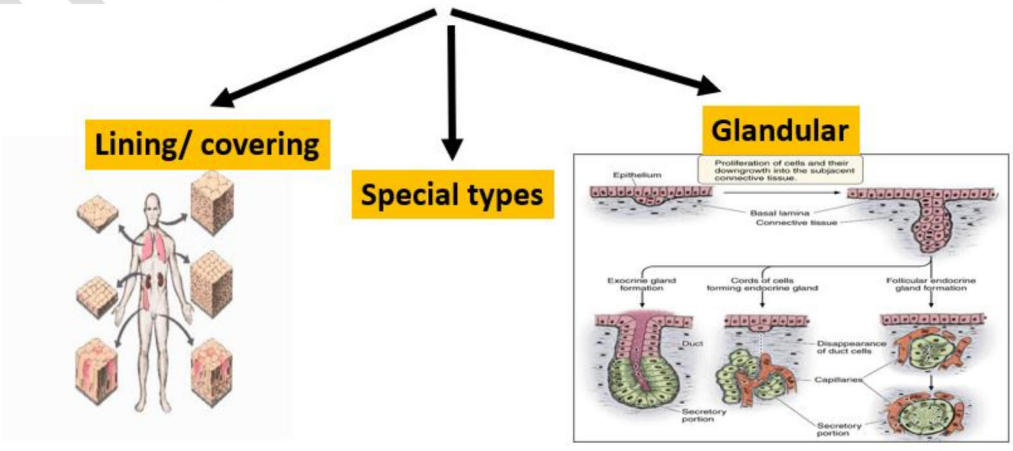

Nervous tissue

Epithelium

Characteristics of Epithelium:

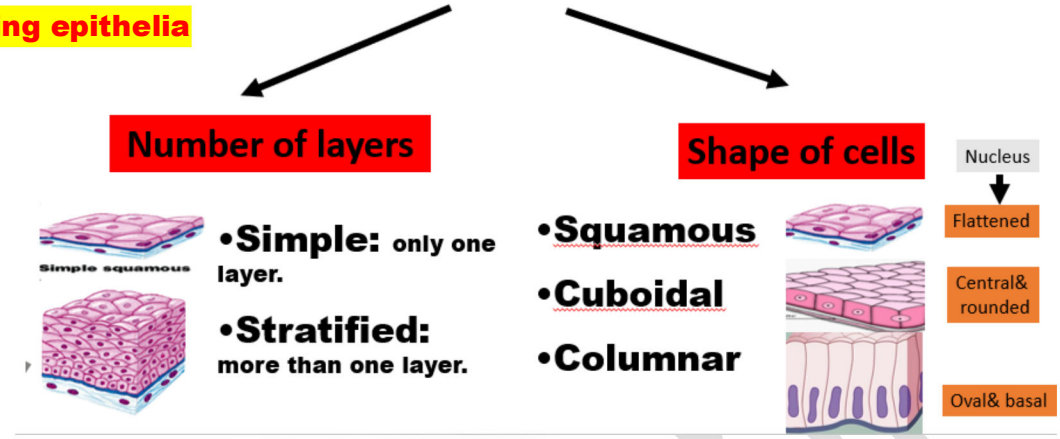


Classification of Epithelium:



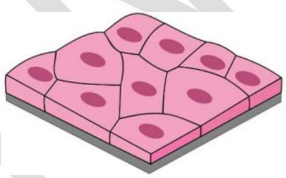
I- Lining Epithelium

Classification of covering epithelia



Simple Epithelium

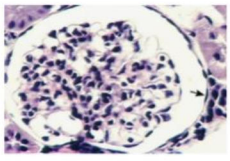
1- Simple Squamous:

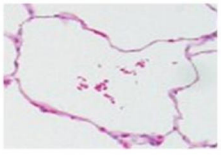


Side view: Flat cells & Flattened nucleus.

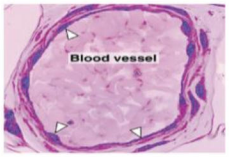
Surface view: polygonal.

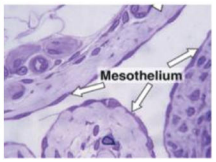
Sites:



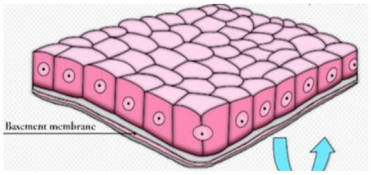


1- *Filtration:* Bowman's capsule of kidney.
2- *Diffusion:* alveoli of lung.
3- *Smooth passage:* endothelium of blood vessels and lymph vessels.
4- *Allows free mobility:* mesothelium.



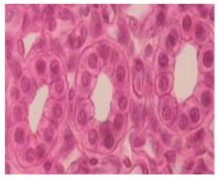


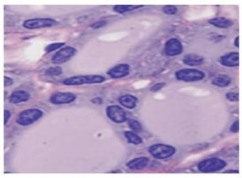
2- Simple cuboidal:



Shape: cubical cells with central rounded nuclei.

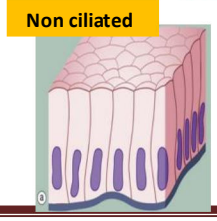
Sites: Kidney tubules & Thyroid follicles (ion exchange).

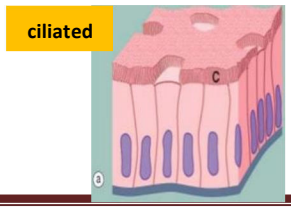




3- Simple columnar:

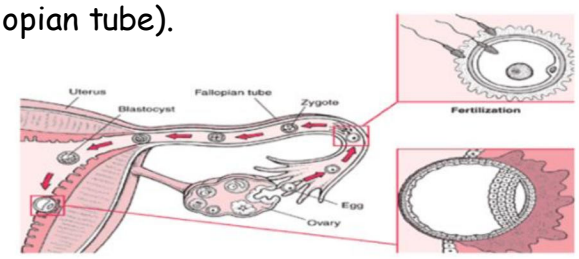
Shape: columnar cells, the nuclei are oval & basal

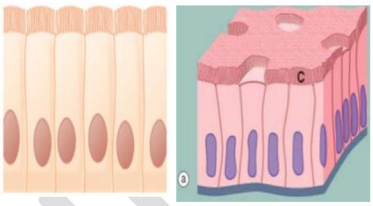




Types & Sites:

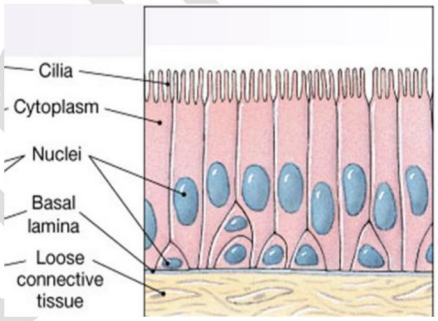
1- *Non ciliated:* Secretion & absorption (stomach, small intestine, gall bladder).
2-*Ciliated:* Secretion (uterus, fallopian tube).





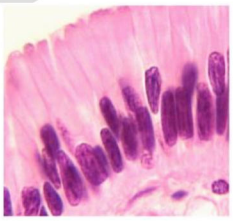
4- Pseudostratified columnar epithelium:

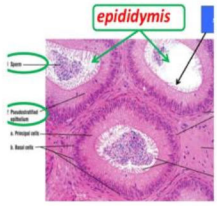
1- *Crowded cells,* all cells lie in contact with the basement membrane, but they do not all reach the surface.
2- The cells that reach the surface are tall ***columnar cell, while*** the other cells which do not reach the surface are short and ***triangular***.
3-*Several layers of nuclei,* each lies at the widest portion of the cell, giving false appearance of stratification.

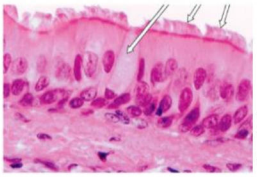


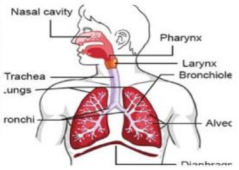
Types & Sites:

1- *Non ciliated:* male genital tract.
2-*Ciliated:* most of respiratory system (pseudostratified ciliated columnar epithelium with goblet cells).





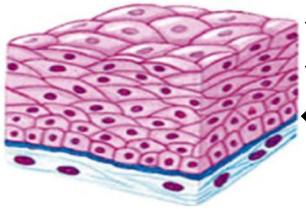




Stratified Epithelium

It is classified according to the shape of the most superficial layer of cells.

1- Stratified squamous:

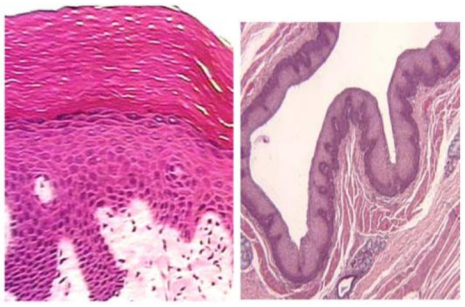


Function: protection.
Structure:

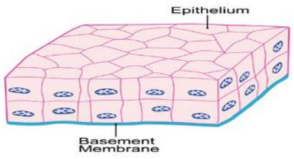
1- *Basal layer:* low columnar; cuboidal cells.
2-*Intermediate layers:* Polygonal cells.
3-*Superficial layer:* Squamous cells.

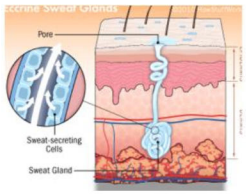
Types:

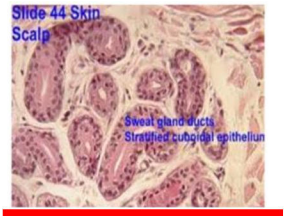
1- *Keratinized:* The superficial cells are filled with keratin (skin).
2-*Non keratinized:* In wet surfaces subjected to wear & tear (cornea, esophagus, mouth cavity & vagina).



2-Stratified cuboidal:





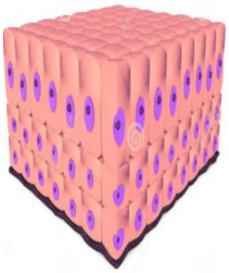


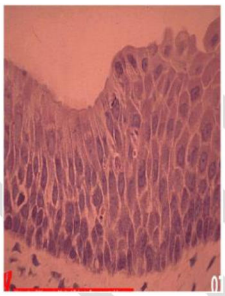
Ducts of sweat glands

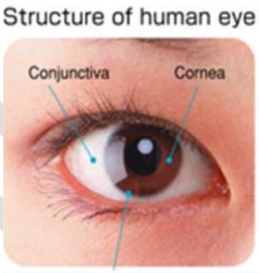
- Uncommon type.
- Two layers of cuboidal cells.

3-Stratified columnar:

- Uncommon type.
- The superficial cells are columnar in shape.



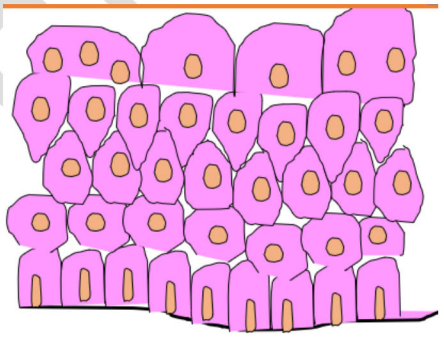




Conjuctival fornix

2- Transitional Epithelium:

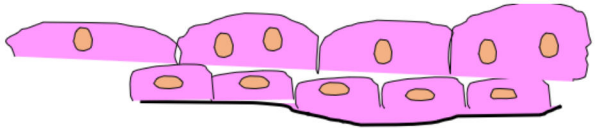
Change its shape and number of layers, according to the functional state of the organ, e.g. urinary bladder& ureter.



Empty bladder

1. ***A basal layer:*** low columnar cells.
2. ***Intermediate layers:*** polygonal cells,tend to be pear-shaped near surface.
3. ***The surface layer:*** large cuboidal (dome-shaped cells; umbrella cells).

Full bladder



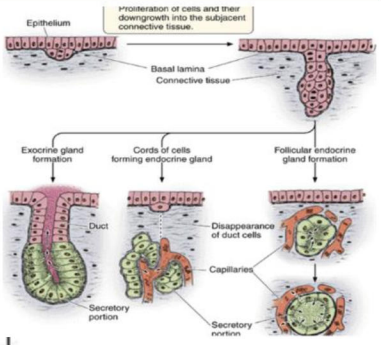
1- ***Superficial***: large, flattened cells.
2- ***Basal***: cuboidal cells.

How does the transitional epithelium adapt to its function?

1- Decrease of number of layers.
2- Flattened cells

} Increase surface area

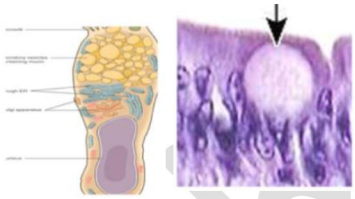
II- Glandular Epithelium



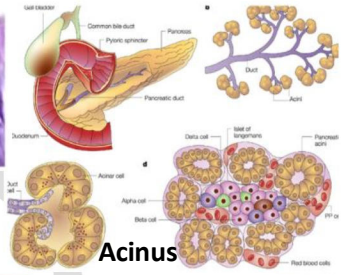
- **Function:** fluid secretion.
- **Origin:** from the covering epithelium

Types Of Glandular Epithelium:

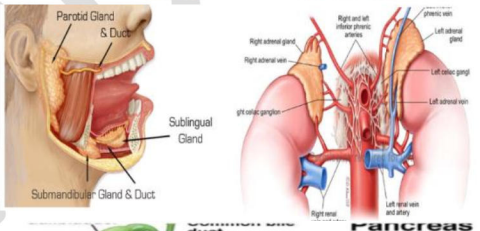
1-According to number of cells:



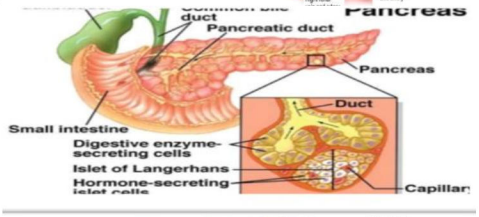
1. *Unicellular glands:* consist of one cell e.g., goblet cells present in the small intestine and the respiratory tract.
2. *Multicellular glands:* consist of groups of cells e.g., most glands of the body.



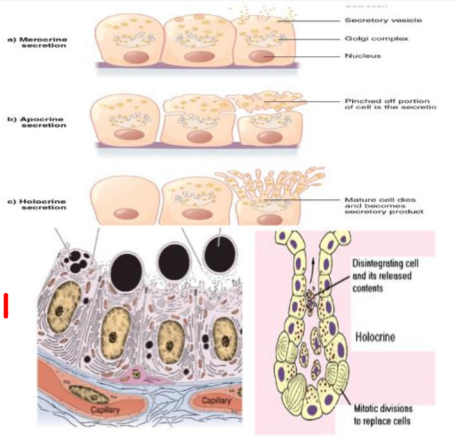
2-According to the presence or absence of a duct system:



1- *Exocrine glands:* in which the secretion is carried by ducts e.g., salivary glands.
2- *Endocrine glands or ductless glands:* in which the secretion is released into the blood vessels e.g., thyroid gland and suprarenal gland.
3- **Mixocrine (mixed exocrine and endocrine) glands:** contain the two types e.g., pancreas.



3-According to the mode of secretion (the secretory mechanism):

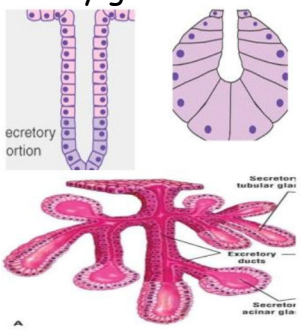


1- *Merocrine glands:* the secretory granules are discharged by exocytosis through the cell membrane **without losing any part of the cell** e.g., pancreas& salivary glands.
2- *Apocrine glands:* the secretion is discharged together **with the apical parts** of the cytoplasm e.g., mammary gland.
3- *Holocrine glands:* the secretion is discharged **with the whole cell** leading to its complete destruction e.g., sebaceous gland.

4-According to the nature of secretion:

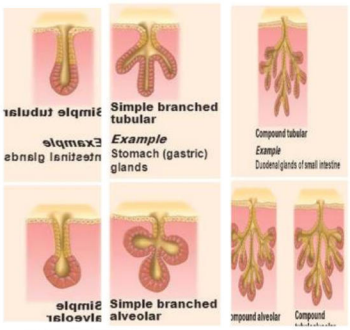
1- *Serous glands:* secrete a watery secretion e.g., parotid salivary gland.
2- *Mucous glands:* secrete mucous e.g., goblet cells and sublingual salivary gland.
3- *Mixed glands:* secrete both mucous and serous secretions e.g., submandibular salivary gland.
4- *Glands with special secretions:* ceruminous glands which secrete ear wax and sebaceous glands which secrete a fatty secretion (sebum).

5-According to the shape of the secretory portion:



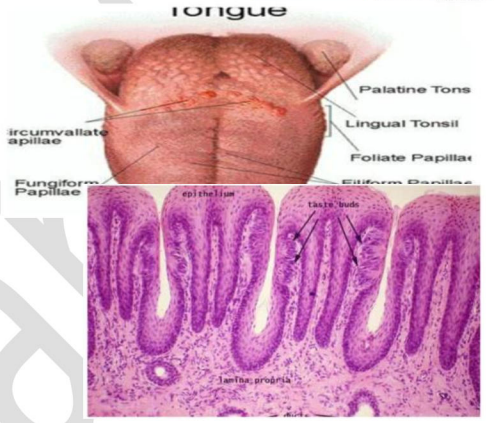
1- *Tubular:* the secretory units are tubular in shape.
2- *Alveolar (acinar):* the secretory units are rounded.
3- *Tubuloalveolar (tubuloacinar):* the secretory units have both tubular and alveolar parts.

6-According to the branching of the ducts and branching of the secretory portion:



1- *Simple glands:* have only one unbranched duct and one secretory unit.
2- *Simple branched glands:* have one unbranched duct and branched secretory units.
3- *Compound glands:* have branched duct system& branched secretory units.

III- Special Types of Epithelium



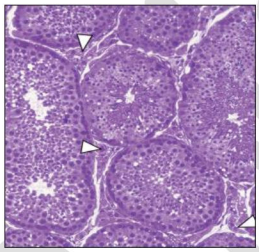
1- Neuroepithelium:

The epithelial cells act as nerve receptors.

Sites:

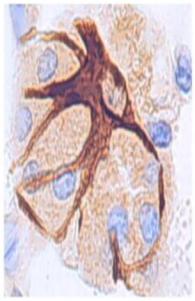
1- The taste buds of the tongue.
2- The organ of Corti in the ear.
3- The retina of the eye.

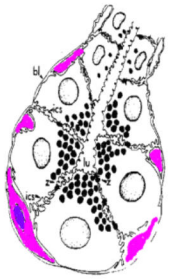
2- Germinal epithelium:



- The epithelium carrying the function of reproduction.
- **Sites:** in the testis and ovary.

3- Myoepithelial cells:





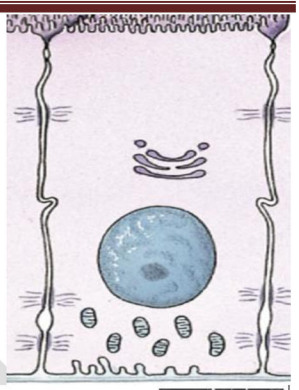
- ***Definition:*** modified stellate epithelial cells which surround the secretory units (the acini) and the ducts of the glands.
- ***Structure:*** contain myosin and actin myofilaments.
- ***Function:*** they are able to contract and squeeze the secretion from the glands.
- ***Sites:***

1- Salivary gland.
2- Mammary gland.

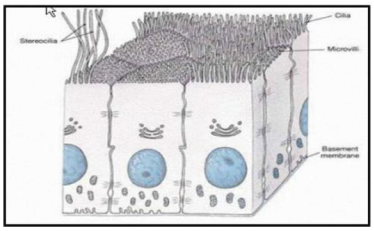
Functions of Epithelium:

1- **Protection (stratified)**
2- **Absorption (simple)**
3- **Filtration (simple)**
4- **Gas diffusion (simple)**
5- **Secretion (glandular)**
6- **Contraction (special)**
7- **Reproduction (special)**
8- **Perception (special)**

Epithelial Cell Polarity

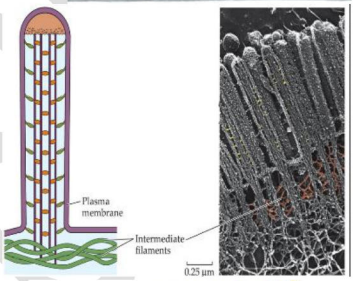


Definition: The epithelial cell has an apical, basal, and lateral surfaces, each surface exhibits special structural modifications to carry out specific functions.



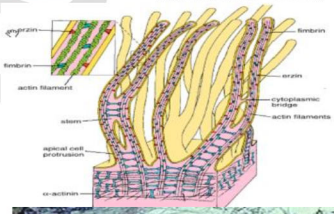
I- Apical Modifications:

1-Microvilli:



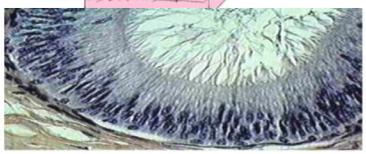
- *Definition:* non-motile, finger like cytoplasmic projections arise from the apical surface of epithelial cells.
- *Structure:* a core of actin filaments.
- *Function:* increase the surface area for absorption.
- *Sites:* The cells of the intestine and kidney tubules.

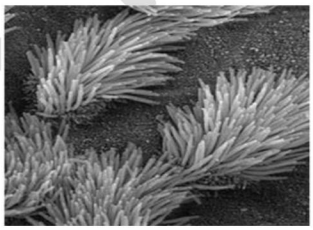
2-Stereocilia:



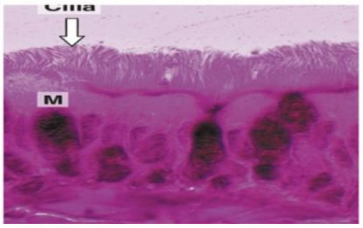
- *Definition:* long, branching microvilli.
- *Function:* increase the surface area for absorption.
- *Site:* the non-ciliated pseudostratified columnar epithelium of the male genital ducts e.g. the epididymis.

3-Cilia الأهداب and flagella:



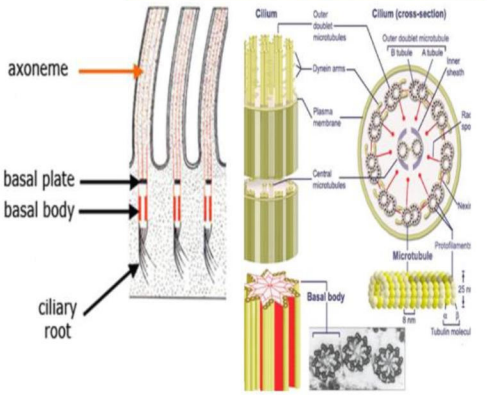


- *Definition:* motile cytoplasmic projections that extend from the cell surface.



- ➢ **Cilia**: are hair-like processes that are longer than microvilli.
- ➢ **Flagella**: resemble cilia in structure but they are much longer and are single for each cell e.g., flagellum of the sperm.

- ➢ **Structure:** each cilium is formed of:

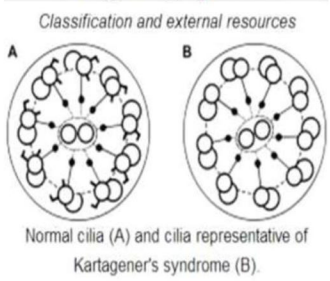


1- ***The basal body:*** replicate of the centrioles **(9 triplets of microtubules)** from which the shaft arises. The basal body is present in the apical cytoplasm.

2- ***The shaft (axoneme):*** extends from the cell surface. It contains **9 peripheral doublets** of microtubules + a central **pair of singlet microtubules** (9x2+2=20 microtubules).

3- ***Rootlets:*** extend from underneath the basal body, in the form of **radiating microtubules** anchoring the cilium into the cytoplasm.

N.B: The immotile cilia syndrome:

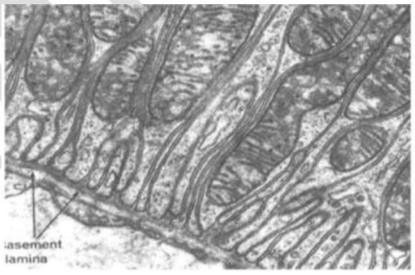


- Abnormal proteins of cilia or flagella resulting from mutation.
- ➢ Male infertility: due to immotile sperm.
- ➢ Chronic respiratory infection : caused by lack of cleaning action of cilia in the epithelium of respiratory tract.

Apical modifications	Microvilli	Stereocilia	Cilia
1- Motility	Non motile	Non motile	Motile.
2- Length	Shorter.	longer	Longer.
3- Shape	Finger like cytoplasmic projections.	Branching microvilli.	Hair like cytoplasmic projections.
4- Structure	Core of actin filaments.	Core of actin filaments.	Consists of basal body, shaft & rootlets, all formed of microtubules.
5- Function	Increase surface area for absorption.	Increase surface area for absorption.	Move a layer of fluid.
6- Most common sites	Intestinal cells & kidney tubules.	Male genital tracts e.g. epididymis.	Respiratory tract.

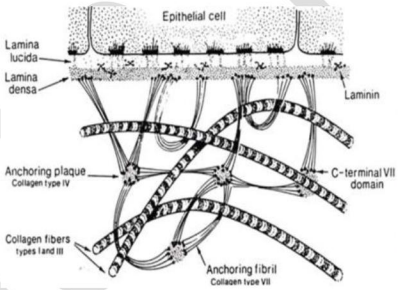
II- Basal Modification:

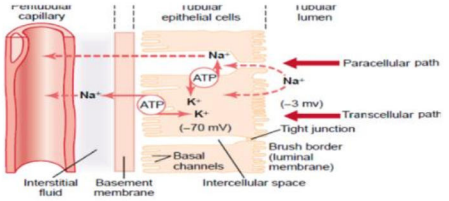
1-Basal infoldings:



- *Definition:* the basal cell membrane is thrown into folds.
- *Function:* increase the surface area for ions transport.
- *Site:* kidney tubules

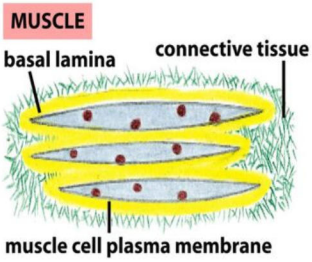
2-Basement membrane:





- *Site:* in the interface between epithelium and connective tissue.
- *Structure:*

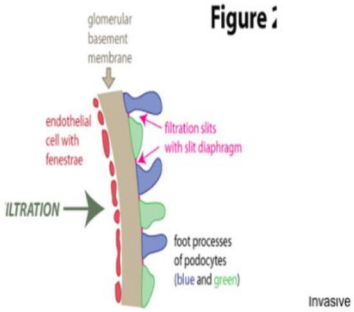
1. ***the basal lamina:*** formed of adhesive glycoprotein.
2. ***the reticular lamina:**** formed of fine network of collagen fibrils.



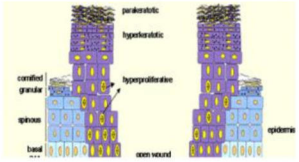
- Some non-epithelial cells are investedمغلفة by a basal lamina like material called ***external lamina*** e.g., muscle fibers, Schwann cell خلية موجودة فى الجهاز العصبى الطرفى مسئولة عن تكوين غلاف الميالين حول الليفة العصبية and adipocytes (the external lamina protects the fat cells from mechanical stress الضغط الحركى).

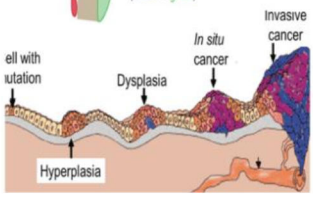
→It is not called basal lamina because these cells have no basal surface.

Functions of Basement Membrane:



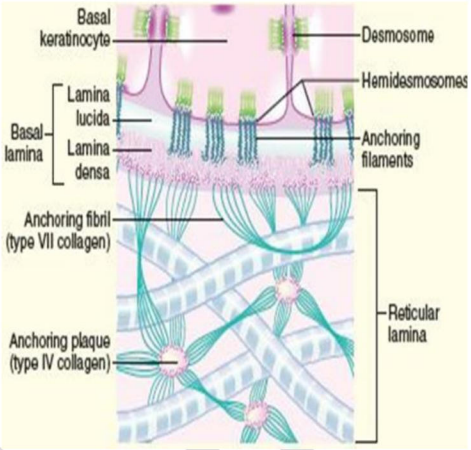
1. ***Structural attachment:*** attachment of the epithelial cells to the underlying connective tissue.
2. ***Filtration:*** regulates exchanges of macromolecules between the epithelium and the surrounding tissues.
3. ***Tissue scaffold:*** it directs the migration of epithelial cells (re-epithelization) during wound repair. It acts as barrier against passage of malignant cells.





3-Basal cell-to-matrix adhesions: Hemidesmosomes

Basement Membrane



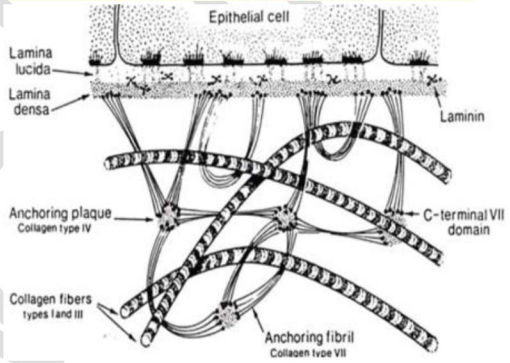
- **Site:** in the interface between epithelium and connective tissue.
- **Structure:**

1-The basal lamina:

- Synthesis: by epithelial cells.
- Structure: formed mainly of proteins (mainly collagen type IV) + glycoproteins (laminin)+ Proteoglycan (heparan sulphate).

2-The reticular lamina:

- Synthesis: by cells of the connective tissue.
- Structure: formed of fine network of collagen fibrils (type III collagen= reticular fibers).



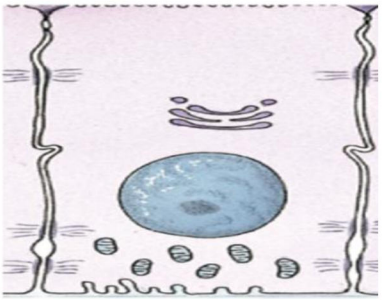
Structures responsible for attachment of the basal lamina to the underlying CT:

- Anchoring fibrils: formed of type VII collagen: extending from the basal lamina to structures called *anchoring plaques* or loop back to the basal lamina.
- This entraps the collagen type III fibers in the CT which ensures strong epithelial anchorage.

N.B. The basal lamina was described as being consists of a pale electrolucent layer (lamina lucida) and an electron dense layer (lamina densa due to presence of condensed collagen type VI). *Recently,* the lamina lucida is considered as an artifact during tissue preparation.

Lateral Specialization & Intercellular Junctions

Lateral Specialization



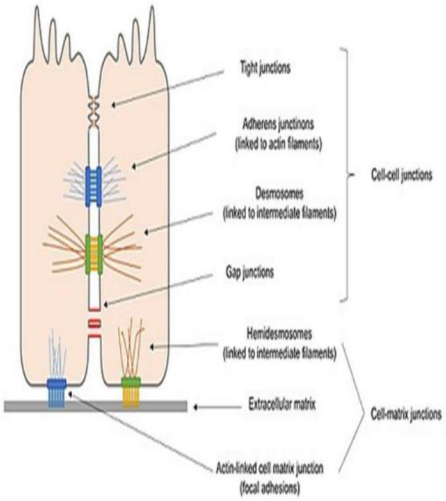
1- *Cellular interdigitations:* increase the surface area for transport.

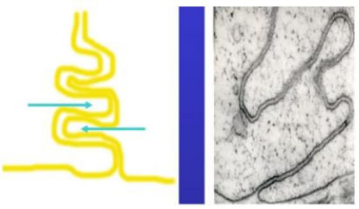
- Sites: cells of the intestine and kidney tubules.

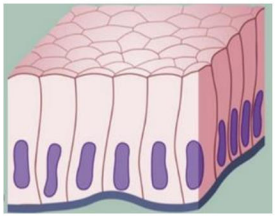
2- *Intercellular junctions:* link the neighboring cells together.

Types Of Cell Junctions

1- Cell to cell adhesion.
2- Cell to matrix adhesion.

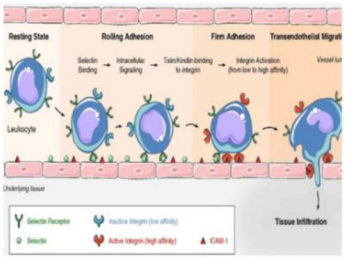


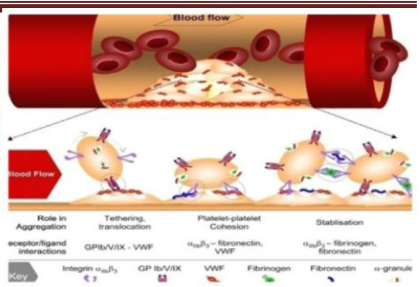


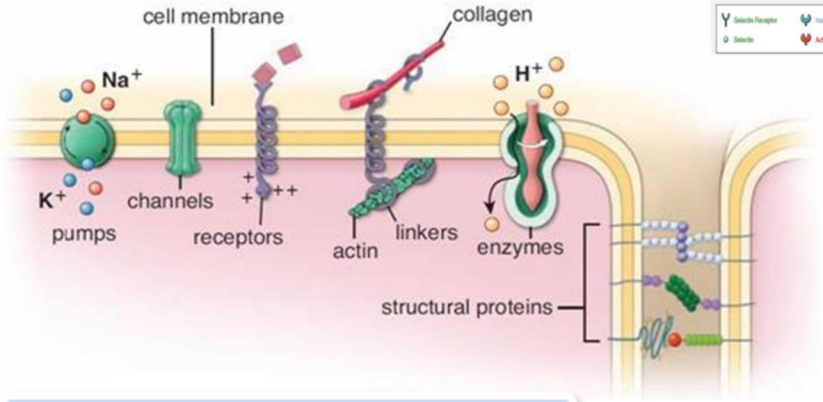


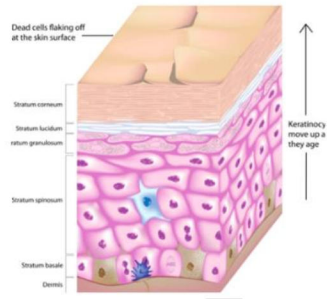
Cell adhesion is a dynamic process:

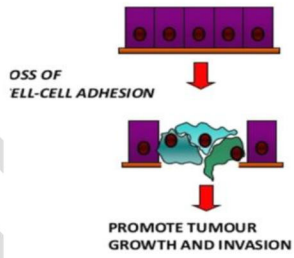
1- Non-adhesive cells become adhesive.
2- Adhesive cells become non-adhesive.





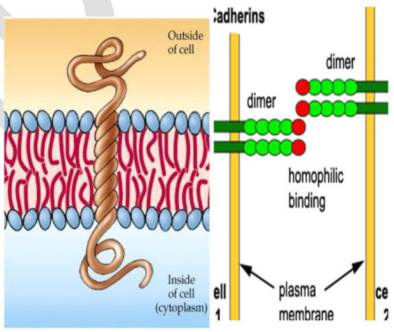






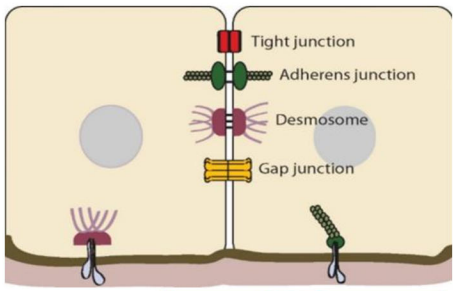
Cell Adhesion Molecules

- **Definition:** transmembrane glycoproteins, consists of three parts (domains):



1- *Extracellular part:* binds with the other CAMs of adjacent cells or extracellular matrix proteins.
2- *Intramembranous (transmembrane)part.*
3- *Cytoplasmic part:* attached to cytoskeleton of the cell through linker proteins.

CAMs may be calcium-dependent, affected by the extracellular calcium ions concentration, while others are calcium independent



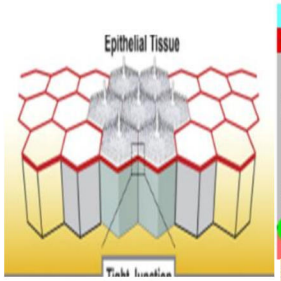
Cell To Cell Junctions

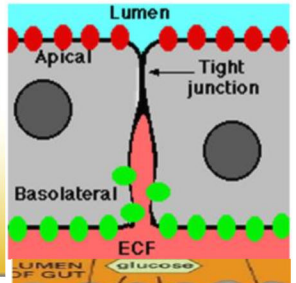
I-Tight junction (occluding Junction, zonula occludens)

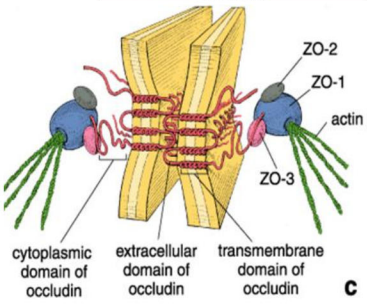
- **Site:** at the apical parts of the cells.
- **Function:** restrict the passage of molecules between the epithelium (***barrier***) e.g. epithelial cells of intestine.
- **Structure:**

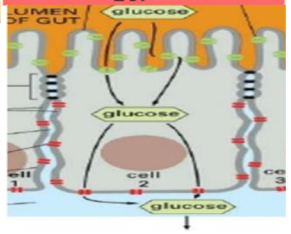
A. The outer leaflets of adjacent cell membranes are ***fused together***, forming a belt- like junction.

B. 2 transmembrane proteins (***occludin*** & ***claudin***) join together to ***seal*** (occlude) the intercellular space → ***no intercellular space*** between the adjacent cells.

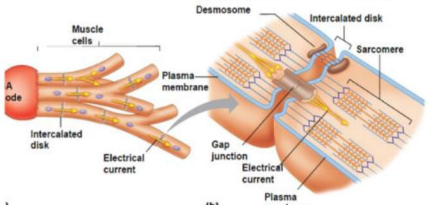




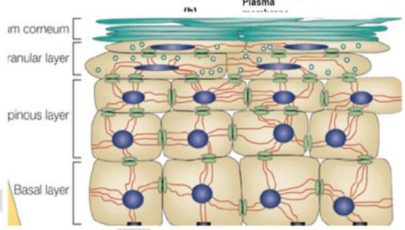




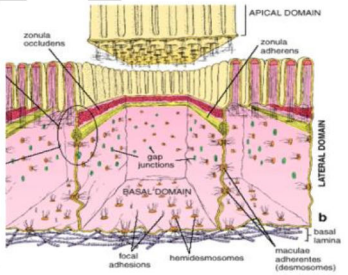
II-Anchoring junctions:



- **Site:** in cells that are subjected to severe mechanical stress e.g. cardiac muscles and epidermis of skin.
- **Function:** provide strong attachment and act as a link between the cytoskeleton of adjacent cells.
- **Histological structure: 2 types:**
- **Zonula adherens:**

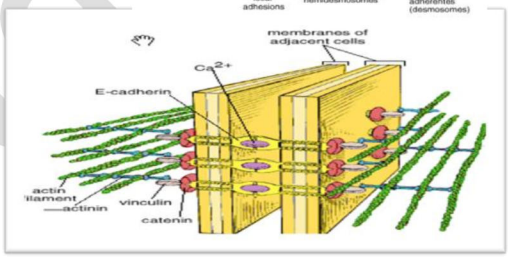


1- ***Belt-like specialization*** that encircles the apical part of the 2 adjoining cells.
2- The intercellular space between the adjacent cell membranes is 20 nm (the usual intercellular space).
3- ***Cadherins*** adhere the two cells together (ca-dependant).
4- The cytoplasmic part of cadherins is attached to ***actin filaments*** inside the cells.

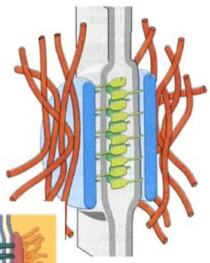


Removal of Ca^{2+} leads to disruption of the junction.

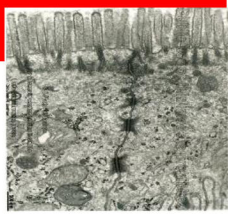
- **Macula adherens (desmosomes):**

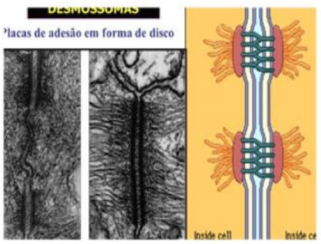


1- A ***spot-like*** specialization of the cell membrane
2- Two ***plaques*** located opposite each other on the cytoplasmic aspects of the adjacent cell membranes , to which ***cytokeratin filaments*** are inserted.
3- ***Cadherins*** connect the two cells together (Ca dependent).
4- the intercellular space between the opposing cell membranes is 30 nm.
5- Dense vertical filamentous material is present in the intercellular space that represents the extracellular domains of cadherins.



In the presence of a calcium chelating agent, the desmosome breaks into 2 halves and the cells separate.



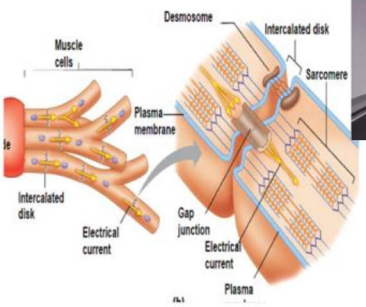


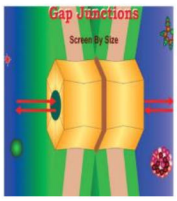
N.B: **Intercellular junctional complexes:**

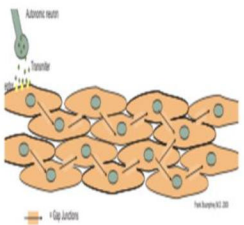
- In several epithelia ***the zonula occludens, the zonula adherens and macula adherens*** are present in a definite order from the apex toward the base of the cell.

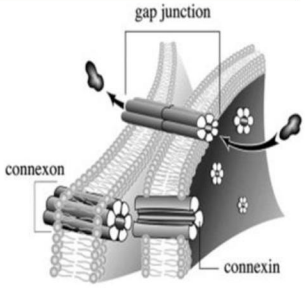
III-Communicating junction (gap junction, nexus):

- **Sites:** in epithelial cells, cardiac and smooth muscle cells.
- **Function:**
  - They permit communication rather than adhesion.
  - They permit the exchange of molecules e.g., ions, amino acids allowing passage of signals involved in contraction and communication from one cell to another.







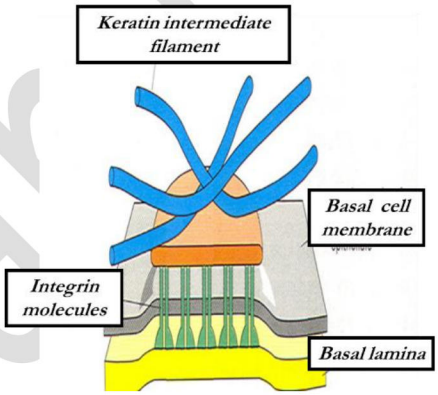


- **Histological structure:**

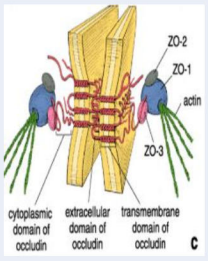
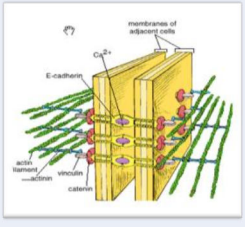
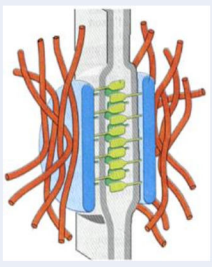
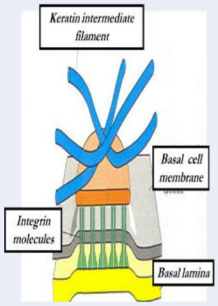
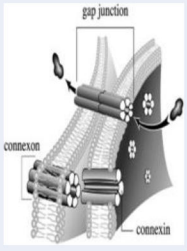
1- ***A spot-like*** junction, formed of protein channels.
2- The channel is called ***connexons*** which are formed of 6 transmembrane proteins called ***connexins***.
3- When two connexons of opposing cell membranes are in register, they form a channel connecting the cytoplasm of adjacent cells.
4- The intercellular space is 3nm.

Cell To Matrix Junctions

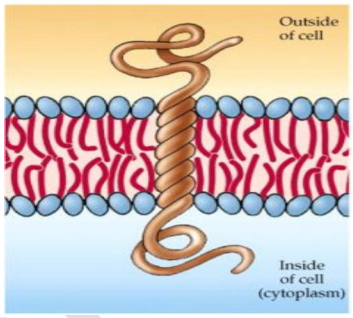
Hemidesmosomes (basal cell polarity):



- **Definition:** half of desmosome but are different functionally and in their content.
- **Site:** at the base of the epithelial cells to connect them with the basement membrane.
- **Structure:** The CAMs are ***integrins,*** their extracellular parts bind to proteins of the basal lamina while the intracellular parts bind to keratin filaments.

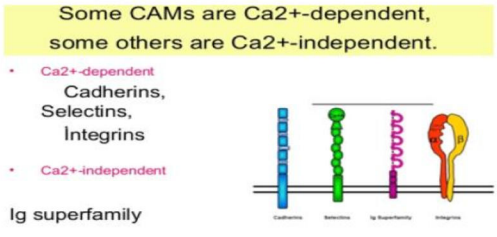
Types of Junctions	Tight junction	Zonula adherence	Desmosomes	Hemi-desmosome	Gap junction
1- Transmembrane protein (structural)	Claudin & occluding.	Cadherin.	Cadherin.	Integrin.	Connexin.
2- Type of attached filaments.	Actin.	Actin.	Keratin.	Keratin.	--------
3- Shape of junction.	Belt like.	Belt like.	Spot like.	Spot like.	Spot like
4- structural features	Fusion of trans-membrane proteins.	Binding of actin filaments on both sides of the adjacent cell membranes by trans-membrane proteins.	Intracellular plaques on both sides of adjacent cell membranes, attached from one side to keratin & other sides to transmembrane proteins.	Half a desmosome on the side of the basal cell membrane.	Connexons are in register to each others.
5- Intercellular space	No space	20 nm.	30 nm.	-------	3 nm.
6- Function	Barrier (prevents passage of molecules in the intercellular space)	Strong attachment between cells.	Strongest attachment between cells.	Binds the basal cell membrane to basal lamina.	Allows exchange of molecules between cells.
7- Most common sites	Cells of intestine. 	Cells subjected to sever mechanical stress such as epidermal cells of skin and cardiac muscles. 	Cells subjected to sever mechanical stress such as epidermal cells of skin and cardiac muscles. 	Epithelial cells. 	Cardiac & smooth muscles. 

Cell Adhesion Molecules (CAMs)



- **Definition:** Transmembrane proteins play important role in cell to cell & cell to matrix adhesion.
- **Structure:** they consist of:
  - Extracellular domain.
  - Intramembranous domain.
  - Cytoplasmic domain: binds to cytoskeleton through linkers proteins
- **Types:**

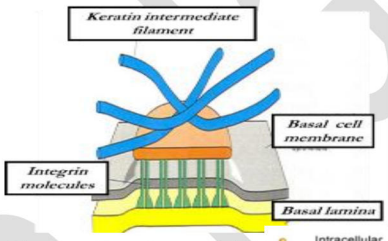
1- *Calcium dependent:* affected by the calcium concentration in the tissue.
2- *Calcium independent*.

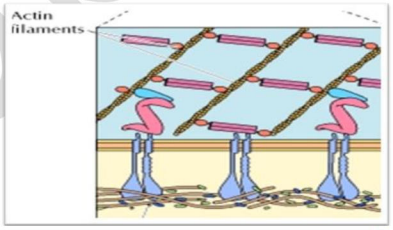


I-Calcium dependent CAMs:

1- Integrins:

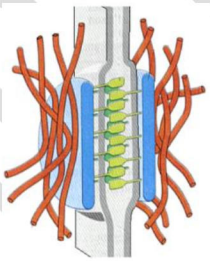
- **Function:** involved in cell to matrix adhesion.
- They are linked indirectly to cytoskeleton through anchoring proteins.

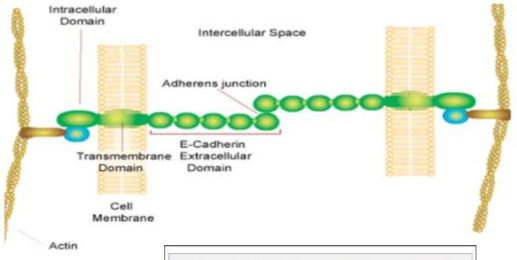




2- Cadherins:

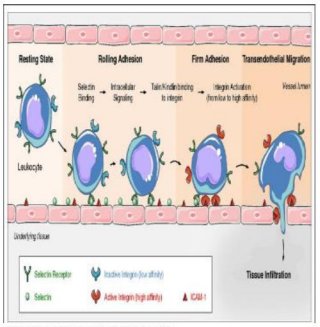
- **Function:** involved in cell-to-cell adhesion.
- They are present in the adhering junction.
- They are linked indirectly to cytoskeleton.





3- Selectins:

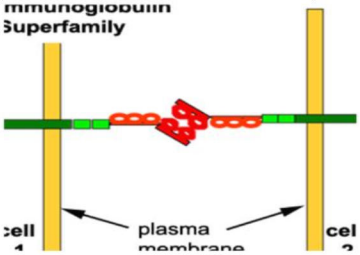
- **Function:** involved in cell to cell adhesion specifically the ***transient*** cell to cell adhesion between neutrophils and endothelial cells of the blood vessels (promote migration of neutrophils from the blood to the connective tissue).
- They bind to specific oligosaccharides on the selectin receptor of another cell.

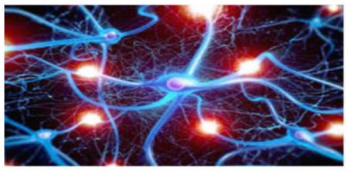


II-Calcium independent CAMs:

Immunoglobulin superfamily:

- **Function:** It has many important functions e.g., Neural cell to cell adhesion molecule, plays an important role in nervous system development.

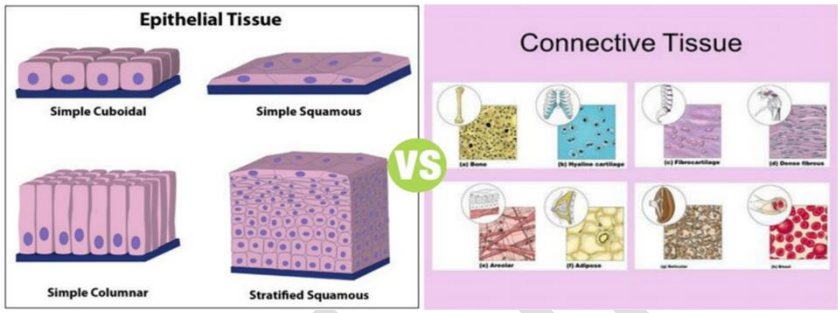




Connective Tissue

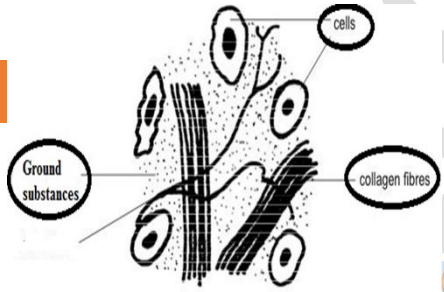
Characteristics of CT:

1. All types of connective tissues arise from the mesoderm.
2. Variable degrees of vascularity.
3. Several types of cells.
4. Extracellular matrix.



Structure of CT:

1- Cells.
2- Ground substance } Matrix
3- Fibers.

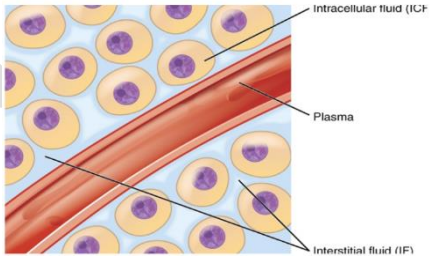


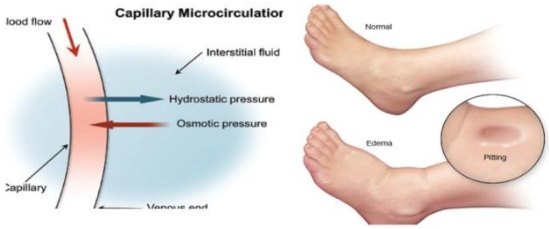
I- Ground Substance:

It is composed of:

1-Interstitial fluid: that escape through the capillary wall as a result of the hydrostatic pressure.

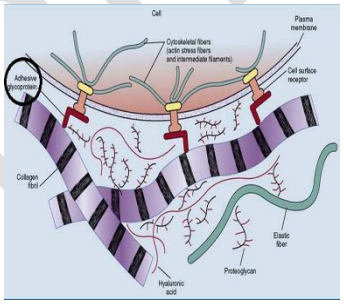
- Edema: an increase in the tissue fluid due to loss of the equilibrium between the tissue fluids entering and leaving the matrix of CT.



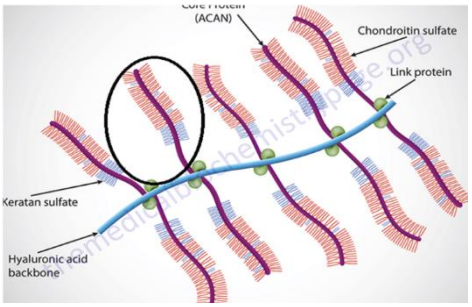


2-Adhesive glycoproteins: They serve as a glue that binds cells to matrix e.g., fibronectin & laminin.

3- Proteoglycans: consist of a protein core + glycosaminoglycans (GAGs, e.g., chondroitin sulfate and keratan sulfate).



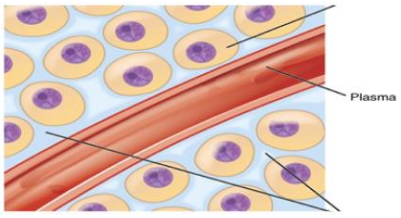
- The proteoglycans attached to hyaluronic acid form *proteoglycan aggregates* (negatively charged) that trap water → viscous gel.
- **Functions:**



A- A medium through which nutrients can diffuse between the blood capillaries and the cells.

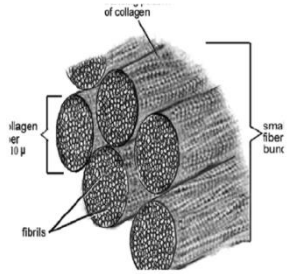
B- Resist compression (shock absorber).

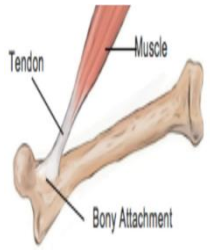
C- A barrier to bacterial penetration: although some bacteria secrete the enzyme hyaluronidase that hydrolyzes the ground substance and facilitates bacterial invasion.

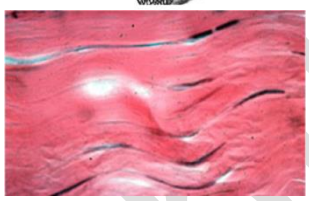


II- CT fibers:

1- Collagen fibers:







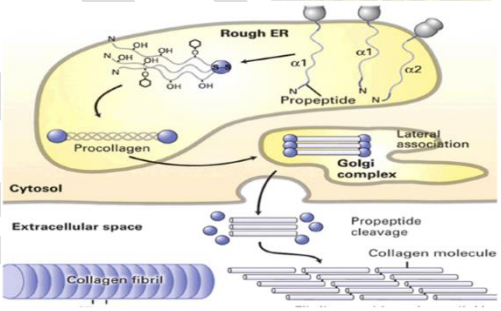
- **Characters:**

1- They are the most abundant CT fibers.
2- They are the strongest type (high tensile strength i.e.the ability to resist longitudinal stress).
3- In fresh state: they have a white appearance (white fibers).

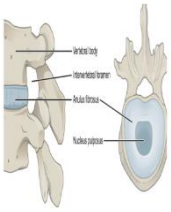
- **Structure:**

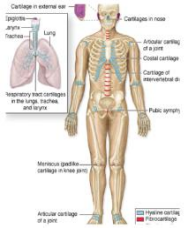
1- Cylindrical structures.
2- Run in wavy bundles.
3- The individual fibers do not branch while the bundles of fibers do.
4- They stain pink with H&E (eosinophilic), blue with Mallory's stain & green with Masson's trichrome stain.

- **Synthesis of collagen:**

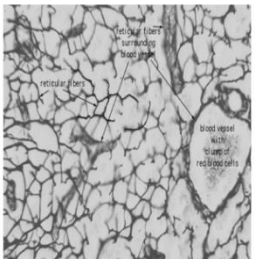


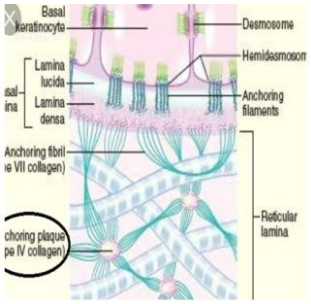
1- *Procollagen* is formed inside the fibroblasts then it is released by exocytosis into the extracellular space.
2- Procollagen is cleaved to form *collagen molecules* which assemble spontaneously into collagen fibrils.
3- *Collagen fibrils* are assembled into collagen fibers.
4- *Collagen fibers* bundled together into *collagen bundles*.





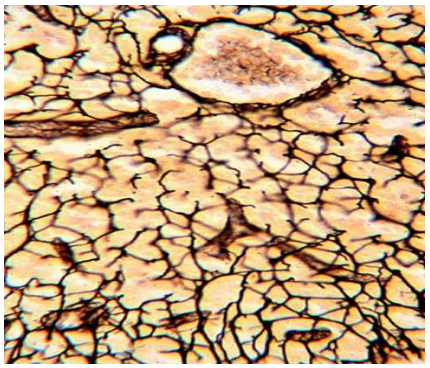
- **Types of collagen:**





- About 20 different types of collagen fibers, differ by their composition, morphology, distribution in tissues and functions.
- **Type I:** in connective tissue proper, fibrocartilage and bone.
- **Type II:** in cartilage.
- **Type III:** reticular fibers.
- **Type IV:** in basement membrane.

2- Reticular fibers:



- They consist of *type III collgen*.
- They are short, thin and branching fibers forming a network.
- They are not stained by H&E, they are stained by silver stain(brown to black).
- They have supportive function (support the cells and blood vessels of the organs).

3-Elastic fibers:

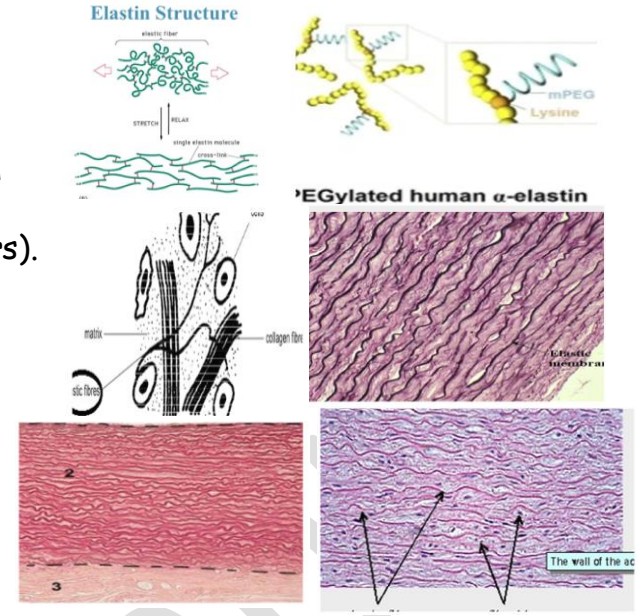
- **Characters:**
  - They contain protein called *elastin* that allows them to stretch and recoil.
  - In fresh state: they appear yellow (the yellow fibers).
- **Structure:**

A. They may exist in two forms:

1- Long and thin branching fibers.

2- Parallel sheets.

B. They stain weakly with H&E, brick red with orcein & dark violet with VVG.



	Collage fibers	Reticular fibers	Elastic fibers
1- Fresh state	White.	---------	Yellow.
2- Stain	H&E : pink. Mallory: blue. Masson: green.	Silver: brown.	H&E: faint. VVG: dark violet. Orcein: brick red.
3- Types	20 types, most common is type I.	Collagen type III.	
4- Description	• Cylindrical. • Run in bundles. • Fibers are not branched but bundles do.	Short branching fibers that form a network.	Either long & thin branching fibers or parallel sheets.
5- Function	Tensile strength.	Support.	Flexibility & elastic recoil (due to elastin protein).

III- CT Cells:

Types of CT cells:

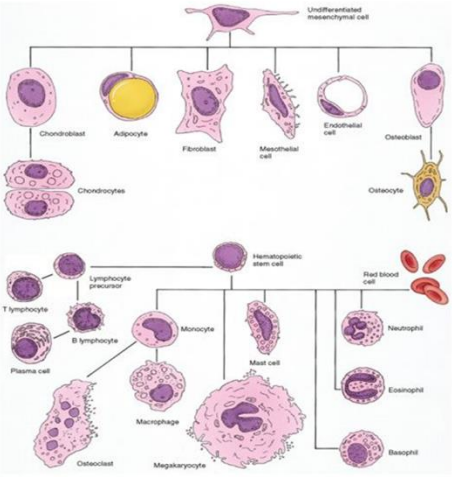
1- Resident (fixed) cells:

- ***Development:*** within the connective tissue.
- ***Characters:*** stable & long-lived.

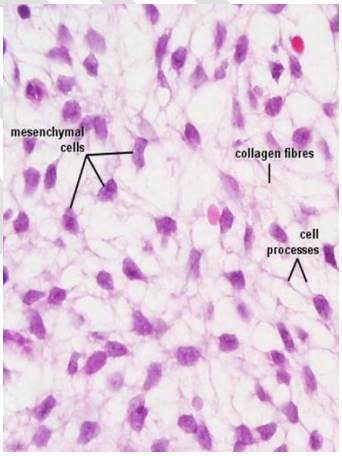
2- Transient(wandering) cells:

- ***Origin:*** in the bone marrow, circulate in the blood and when they receive a stimulus, they leave the blood and migrate into the connective tissue to perform specific functions.
- ***Characters:*** motile, short-lived and replaced by stem cells.

Resident (Fixed) CT cells	Transient (Wandering) CT cells
1- Undifferentiated mesenchymal stem cells. 2- Fibroblasts. 3- Fibrocytes. 4- Adipocytes. **Mast cells& Macrophages???**	1- Plasma cells. 2- Leukocytes.



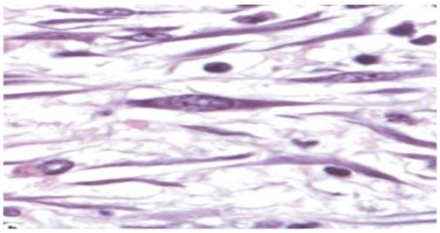
1-Undifferentiated Mesenchymal Cells:



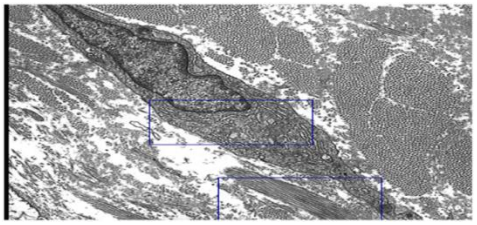
- **Origin:** mother cell of CT.
- **Function:** Stem cells that divide and differentiate into many types of CT cells.
- **Structure:**
  - Shape: stellate with few processes.
  - Nucleus: pale.
  - Cytoplasm: pale basophilic (polysomes).

2-Fibroblasts:

- They are the most common cells in CT.
- **Origin:** UMC.
- **Function:** Secrete the ground substance &the fibers of the matrix.
- **Structure:**



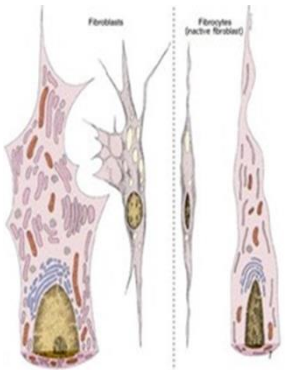
LM:
- Shape: spindle with processes.
- Nucleus: large& pale.
- Cytoplasm: deeply basophilic.



EM: protein synthesizing cells
- numerous rough endoplasmic reticulum & well developed Golgi but no <u>*secretory granules.*</u>

After they synthesize the matrix, they become quiescent and are called fibrocytes.

3-Fibrocytes:



- **Origin:** Less active fibroblast.
- **Function:** maintenance of the matrix.
- **Structure:**

LM:
- Shape: smaller with fewer processes.
- Nucleus: small & dark.

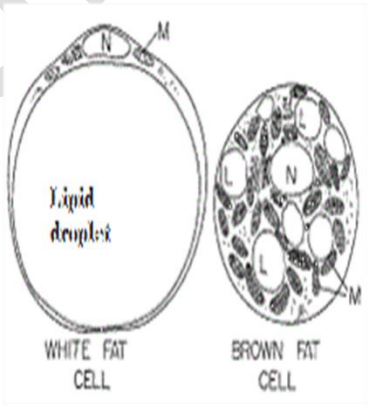
- Cytoplasm: eosinophilic.

EM: fewer organelles (fewer rER and small Golgi).

If the matrix is injured, they can return to their more active state (fibroblast) to repair the matrix

	Fibroblast	Fibrocyte
1- Origin	Undifferentiated mesenchymal cells.	Fibroblast after being less active.
2- Function	Secretes ground substances& fibers.	Maintains matrix.
3- LM A- Shape B- Nucleus C- cytoplasm	 Spindle with processes. Large & pale. Deep basophilic.	 Smaller with fewer processes. Small & dark. Acidophilic.
4- EM	Protein synthesizing cells: Many rER, well developed Golgi but no secretory granules.	Less active cell: Few rER, small Golgi

4-Fat cells (adipocytes):



- **Origin:** UMC.
- **Function:** storage of fat.
- **Structure:**

1- Unilocular adipocytes:

- **Shape:** large cells, spherical.
- **Cytoplasm:** occupied by a single large lipid droplet that pushes the cytoplasm to a thin peripheral rim with peripheral flattened nucleus giving them *a signet ring appearance.*

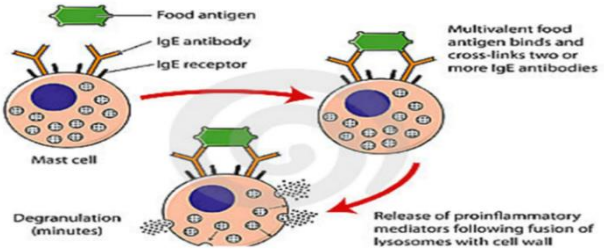
2-Multilocular adipocyte:

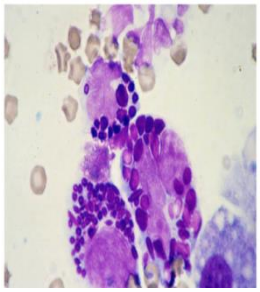
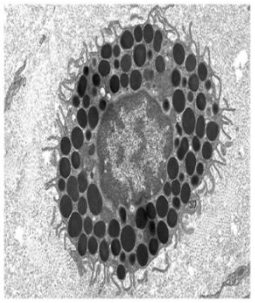
- **Shape:** polygonal and smaller.
- **Nucleus:** central rounded.
- **Cytoplasm:** numerous small lipid droplets and numerous mitochondria.

	Unilocular fat cell	Multilocular fat cell
1- Shape	Large rounded or polygonal.	The same but smaller.
2- Cytoplasm	Contains single, large lipid droplet.	Contains numerous lipid droplets & numerous mitochondria.
3-Nucleus	Flattened & peripheral (signet ring appearance).	Rounded & central.
4- Function	Storage of energy.	Production of heat.

5-Mast cells:

- **Origin:** Haemopoietic stem cells.
- **Function:** Secrete histamine and heparin that initiate allergic and local inflammatory response.

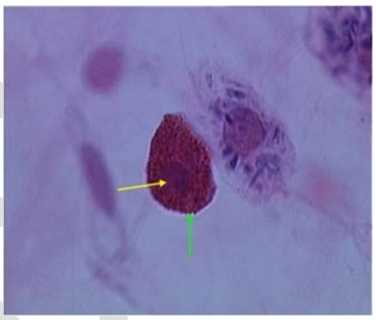


- **Structure:**

LM:

- Shape: a large cell.
- Nucleus: rounded and central.
- Cytoplasm: contains basophilic granules that may obscure the nucleus.



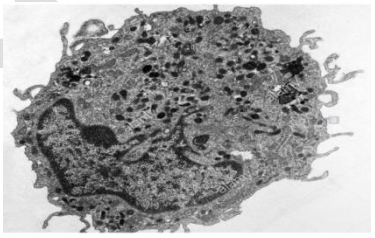
EM: numerous secretory granules (release their contents by degranulation in response to allergen).

- ***Metachromasia***: A certain stain give to their granules a color differs than that of the dye e.g., toluidine blue stain gives a purple color instead of blue, due to the chemical composition of the secretory granules(heparin).

6-Macrophages:

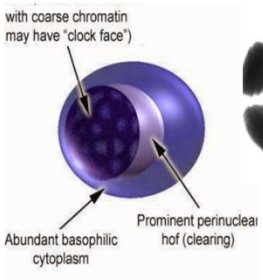
- **Origin:** Blood monocytes.
- **Function:** phagocytosis of foreign materials including bacteria& dead cells.
- **Structure:**

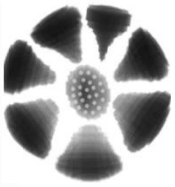
- **Shape:** large& irregular.
- **Nucleus:** eccentric kidney shaped.
- **Cytoplasm:** numerous lysosomes.



7-Plasma cells:

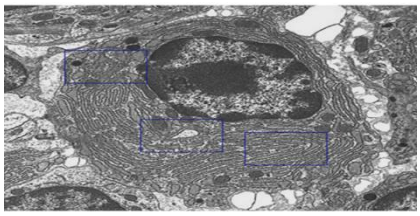
- **Origin:** B lymphocytes.
- **Function:** synthesis of antibodies against foreign bodies entering the CT.
- **Structure:**





LM:

- Shape: large oval.
- Nucleus: spherical and eccentric with ***a cartwheel*** appearance (due to arrangement of chromatin).
- Cytoplasm: basophilic with ***negative Golgi image*** (prominent juxtanuclear Golgi apparatus appears unstained against the deeply basophilic cytoplasm).



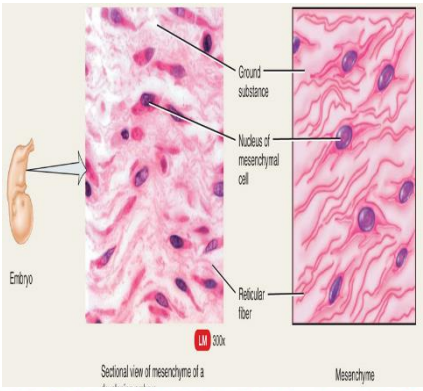
EM:Protein synthesizing cells: numerous rER, large well-developed Golgi but <u>no secretory granules.</u>

	Mast cell	Macrophage	Plasma cell
1- Origin	Hemopoietic stem cell.	Monocyte	B- lymphocyte.
2- Function	Secretes histamine & heparin	Phagocytosis.	Secretes antibodies.
3- LM A- Shape B- Nucleus C- Cytoplasm	Large. Rounded & central. Basophilic with large granules, showing metachromasia.	Large & irregular. Kidney shaped & eccentric.	Large & oval Spherical, cartwheel & eccentric. Basophilic with negative Golgi image.
4- EM	Secretory granules.	Lysosomes.	Protein synthesizing cells: many rER & well-developed Golgi but no secretory granules.

Connective Tissue Types

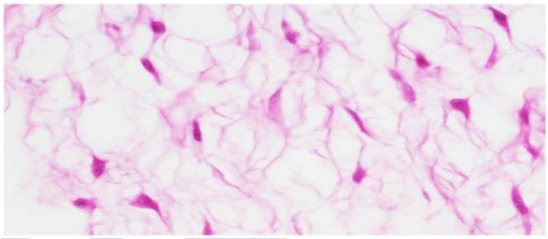
I-Embryonic CT:

1- Mesenchymal CT:



Structure:

- **Cells:** UMSCs with their processes come in contact with each other forming a network.
- **Fibers:** reticular fibers.
- **Ground substance:** gel-like.

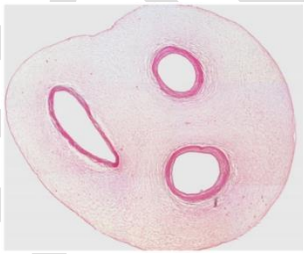


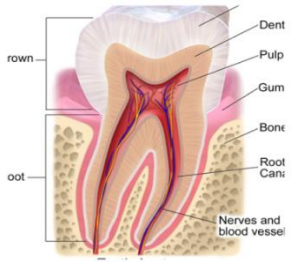
Site: embryo.

2- Mucoid CT:

Structure:

- **Cells:** UMSCs (spindle) appear like fibroblasts.
- **Fibers:** unapparent collagen (have the same refractive index as the matrix).
- **Ground substance (Wharton jelly):** abundant, basophilic & homogenous composed of hyaluronic acid.



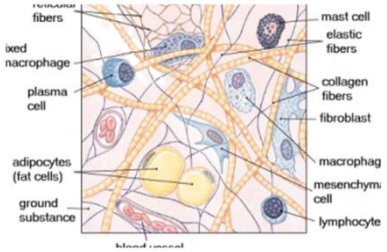


Site: umbilical cord, pulp of growing teeth.

Embryonic CT	Mesenchymal CT	Mucoid CT
1- Cells	Undifferentiated mesenchymal cells (stellate with processes).	Undifferentiated mesenchymal cells (spindle resembles fibroblast).
2- Fibers	Reticular.	Unapparent collagen.
3- Ground substance	Gel like.	Abundant, homogenous & basophilic (called Wharton jelly).
4- Sites	Embryo.	1- umbilical cord. 2- Dental pulp.

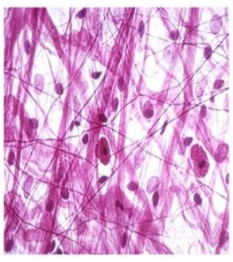
II-CT Proper:

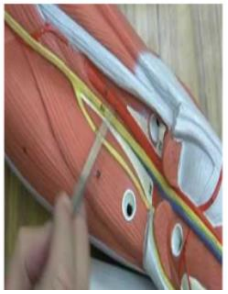
1- Loose areolar CT:



Structure:

- **Cells:** All types cells especially fibroblasts & macrophage.
- **Fibers:** All fibers (collagen, elastic& reticular).
- **Ground substance:** Abundant



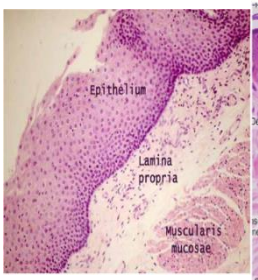


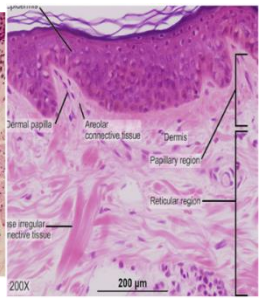
Function:

1- Fibers: supports and binds tissues.
2- Ground substance: nutrition.
3- Cells: defends against infection (by its white blood cells, plasma cells, mast cells and macrophages).

Sites: it is the most widely distributed connective tissue in the body.

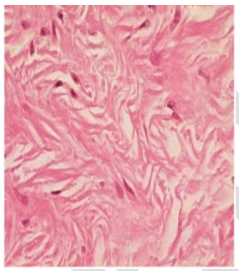
1- Under the epithelium in all mucous membranes.
2- The papillary layer of dermis.
3- It surrounds glands, blood vessels and nerves.

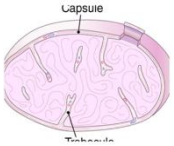


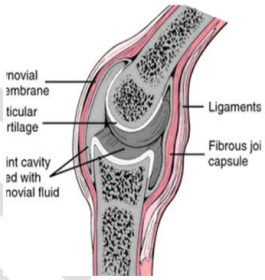


2- Dense Irregular CT:

Structure:
- **Fibers:** collagen run in all directions (irregular).
- **Cells:** few fibroblasts.
- **Ground substance:** little.





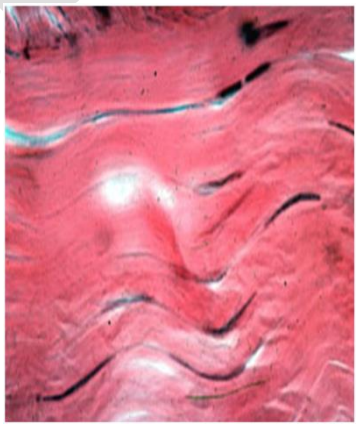


Function: resist tension in different directions.

Sites:

1- the reticular layer of dermis of the skin.
2- the capsules of the organs.
3- the fibrous capsules of the joints.

3- Dense regular CT (White fibrous CT):



Structure:
- **Fibers:** collagen bundles, wavy, parallel in one direction.
- **Cells:** rows of flattened fibroblasts (tendon cells).
- **Ground substance:** little.

Function: resist pulling force in one direction.

It is poorly vascularized

Sites:

1- Tendons.
2- Ligaments.

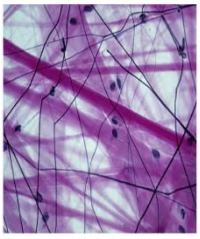
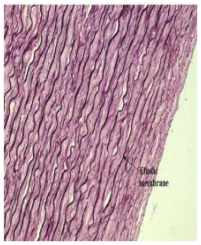
CASE

A 12-year-old boy admitted to the hospital, suffering from severe pain in his knee joint and inability to move it after playing a football match. After examination and investigations, he was diagnosed as a tear in the posterior cruciate ligament.
1- What is the type of tissue affected in this case?
2- What is your expectation for the healing of this tear? Explain your answer.
Answer:

1- **White fibrous CT.**
2- **If the tear is mild: healing can occur spontaneously with conservative treatment, but if the tear is severe, it needs surgical interference because this type of tissue is poorly vascularized.**

	Loose areolar CT	Dense regular CT	Dense irregular CT
1- Cells	All types especially fibroblast & macrophage.	Flattened fibroblast (tendon cells).	Fibroblasts.
2- Fibers	All types.	Collagen in wavy parallel bundles.	Collagen run irregularly.
3- Ground substance	Good amount	Little	Little.
4- Vascularity	Highly vascular.	Poor.	Poor.
5- Function	1- support & bind tissues. 2- Nutrition (high vascularity). 3- defense against infection.	Resists pulling force in a single direction.	Resists tension in all directions.
6- Sites	1- papillary dermis. 2- beneath epithelium. 3- around blood vessels & nerves.	Tendon & ligaments.	1- reticular dermis. 2- capsules of organs & joints.

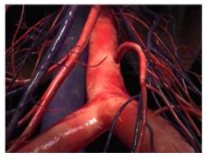
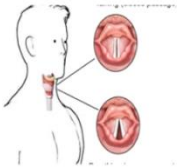
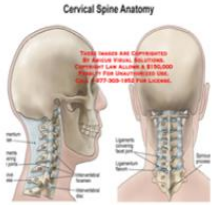
4- Elastic CT:

Structure:

- Elastic fibers that run in all directions or they may form fenestrated membranes.

Function: flexibility and elastic recoil.

Sites:

1- arteries.
2- vocal cords.
3- ligamenta flava & ligamenta nuchae.

5- Reticular CT:

Structure:

- **Fibers**: Reticular fibers forming a network.
- **Cells**: Reticular cells (fibroblasts).

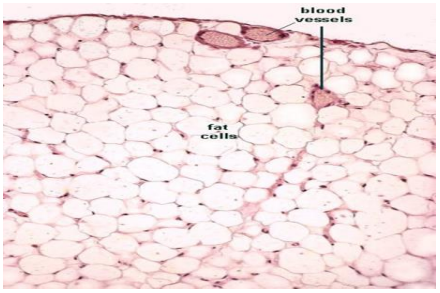
Function: Form framework to support cells of an organ.

Sites:

1- Liver.
2- Spleen, lymph nodes & bone marrow.

	Elastic CT	Reticular CT
1-Cells	----------	Reticular cells.
2- Fibers	Elastic fibers.	Reticular fibers.
3- Function	Flexibility & elastic recoil.	Support.
4- Site	1- arteries. 2- vocal cords. 3- elastic ligaments of the vertebral column.	Bone marrow, liver, spleen & lymph nodes.

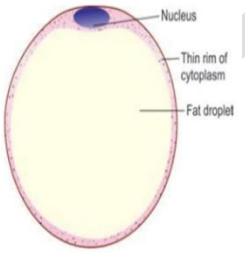
6- Adipose CT:



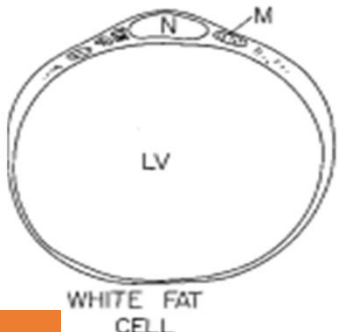
Structure:

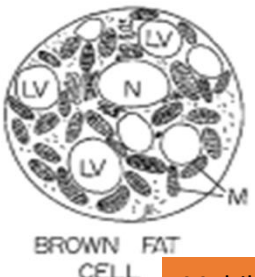
- **Cells**: Adipose cells.
- **Fibers**: Reticular fibers.
- **Ground substance**: Sparse.

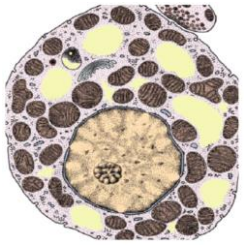
It is highly vascular



Unilocular adipocytes



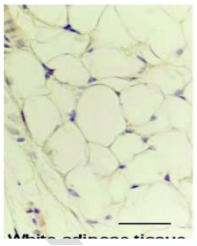




Multilocular adipocytes

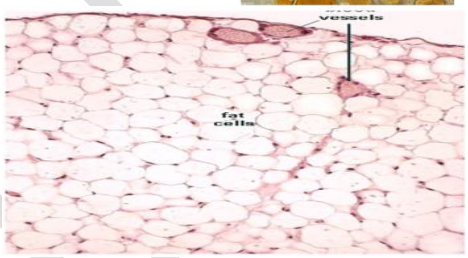
Types Of Adipose CT:

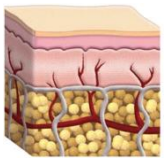
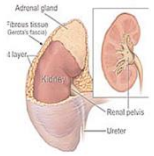
A-Unilocular (White adipose CT):

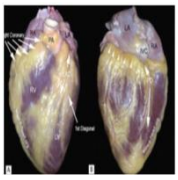



- **Color:** varies from white to yellow due to the presence of carotenoids dissolved in fat droplets of the cells.
- **Structure:** It is formed of unilocular adipocytes.
- **Sites:** All the subcutaneous tissue of the body& around vital organs.
- **Functions:**

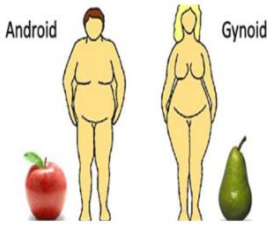
1- Storage of energy.
2- Shaping body.
3- Shock absorber (especially in palm& sole).
4- Support vital organs e.g., heart & kidney.
5- Thermal insulation (due to the poor heat conduction of adipose tissue).

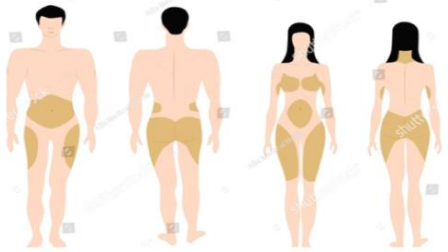




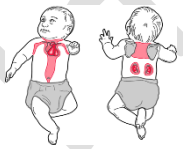
Distribution of Subcutaneous Fat in Males and Females



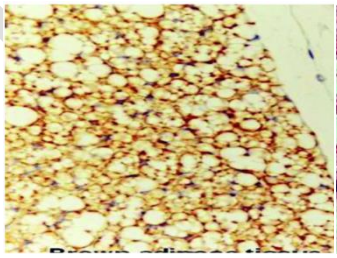
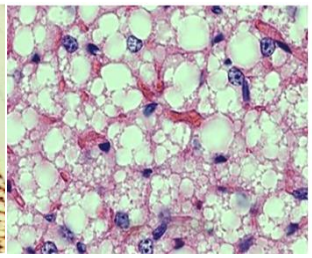


B-Multilocular (Brown adipose CT):

- **Color:** brown due to the large number of blood capillaries and the colored cytochromes inside the numerous mitochondria.
- **Structure:** multilocular adipocytes.
- **Sites:** in certain areas in the abdomen and neck of the human embryo and the newborn.



- **Function:** *Thermogenesis*
  Production of heat to protect the newborn against cold.

As children grow, the lipid droplets coalesce together and the brown fat changes into white fat.

	Unilocular adipose CT	Multilocular adipose CT
1- Cells	Unilocular fat cells.	Multilocular fat cells.
2- Fibers	Reticular.	Reticular.
3- Ground substance	Little in amount, highly vascular.	Highly vascular.
4- Color	Yellow due to carotenoids inside fat droplets.	Brown due to the color of blood inside blood vessels & cytochrome inside numerous mitochondria.
5- Site	1- all subcutaneous tissues. 2- around vital organs.	Abdomen & neck of the human embryo and newborn.

6- Functions	1- storage of energy. 2- shock absorber. 3- shaping of the body. 4- support vital organs. 5-thermal insulation.	Thermogenesis (heat production).

Skin

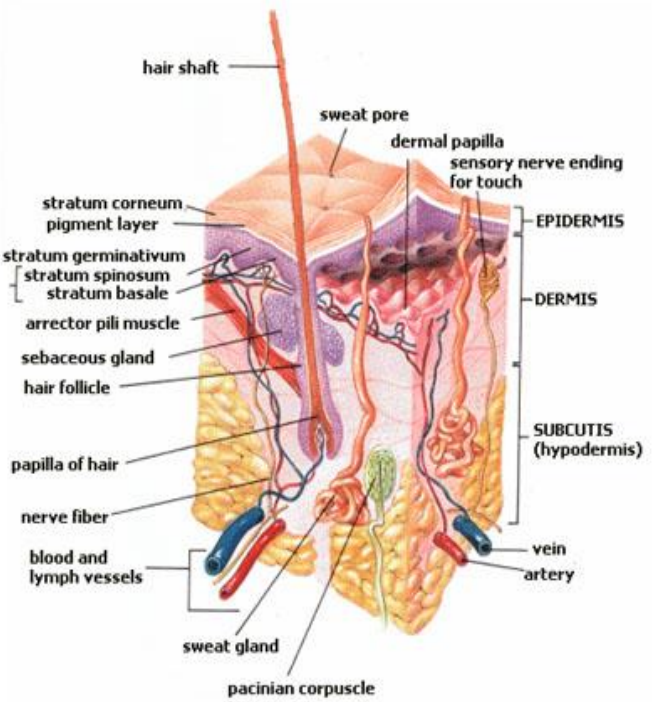
The integumentary system: الجهاز الغلافى

It consists of:

1- The skin.

2- The skin appendages:

- Hair.
- Nail.
- Sweat, sebaceous & mammary glands.

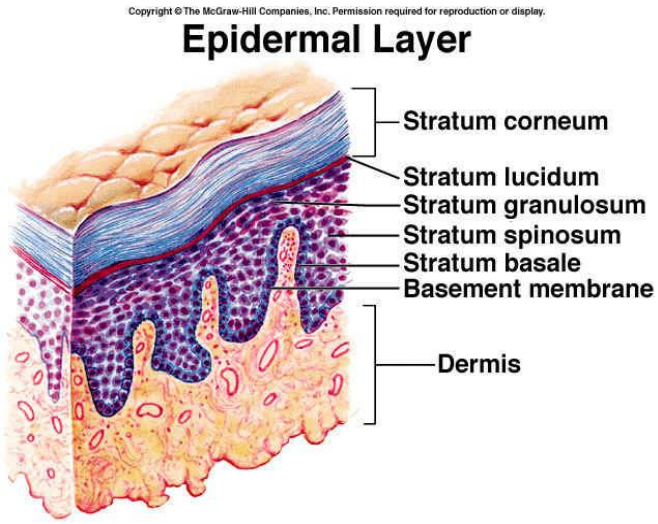


SKIN:

- ***It consists of two layers:***

1- The epidermis: the superficial epithelium derived from ectoderm. It is avascular but rich in sensory nerve endings especially for pain.

2- The dermis: the deeper vascular connective tissue layer derived from mesoderm.



I-The epidermis:

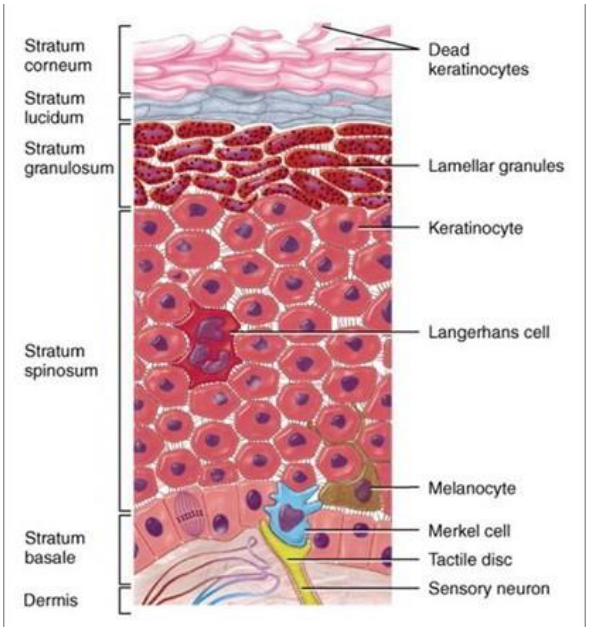
- **It is a keratinized stratified squamous epithelium.**
- **It consists of four types of cells:**

1-Keratinocytes.

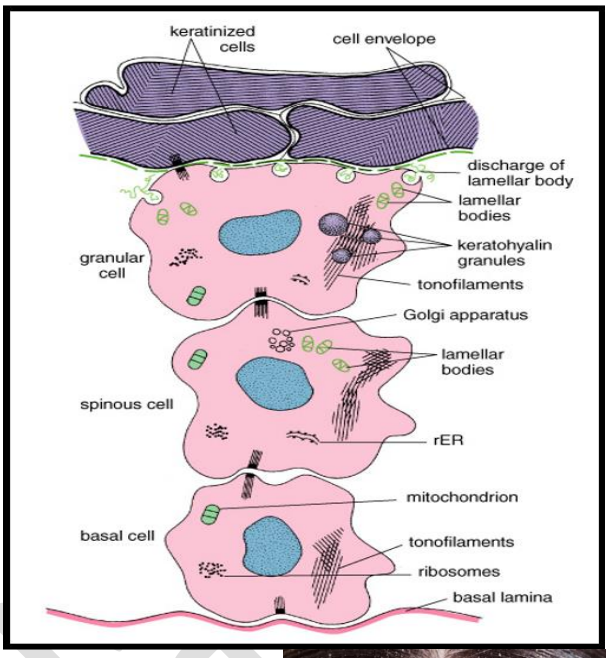
2-Melanocytes.

3- Langerhans cells.

4- Merkel's cells.



A-Keratinocytes:



- They are the most abundant cells in the epidermis.
- **Keratinization (15-30 days):**

➢ The superficial epithelial cells are shed off at the surface and are replaced by cells arise from stem cells in the basal layer.

➢ ***As the cells move upwards:***

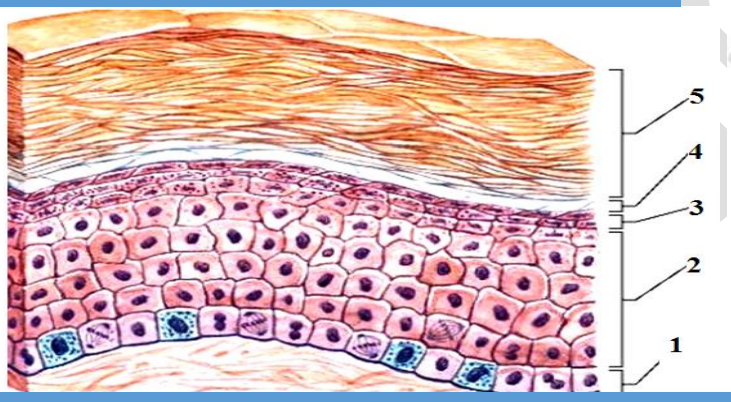
1- The keratin filaments (cytokeratin filaments) accumulate inside the cells.

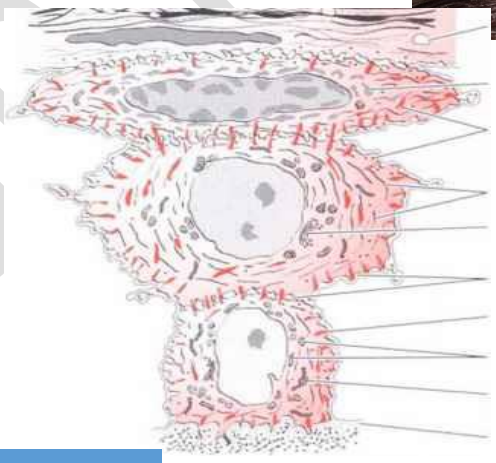
2- The nucleus and organelles are disappearing.

3- The cells die.

- **If the process of keratinization occurs more rapidly (one week):** The superficial keratinized cells will accumulate and desquamate forming thick scales (***dandruff***).

The keratinocytes are arranged in 5 layers:





1-Stratum germinativum =Stratum basale:

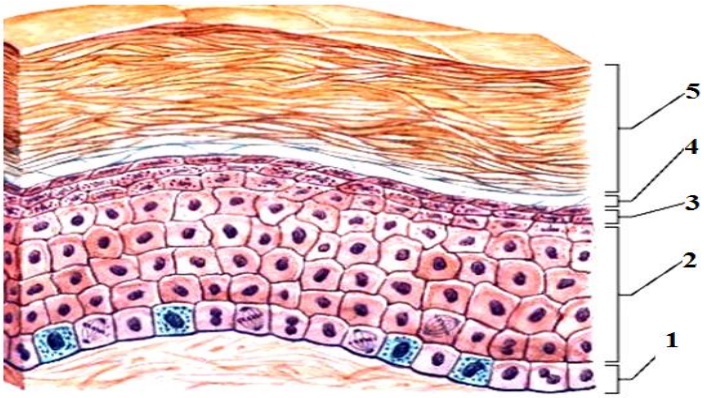
- ***Number of layers:*** **one layer.**
- ***Structure:***

1- *Shape of cells:* **low columnar.**

2- *Nucleus:* **large oval.**

3- *Cytoplasm:* **deep basophilic (numerous polysomes).**

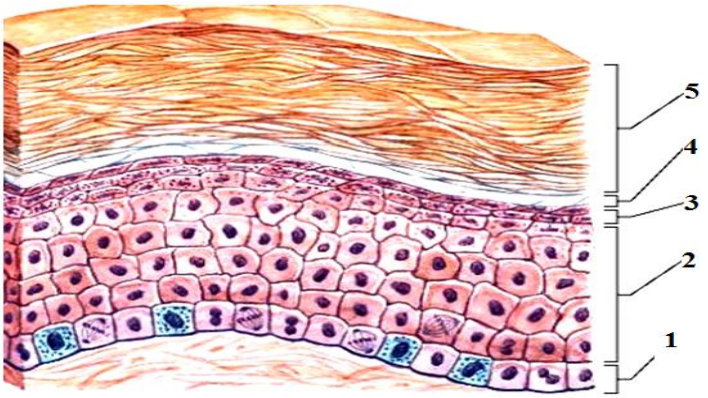
4- **The cells are attached together by** *desmosomes* **and to the basement**



membrane by *hemidesmosomes*.

5- Frequent *mitotic figures*.

- ***Function:*** renewal of keratinocytes.



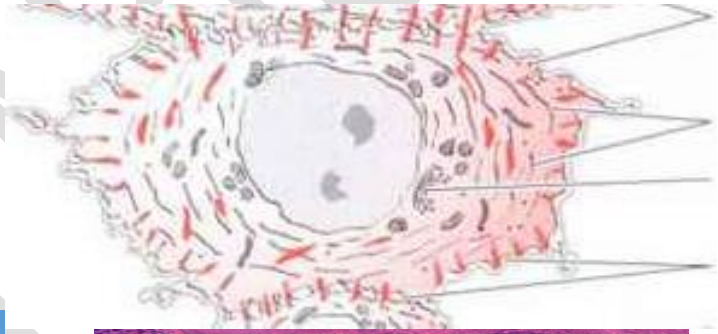
2-Stratum spinosum = Prickle cell layer:

- Number of layers: 5-10.
- Structure:

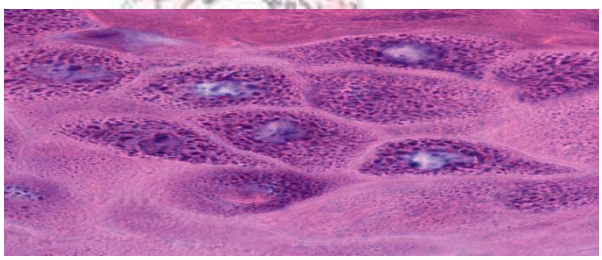
1- *Shape of cells:* polyhedral.

2- Multiple *spinous processes* which interdigitate the similar processes of adjacent cells by *numerous desmosomes*.

- Function: resisting the effects of friction and pressure.



3-Stratum granulosum = granular layer:



- Number of layers: 3-5.
- Structure:

1- *Shape of cells:* diamond shaped.

2- *Nucleus*: flattened.

3- *Cytoplasm:* deeply basophilic& granular, contains:

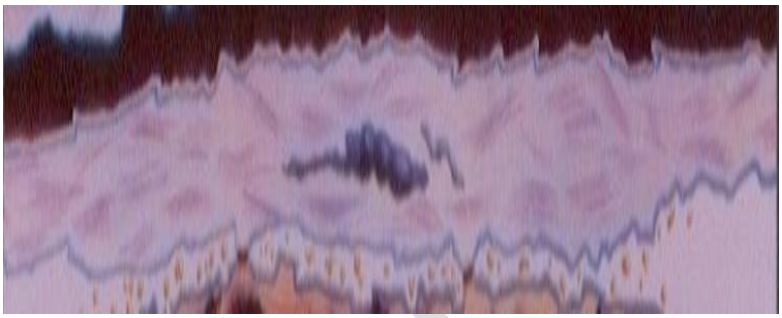
a. ***Keratohyaline granules:*** non-membrane-bounded granules (packing keratin filaments together).

b. ***Membrane-bounded lamellated granules:*** Its synthesis starts in stratum spinosum and they increase in number in stratum granulosum, collect near the cell membrane then discharge their contents in the intercellular spaces.

- Function: waterproof-barrier of the skin.

4-Stratum lucidum = clear zone:

- Structure: 2-3 layers.



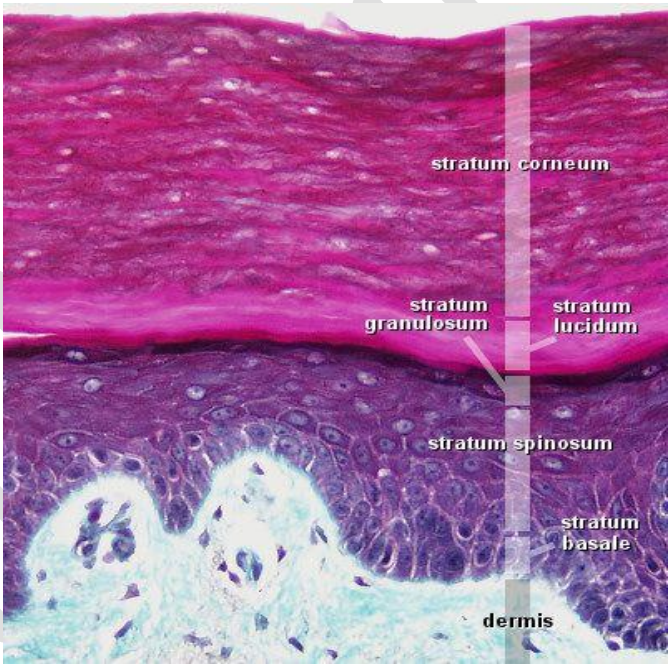
- **Structure:**

1- *Shape of cells:* flattened & pale.

2- *The nuclei and the organelles:* are degenerating.

3-*The cytoplasm:* contains densely packed keratin filaments.

5-Stratum corneum = horny layer:



- **Number of layers: 20-30.**
- **Structure:**

1- *Shape of cells:* flat cells in the form of eosinophilic horny scales.

2- *The nuclei and organelles:* degenerated.

3- *Cytoplasm:* contains densely packed keratin filaments.

4- The cells adhere to each another by *remnants of desmosomes*.

B-Non keratinocytes:

2-Melanocytes:

- ***The color of the skin depends on the interaction of three factors:***

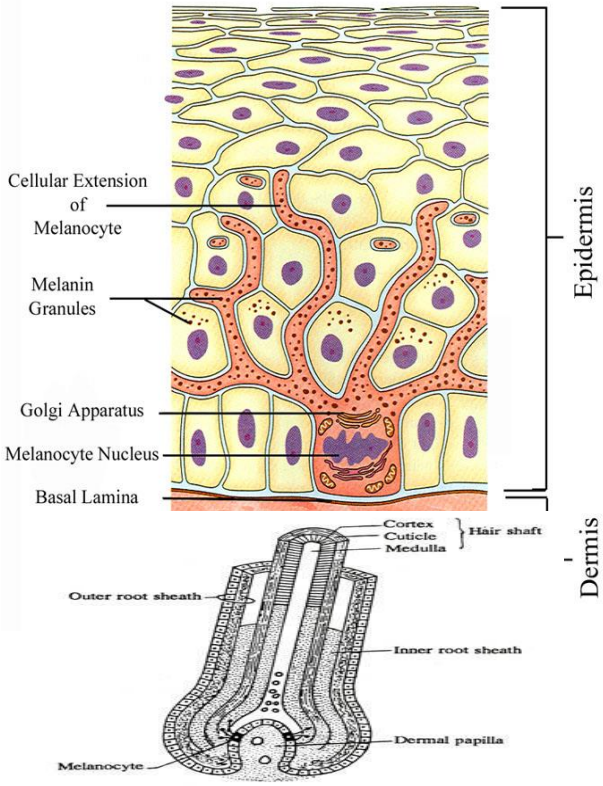
1- The content of *carotene* (yellow).

2- The oxygenated *hemoglobin* in the capillaries (red).

3- The *melanin pigments* (brown to black).

- ***Features:***

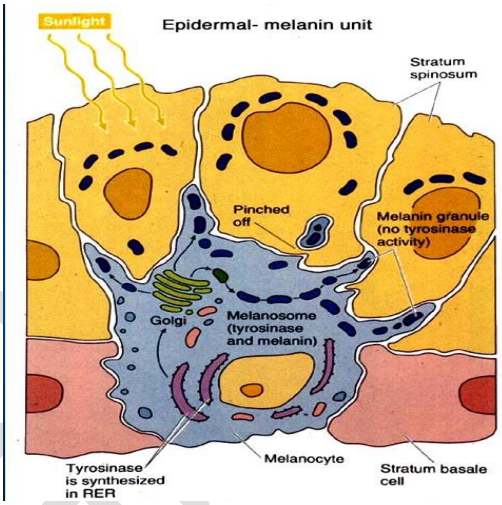
1- *Site:* in the epidermis, between the cells of the stratum basale (also found in the hair follicle).



2- Structure: **branching cell, its cytoplasm contain melanosomes.**

- ***Function:***

Melanin formation which protect against the harmful effect of ultraviolet rays, thus exposure to sun light accelerates the rate of melanin production.



- **Cytocrine secretion: unusual mode of secretion, in which the cytoplasmic processes of melanocytes transfer the melanosomes into the neighboring epidermal cells.**

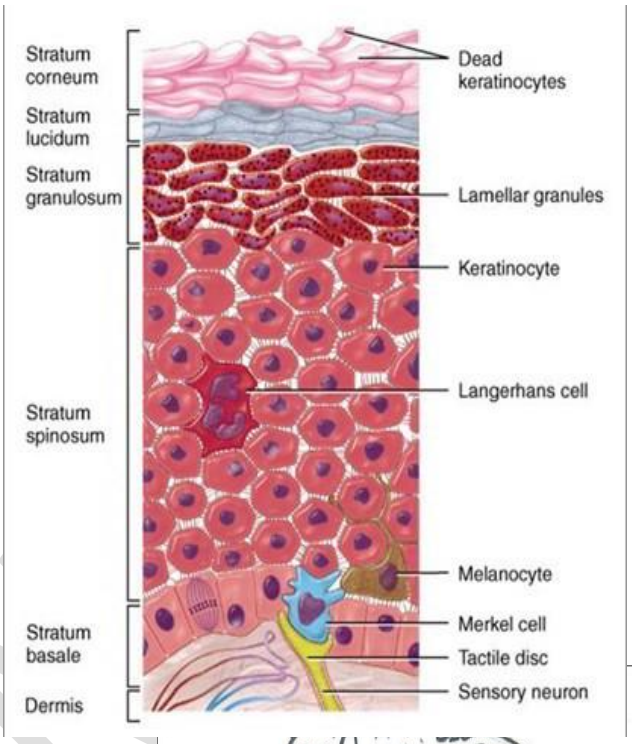
- **The number of melanocytes: Nearly the same in all races. Although, hereditary and racial factors control the amount and size of melanosomes and the rate of transfer by melanocytes.**

Disorders of Melanocytes:

1- *Albinism:* Lack of pigmentation, in which the melanocytes fail to form melanin.

2- *Vitiligo:* a depigmentation disorder occurs due to degeneration of melanocytes.

3-Langerhans cells:



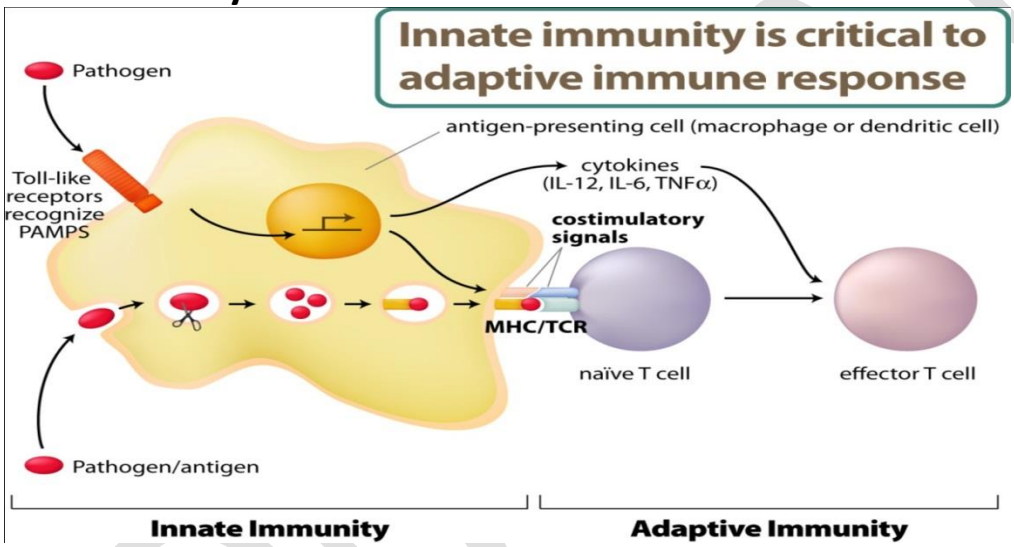
- **Origin:** blood monocytes (mononuclear phagocytic system)
- **features:**

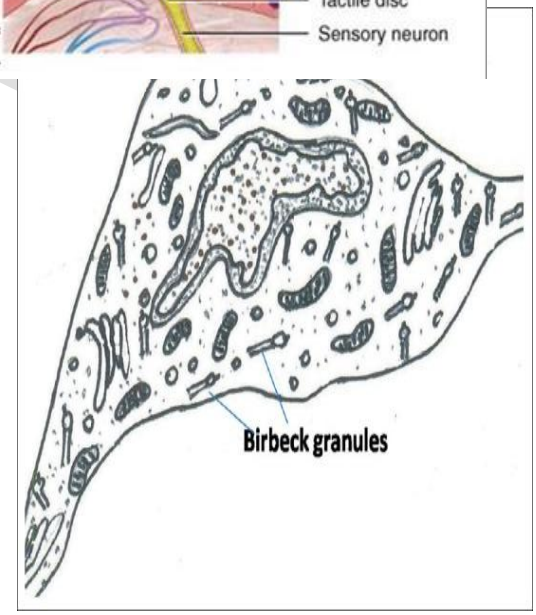
1- LM:

- ***Shape:*** branching cells with multiple cytoplasmic processes.
- ***Nucleus:*** folded & irregular.
- ***Cytoplasm:*** pale.
- ***Site:*** between the cells of stratum spinosum.

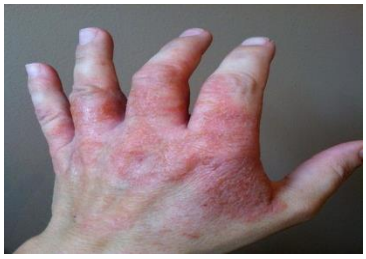
2- EM:

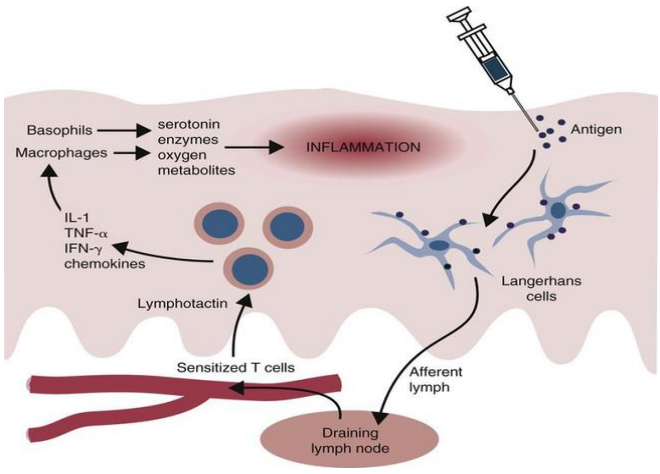
- numerous *lysosomes*.
- *2 Nos:* No keratin & No desmosomes between the Langerhans cells and keratinocytes.



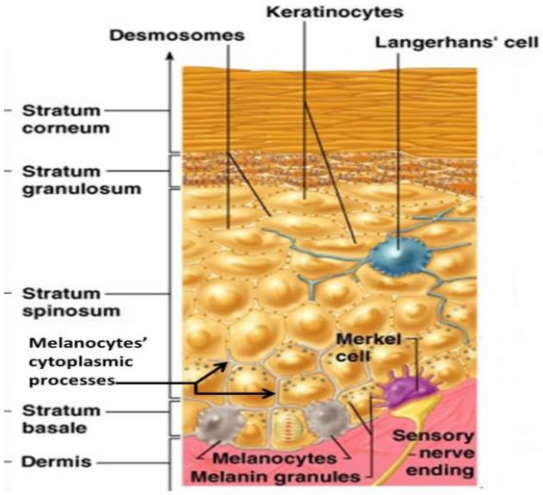


- ***Function:*** *Immune function* Antigen presenting cells (binding, processing and presenting the antigen to T lymphocytes). They are involved in ***the cutaneous contact hypersensitivity reaction***.





4-Merkel's cells:



- ***Features:***

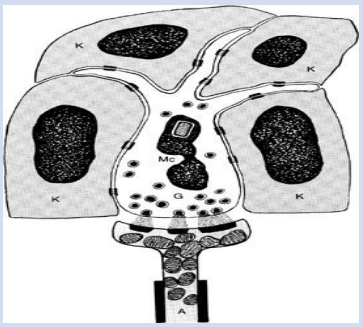
➢ ***Shape:*** **large cells with short processes.**

➢ ***Site:*** **the basal layer of the epidermis.**

➢ **They are attached to the keratinocytes by *desmosomes.***

➢ **The sensory nerve fibers pierce the basement membrane, end as expanded discs near the Merkel's cells**

- ***Function:*** **Receptors for fine touch sensation.**

	Melanocyte	Langerhan ′s cell	Merkel ′s cell
1- Site	Basal layer.	Stratum spinosum.	Basal layer.
2- Function	Melanin secretion which acts as a screen against UV radiation.	Antigen presenting cell responsible for cutaneous hypersensitivity.	Receptors for light touch.
3- Structure	Branching cells. Cytoplasm contains melanosomes. 	Branching cells with irregular nucleus. Cytoplasm contains lysosomes.	Large cell with short processes. Connected to keratinocytes by numerous desmosomes. 

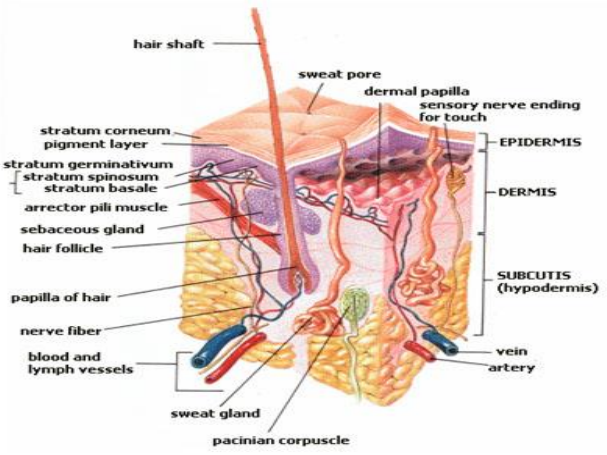
II-The Dermis:

- It is a connective tissue layer.
- *It contains:*

1- <u>Epidermal downgrowths:</u> the hair follicles, the sweat glands & the sebaceous glands.

2- <u>Sensory nerve endings</u> (receptors).

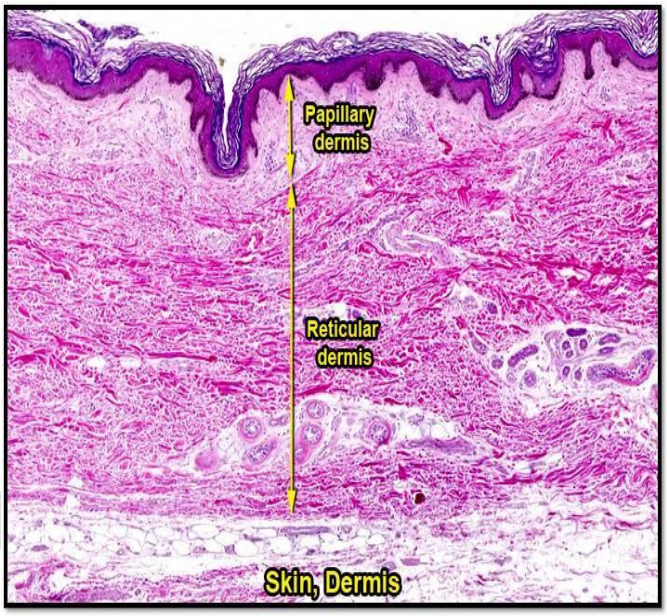
3- <u>Numerous capillaries</u>: for thermoregulation and nutrition.



- **The dermis is formed of two layers:**

I-Papillary layer:

- **It is the thin superficial layer, interdigitating with the basement membrane of the epidermis.**
- ***Structure:*** *loose connective tissue* **rich in blood capillaries & receptors for fine touch and temperature sensation.**

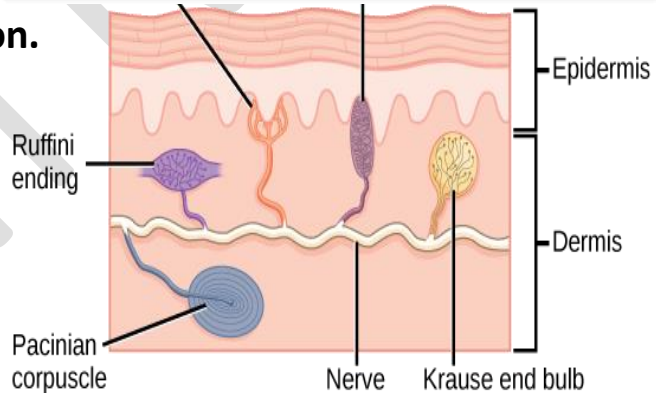


II- Reticular layer:

- **It is the deep thick layer.**
- ***Structure:*** *dense irregular connective tissue* **(more fibrous and less vascular than the papillary layer)** *contains:*

1-Collagen& elastic fibers.

2- Sensory nerve endings for pressure sensation.



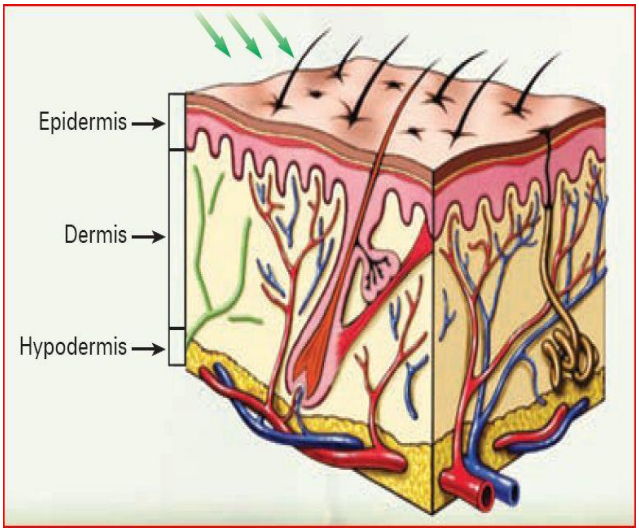
III–The hypodermis:

- **It is a subcutaneous layer lies under the dermis (it is not a part of the skin).**
- ***Structure:*** **loose connective tissue rich in fat cells.**
- ***Functions:***

1- Attaches the skin to the underlying tissue.

2- Storage of fat.

3- Contains the large blood vessels that supply the skin.

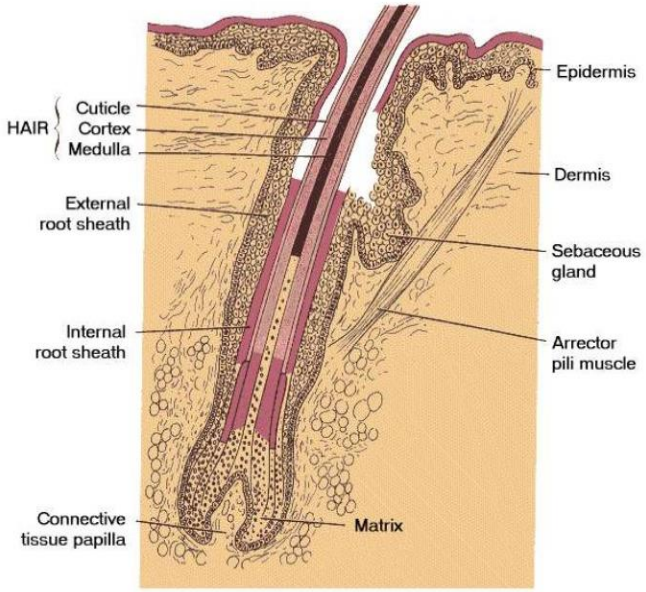


4- Allows a great mobility of the skin (except in palm& sole).

IV–Skin appendages, Hair &Nail

1-Hair

A-Hair follicle:



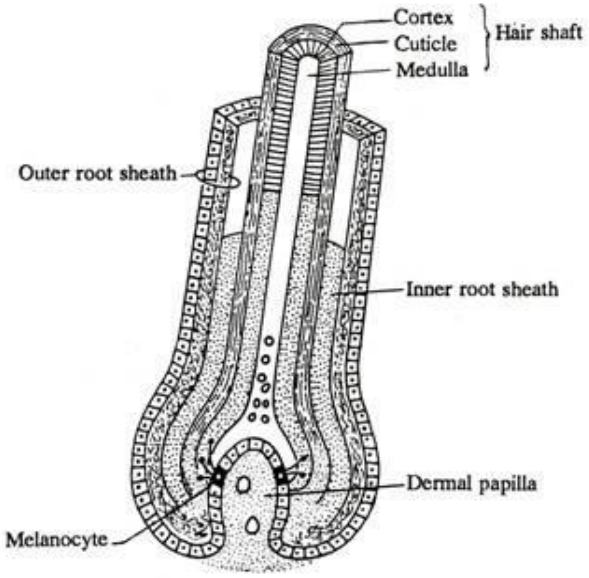
- **Definition:** an epidermal down growth into the dermis, containing the hair.
- **Function:** it is responsible for production & growth of hair.
- **Structure:**

1- It is an epidermal down growth into the dermis, ends by *the hair bulb* (terminal dilatation).

2- The hair bulb is invaginated by a vascular connective tissue called *dermal papilla* (if the dermal papillae are destroyed, the hair follicle dies and the hair will not grow again).

2- The cells of the hair bulb is called the *matrix* (containing stem cells, its proliferation results in growth of the hair).

3- The color of the hair is due to the activity of *the melanocytes* present in the hair matrix (white hair is due to lack of formation of melanin pigment in these cells).



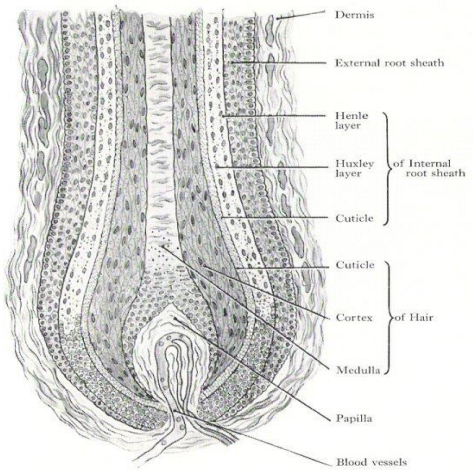
B-Hair:

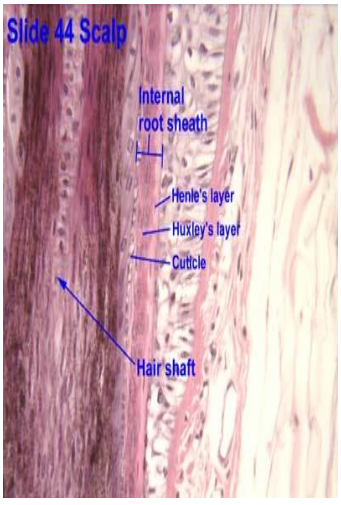
- Each hair has:

A- Root: embedded into the skin.

B- Free shaft: protruded beyond the skin.

- **Structure of hair:** Epidermal cells arranged in 3 concentric layers: Medulla, Cortex& cuticle.

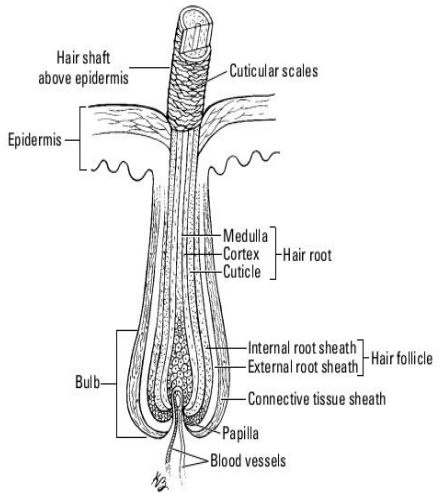




1- Medulla:

➢ Central core.

- Formed of ***moderately keratinized*** large polyhedral cells (contains soft keratin).
- It is absent in fine hairs.



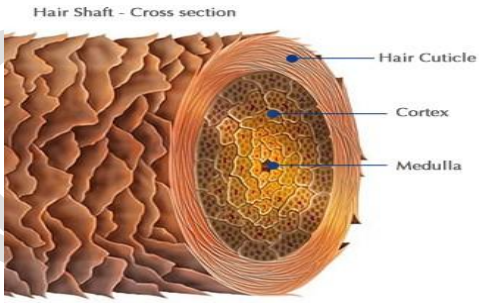
2- Cortex:

- Surround the medulla.
- Formed of ***heavily keratinized*** (hard keratin) tightly compact fusiform cells containing ***melanin pigment***

(Transferred from the melanocytes in the matrix) which gives the color of the hair.

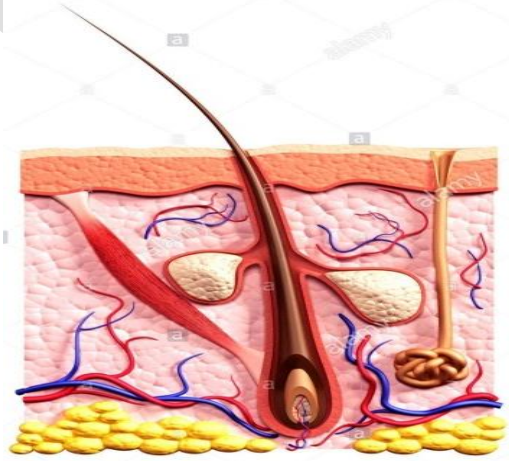
3- Cuticle:

- Surround the cortex.
- Formed of a single layer of flat cells containing ***hard keratin***. These cells form hard horny scales.
- ***Function:*** protects the hair from physical & chemical damage.

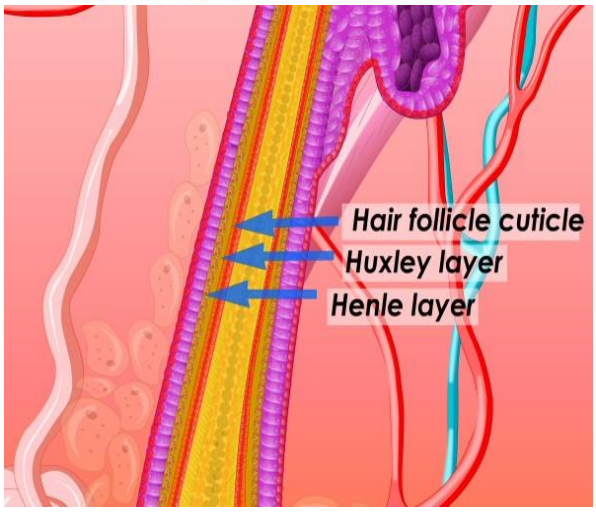


Arrector pilli muscle:

- It is attached to the hair follicle.
- **Function:** When the body is under some form of stress (Fear or low temperature)→ Stimulation of the nerve endings (of the autonomic nervous system) → contraction of these muscles→ pulls the bulb of the hair follicle towards the end of the arrector pili muscle→Erection of the hair.



The hair root is surrounded by two sheaths:

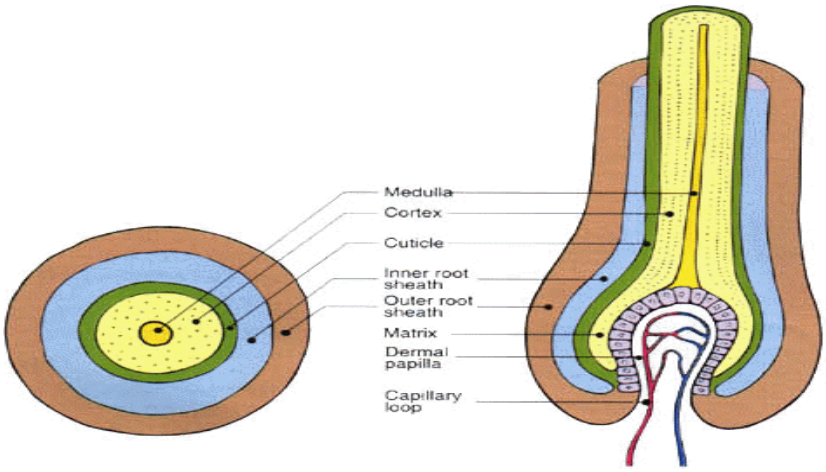


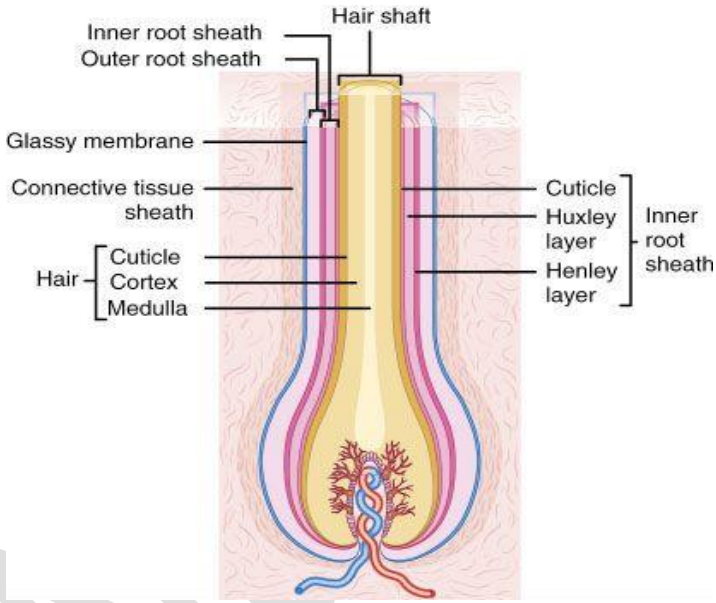
1- Internal root sheath: Multilayered cellular covering that surrounds the deep part of the hair root, consist of 3 layers:

- **Henle's layer:** an outer single layer of cuboidal cells.
- **Huxley's layer:** 1 or 2 layers of flattened cells.
- **The inner root sheath cuticle:** squamous cells.

2- External root sheath: corresponds to the stratum basale & spinosum of the epidermis.

- A thick basal lamina called **Glassy membrane** separates the hair follicle from the dermis.



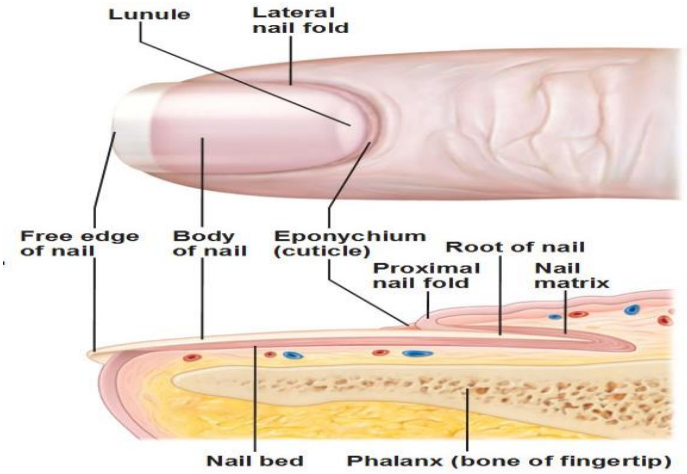


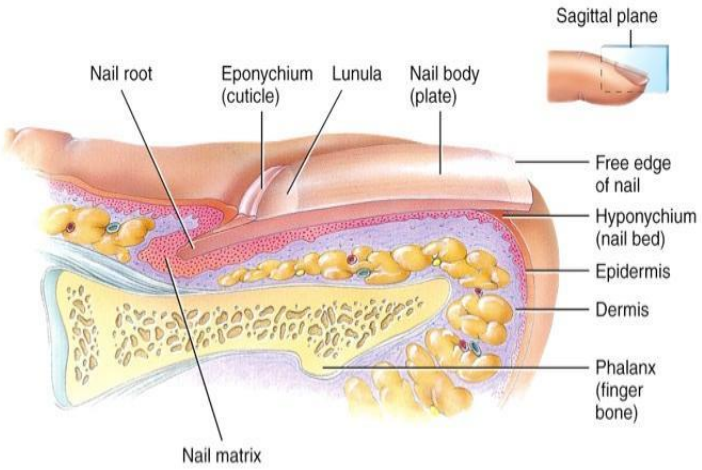
2-Nail

Definition: horny plates present on the dorsal surfaces of the terminal phalanges of fingers& toes.

Development& structure: epidermal invagination into the underlying dermis forming *the nail groove*.

- The cells of the nail groove is called nail matrix.
- Proliferation of nail matrix results on development of *nail plate* (closely packed hard heratin).
- *A soft cuticle* overlaps the proximal border of the nail plate to protect the nail matrix from microbes.
- The epidermis under the nail plate is called *nail bed* (formed of stratum basle& spinosum).
- The dermis of the nail bed is *highly vascular* (reflected in the pale pink color transmitted through the translucent nail) which is useful indication of the degree of blood oxygenation.





Which statement is the best to describe the medulla of the hair?

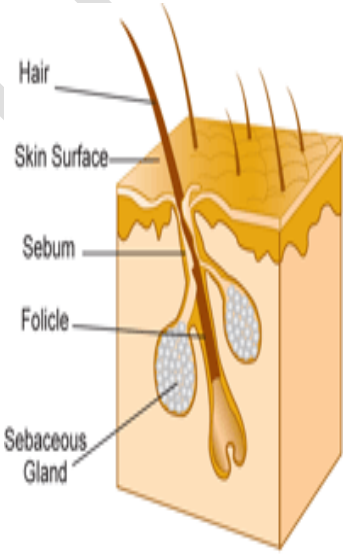
1- It consists of tightly packed fusiform cells.

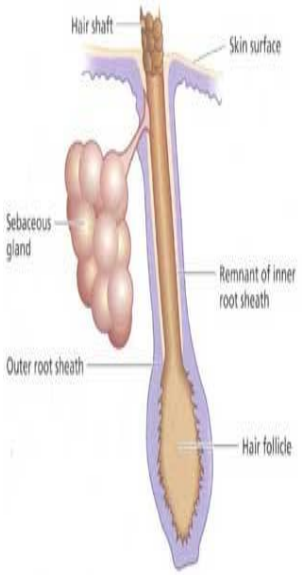
2- It is responsible for protection of the hair.

3- It is present in thick hair.

4- Proliferation of its cells is responsible for growth of the hair.

3-Sebaceous Glands:

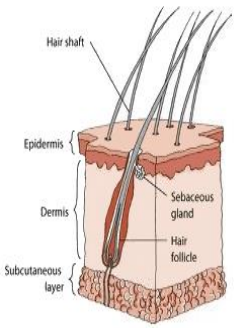


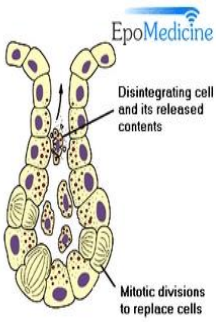


- ***Origin:*** **from the upper third of the hair follicle.**
- ***Sites:*** **They are most numerous over the head and ano-genital area.**
- ***Type:*** **simple or simple branched alveolar, holocrine glands.**
- ***Activity:*** **they are relatively inactive until puberty when they are stimulated by elevated sex hormones.**
- ***Structure:***

A- The secretory portion:

- **It is pale & alveolar in shape.**
- **It is lined by a layer of flattened *germinal cells* resting on a basement membrane.**
- **This layer proliferates & differentiates, becomes polyhedral and accumulate *sebum*.**
- **Then they are pushed to the center, where they degenerate while discharging their secretion.**





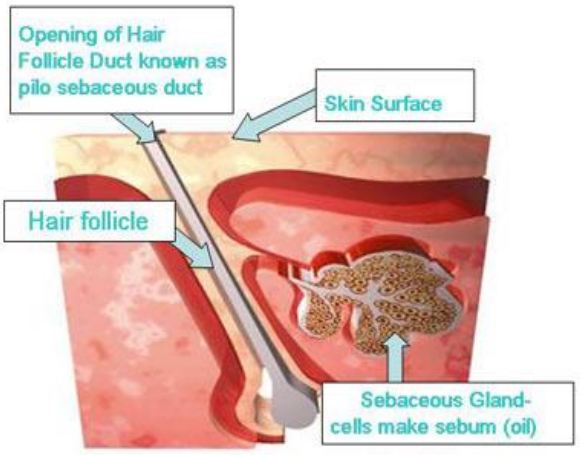
- ***Sebum:***

➢ ***Definition:*** **fatty substance+ cell debris + keratin.**

➢ ***Functions:***

1- Lubrication of the skin surface and hair.

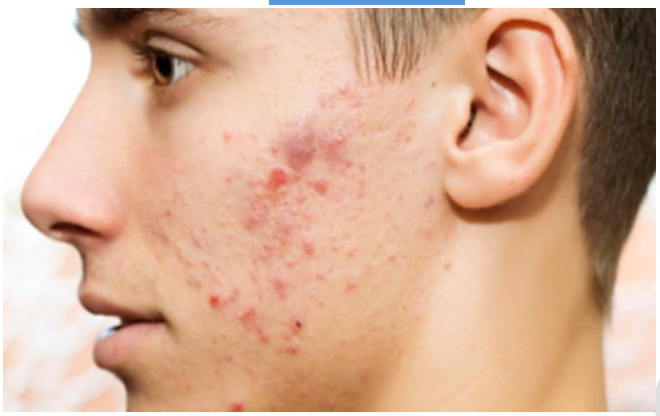
2- Has a bactericidal effect.



B-The excretory duct:

- **It is short and wide, opens obliquely into the upper third of the hair follicle; directly into the skin surface.**
- **It is lined by stratified squamous epithelium.**

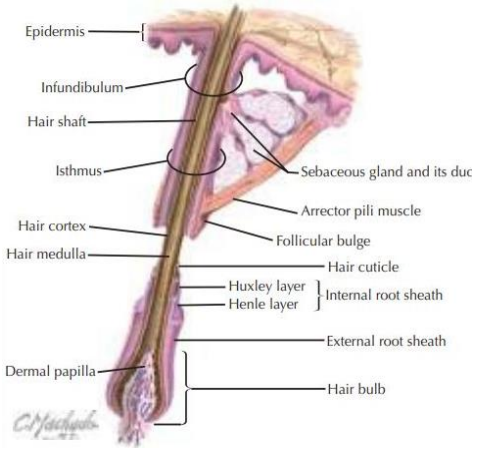
Acne:



Chronic inflammation of the obstructed sebaceous glands due to disturbance of the normal flow of sebum which occurs at adolescence.

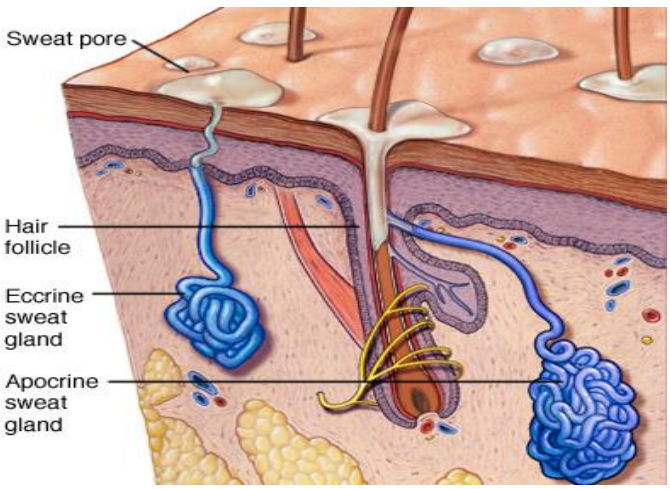
Pilosebaceous unit:

- It consists of the hair follicle, the sebaceous gland and the arrector pili muscle.



4- Sweat Glands:

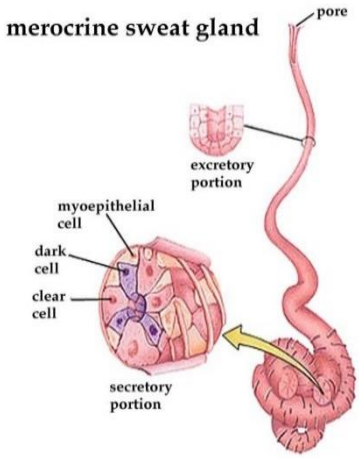
- ***Type:*** simple coiled tubular glands.
- ***Site:*** deep in the dermis or the hypodermis.
- ***Classification:*** the eccrine & the apocrine glands.

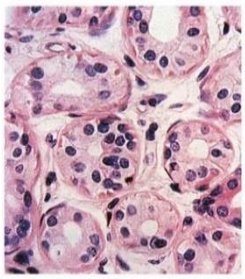


A-The eccrine sweat glands:

- ***Site:*** all over the body.

- ***Secretion:*** watery rich in sodium chloride.
- ***Activity:*** since birth.
- ***Structure:***





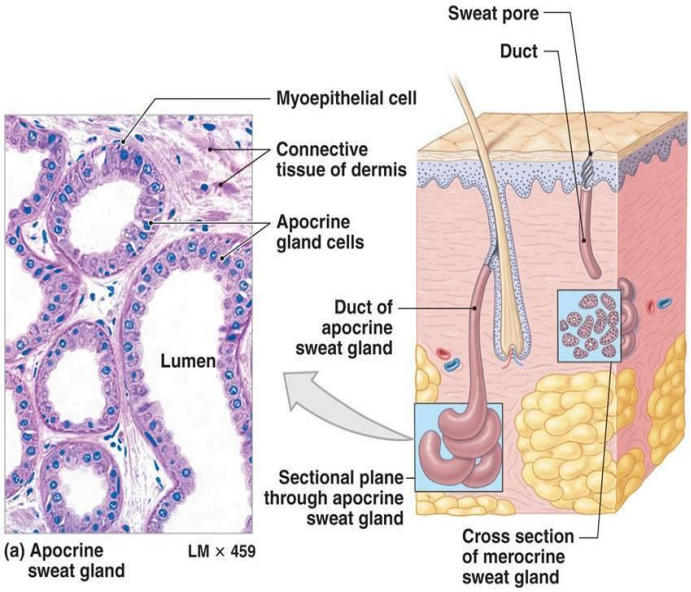
1- The secretory portion: small rounded acini with narrow lumen and composed of three cell types:

- Dark pyramidal cells: secreting glycoprotein (mucoid).
- Clear cuboidal cells: secreting a watery secretion.
- Myoepithelial cells: move the secretion into the ducts.

2- The excretory duct: lined by stratified cuboidal cells. It ascends in a helical course to the epidermis where it opens on the skin surface.

B-The apocrine sweat glands:

- ***Sites:*** in the skin of axilla, areola of the breast, and perianal region.
- ***Secretion:*** viscous, has a characteristic odor.
- ***Activity:*** at puberty.
- ***Structure:***



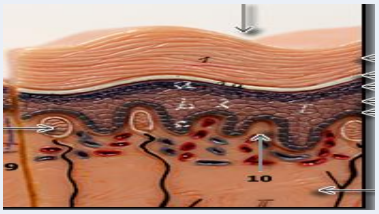
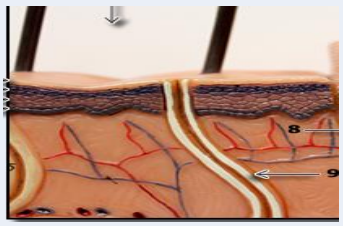
1- The secretory portion: acini which are larger and of wider lumen than the eccrine gland, composed of two types of cells:

- cuboidal cells with apical secretory granules.
- myoepithelial cells.

2- The excretory duct: lined by stratified cuboidal cells, opens into the hair follicle.

	Eccrine sweat gland (ec= outside)	Apocrine sweat gland
1- Site	All over the body.	Axilla , perianal region & breast.
2- Activity	Since birth.	At puberty.
3- Secretion	Watery.	Viscous with odour.

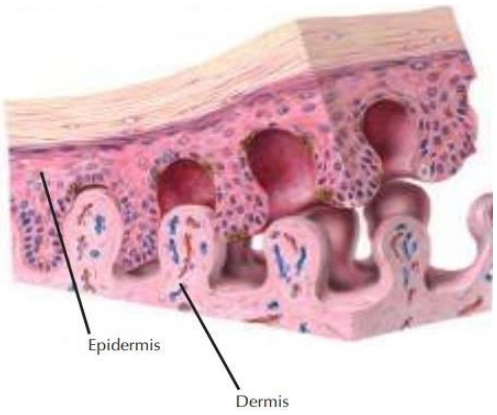
4- Secretory portion	• Smaller with narrow lumen. • Consists of 3 types of cells: 1. dark pyramidal: gives mucous secretion. 2. clear cuboidal: gives watery secretion. 3. myoepithelial cell: squeeze secretion into the duct.	• Large with wider lumen. • Consists of 2 types of cells: 1. cuboidal cell: gives mucous secretion. 2. myoepithelial cell.
5- Duct	Opens into skin surface.	Opens into hair follicles.

	Thick skin	Thin skin
1- Thickness	Thicker (5 layers).	Thinner (4 layers, stratum lucidum is absent).
2- Stratum corneum	Thicker.	Thinner.
3- Hair follicles	Absent.	Present.
4- Sebaceous glands	Absent	Present.
5- Sweat glands	More.	Less.
6- Sites	Palm & sole. 	The rest of the body. 

Dermo-epidermal junction

Definition: The boundary between epidermis & dermis.

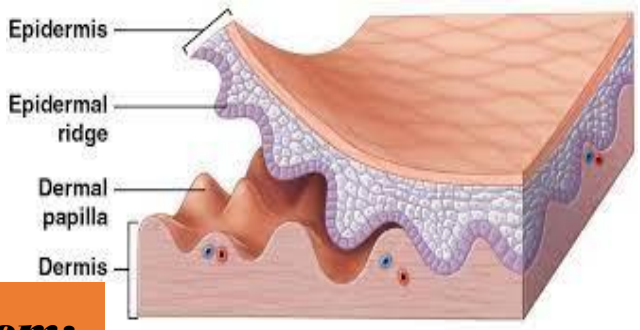
- It shows:



1- *Dermal papillae:* finger-like connective tissue protrusions projecting into the under surface of the epidermis.

2- *Epidermal ridges:* Similar epidermal protrusions projecting into the dermis.

In thick skin: the epidermal ridges are deeper, the dermal papillae are longer and more closely spaced.



Functions of the integumentary system:

1- Protection of the body against any injurious agents (Keratin in stratum corneum).

2- Water proof-barrier: lipid-rich extracellular material in stratum granulosum&corneum.

3- Screening against ultraviolet rays: melanin pigments.

4- Perception of stimuli: sensory nerve endings.

5- Excretion of nitrogenous products and sodium chloride: in sweat.

6- Formation of vitamin D: mainly in stratum basale and spinosum.

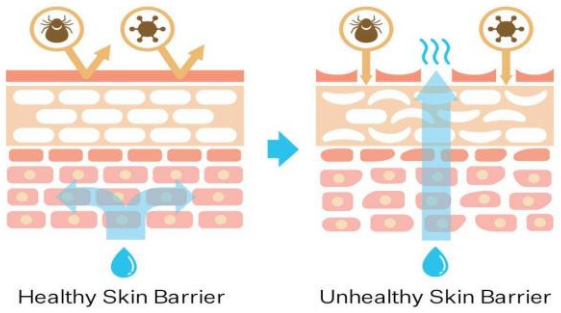
8- Regulation of the body temperature:

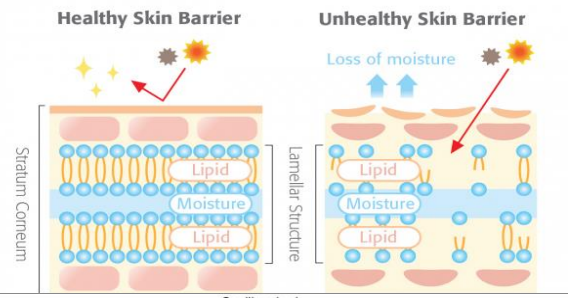
- ***In hot weather:***

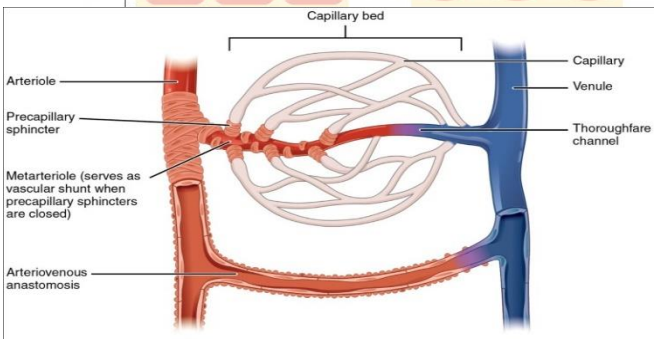
1- Increase sweating.

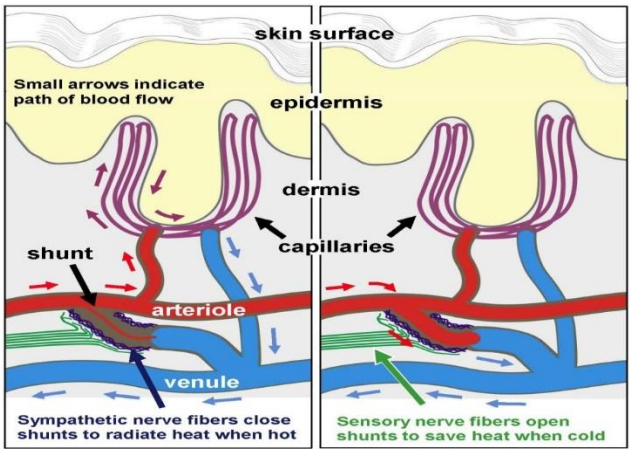
2- Vasodilatation of the dermal capillaries & closure of the arteriovenous shunt→ increase cutaneous blood flow& increase heat loss.

- ***In cold weather:*** **constriction of dermal blood vessels and opening of the arteriovenous shunts→ decrease cutaneous blood flow and decrease heat loss.**









Which structure is responsible for water proof barrier of the skin?

1- Cytokeratin in the stratum corneum.

2- Keratohyaline granules in the stratum granulosum.

3- Desmosomes in the stratum spiosum.

4- Lamellated granules in the stratum granulosum.

اللَّهُمَّ ارْزُقْنَا العِلْمَ النَّافِعَ وَالعَمَلَ الصَّالِحَ وَارْزُقْنَا

الإِخْلَاصَ فِي القَوْلِ وَالعَمَلِ وَوَفِقْنَا لِمَا تُحِبُ وَتَرْضَى ..

جزى الله كل خير

الأستاذة الدكتورة: إيمان نبيل

ومن عمل على كتابته وتصميمه ليخرج بهذا الشكل

فلا تنسوه من دعواتكم في ظهر الغيب ..

تم تجميعه بواسطة: ميّ قدري