



# GENERAL HISTOLOGY

*By Data Zone\_SWG*



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ME

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شرح نجاح



Data Zone

**إزاي أذاكر صح ؟**

نستعين بالله ونطلب منه التوفيق والبركة في السعي والوقت.

نسمع حد بنفهم منه كوييس عشان المذاكرة تبقى سهلة.

ميففععش تذاكر الهستو من غير صور (diagrams).

نركز على الكلام المهم (**الملون**) ومواقع الأسئلة.

نذاكر أول بأول ومنراكمش المحاضرات.

ميففععش تهمل الهستو؛ لأن كمية درجاتها مش قليلة.

شابتر 4&amp;5 فيهم تفاصيل محتاجة تتذاكر في شكل مقارنات عشان تثبت.

لازم تطبق على مذاكريك بالحل.. والأهم أسئلة **كتاب القسم** ونبعد عن الأسئلة الغريبة.



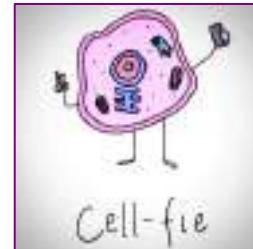
# ch 1 : MICROTECHNIQUE AND MICROSCOPY

**Objectives:** By the end of this chapter, the student should be able to know:

1. The meaning of microtechnique.
2. Steps of paraffin section preparation and the importance of each step.
3. Basic idea of other types of tissue section preparation.
4. Major differences between tissue section preparation for light microscope and for electron microscope.
5. Steps of H&E staining.
6. The idea of different types of staining.
7. The idea of histochemistry, immunohistochemistry, Immunocyto- chemistry and autoradiography.
8. Structure and idea of ordinary light microscope working.
9. Basic idea of other different types of microscopes.

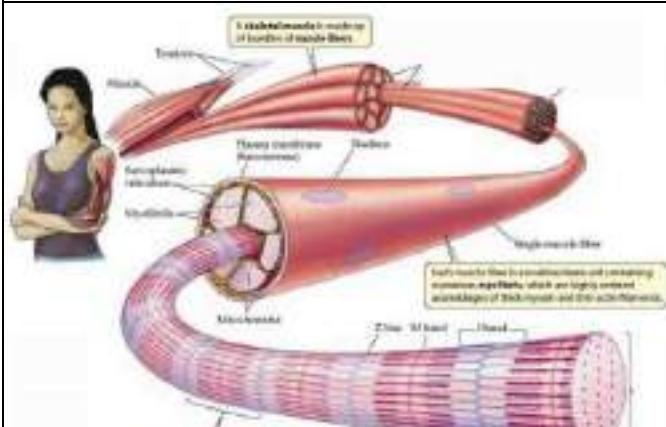
## Histology and cell Biology

 Histology (Gr. **Histo**= tissue + **logos**= study) علم دراسة الأنسجة → is the study of the microscopic structure of tissues so it is the **microscopic anatomy** of the tissues (Fig. 1-1).

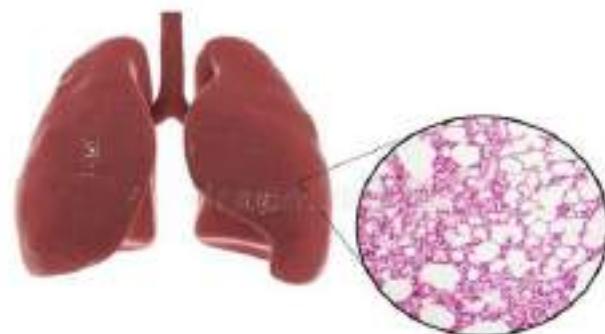


 **Histology and Cell Biology** is: the study of the **structure and behavior** of cells and body tissues, usually involving microscopic examination of tissue slices.

(Fig. 1-1).



Anatomy & Microscopic anatomy of (Muscles)



Anatomy & Microscopic anatomy of lung

# Microtechniques

Microtechnique is the art of **preparing** tissues for examination under the microscope (light & electron microscopes) and of **preserving** objects so prepared.

## 1. Selection and obtaining tissue

- Samples must be obtained from **living** tissue (**biopsy**) or very soon **after death** (**autopsy**).
- Samples are taken using **very sharp razors** to prevent distortion of tissue during cutting.
- Samples should be **small in size** to allow the penetration of fluid through it up to the most **interior part**. لازم العينة يكون حجمها صغير؛ لأن الخطوة اللي بعد دي هي إننا هنحط العينة في مثبت (حاجة زي المادة الحافظة)، ومحاجينه يتغلغل لأعمق العينة.

## 2. Fixation

- The tissue is put immediately in a suitable fixative.
- Fixation is the process of tissue **preservation** through coagulation of the protoplasm.
- The most commonly used fixative is **formalin** (buffered 10%), **Susa**, **Zenker**, **Bouin** & **Carnoy's fluid**.



### Purpose of fixation:

1. Prevent **autolysis** التحلل الذاتي as it destroys lysosomal enzymes.
2. Prevent **putrefaction** التعفن by killing bacteria.
3. **Coagulate** the proteins and **harden** the tissue → making it easier for cutting into thin sections.
4. **Preserve** the relation of the various tissue components.
5. Some fixatives have **mordanting** effect (increase the affinity of tissue for stains).



## Paraffin technique

It is the routine method of histological sections preparation for light microscope (LM).

## 3. Washing

- After the tissue is fixed for the proper length of time, excess fixative is washed out.
- Washing also removes substances in the fixative which might interfere with the subsequent processing.



## 4. Dehydration

- Removal of water is a necessity to embed the tissue in a **wax** or resin material to be ready for sectioning.
- Since the embedding media are immiscible with water, dehydration (removal of water) must be undertaken to prepare the wax block.
- Dehydration is usually done by **ascending grades of ethyl alcohol** (50, 70, 90, 100%).
- The gradual ascending concentrations are used to prevent sudden withdrawal of water which may cause distortion and damage of the tissue.



الألكحول بيسحب الماء من النسيج؛ عشان كدا أيام كرونا لما كنا بنستخدم الألكحول كثين، كانت البنات بتتحس بجفاف في إيديها وبينزعجو من الموضوع دا (")





## 5. Clearing

- Paraffin is not soluble in alcohol.
- The alcohol is replaced by a substance in which paraffin is soluble, such as xylene, toluene, or benzene.



## 6. Infiltration and Embedding

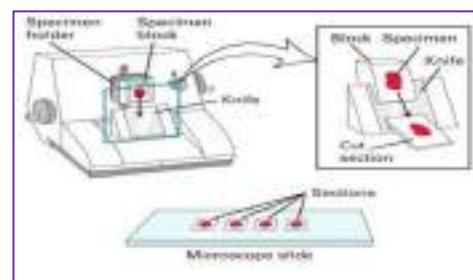
- The transformation of the cleared tissue into a **paraffin block** is termed **embedding**.

- If the tissue is only **surrounded** with wax, sectioning will cause the tissue to be separated from its surrounding wax medium. Wax, thus, must be **surrounding** and passing into the **inside of the tissue**; the latter is termed **infiltration**.



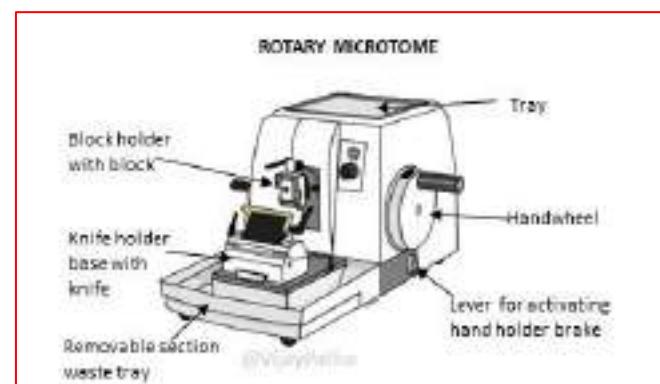
جطعة فزلكة معلش: وجود الشمع حول النسيج كدا انت دفنت النسيج (إمدينج) ، لكن وجود الشمع داخل النسيج وتغلغله فيه: دا كدا إنفلترشن

- Infiltration is done first by some sort of low molecular weight wax (**soft paraffin**).
- Soft paraffin, thus, replaces the clearing agent and hard paraffin is used in the following step to conform the block around the tissue.



## 7. Microtomy and Sectioning

- Sectioning is done using the **microtome**.
- Microtomes in common use are usually the rotary types, although other types are used in tissue preparation such as the **sliding microtome** usually used in sectioning of **dense** tissue (bone and skin).
- Section thickness usually suitable for routine histological study is 4-10 um.



## 8. Mounting

Sections are mounted onto a glass slide and left to dry

Advantages of paraffin technique	Disadvantages of paraffin technique
1- It takes a short time. 2- It gives serial sections (ribbon). 3- It gives very thin sections. 4- The sections are easily stained.	1- The fixatives and heat used may damage the tissues. 2- The fat contents of the cells is dissolved during preparation. 3- It is not suitable for histochemistry. 4- It cannot be used for large pieces of tissues with large cavities.

## Other methods of preparation of histological sections for LM:



### Celloidin method

- The tissue is embedded in celloidin .
- The sections are cut with a **sliding microtome**.



Fig. 1-8: Sliding microtome.

Advantages of Celloidin method	Disadvantages of Celloidin method
1. It preserves the relations of the tissues because no heating is used. 2. It can be used for cutting large organs with plenty of folds and lumina.	1. Time-consuming. 2. No serial sections can be obtained. 3. The sections are very difficult to be stained.



### Freezing technique

- It is used to cut **fresh** specimen.
- The specimens are frozen at about **-150 °C**, hardened and cut by the **cryostat** (is an electrical freezing and cutting apparatus widely used to prepare frozen sections)



cryostat

Advantages	Disadvantages of Celloidin method
1- It is used in hospitals to study specimens during <b>surgical</b> procedures. 2-Allows stained sections to be prepared rapidly (within a few minutes). 3- It is effective in the <b>histochemical</b> study of enzymes since freezing does not inactivate most enzymes. 4- It <b>preserves lipids</b> .	1- Producing <b>thick</b> sections. 2- Does not give serial sections. 3- The section may <b>fragment</b> into small pieces.



Tissue processing





# Staining procedure



## 9. Deparaffinization

- Most stains in common use are **natural salts** having a basic and acidic radical.
- Such stains are usually in the form of aqueous solutions.
- Sections on the slide is surrounded and infiltrated with paraffin which immiscible with water.
- Paraffin is removed by xylol

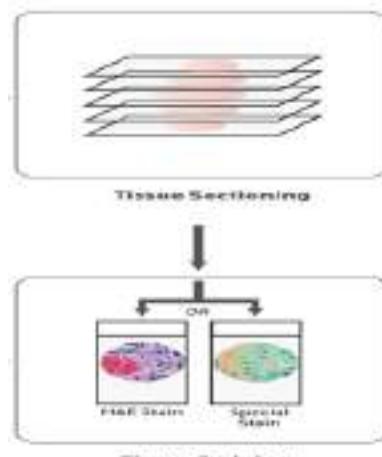
## 10. Hydration

- Hydration of the tissue is a necessity to enable the stain reach and react with the tissue components.
- Rehydration of the tissue is achieved by **descending grades** of alcohol (100, 90, 70, 50%), distilled water is then used to replace the alcohol.



## 11. Staining

- The **nucleus** is stained first (by **hematoxylin**) because the use of acidic dyes (e.g. **eosin**) to stain the **cytoplasm** may impart some color which prevents perfect staining of the nucleus.  
So, haematoxylin (H or Hx) is used first then eosin (E).
- Washing with water is done between the two steps and after eosin.



## 12. Dehydration

- by **ascending** grades of ethyl alcohol (50, 70, 90, 100%).



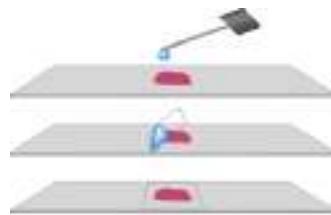
## 13. Clearing

- by **xylene**, it makes the stained tissue sections transparent.

## 14. Mounting

- to convert the slide into a permanent preparation used in the study of section for months or even years, the section is mounted (covered) with a very thin cover slip using a sticky mountant (**Canada balsam** or **De Pe Xe**).

## 15. Cleaning and Labeling

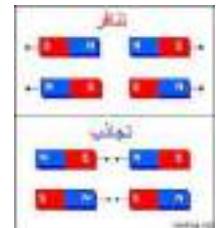


## Types of histological stains

### Basic dyes

- Tissue components that stain more readily with basic dyes are known as **basophilic**. يُحب
- The tissues stain with basic dyes because of acids in their composition (nucleic acids, acid glycoproteins).
- Basic dyes as **Hematoxylin** and **methylene blue**.
- Basic dyes have a **positive** charge so it is called **cationic**.

زي أقطاب المغناطيس  
هتلaci الغضيات اللي بتتركب من أحماض  
بتحب الصبغة القلوية، والعكس للعكس



### Acid dyes

- Tissue components that stain more readily with acidic dyes are known as **acidophilic**.
- Acidophilic component of tissues such as mitochondria, secretory granules and collagen.
- Acid dyes as **orange G, eosin** and **acid fuchsin**.
- Acid dyes has a **negative** charge so it is called **anionic**.

### Hematoxylin and Eosin (H&E)

The combination of H&E is the most commonly used. 🌟

**Hematoxylin**: is a **basic dye**, stains the cell nucleus and other acidic structures **blue**.

**Eosin**: is an **acidic dye**, stains the cytoplasm and other basic structures **pink**.

### Vital stains

- Vital staining is the staining of the **living** cells within the living animal (i.e. in **vivo**). حيوي
- It is done by injecting a nontoxic dye into living animals.
- e.g. staining of phagocytic cells with **trypan blue** or **Indian ink**.



### Supravital stains

Supravital staining is the staining of living cells outside the body (i.e. in **vitro**).

e.g. staining of reticulocytes with brilliant cresyl blue and mitochondria with Janus green B.

### Neutral stains



It is a **mixture** of acidic and basic stains.

Are used to stain the **blood elements** in a blood film, e.g. **Leishman's stain**.

### Trichrome stains

blood film

Three (3) stains are used in combinations to give 3 colors to different tissue components.

In addition to staining the nuclei and cytoplasm can differentiate collagen from smooth muscle.

Examples:

**Mallory's** stain: stains **collagen blue**, **smooth muscle yellow**, **cytoplasm red**.

**Masson's** stain: it stains **collagen green**, **nuclei blue** and **cytoplasm red**.





## Metachromatic staining

- It is the staining of certain cell components with a color which is different from that of the dye used.
- The phenomenon of altering the color is called **Metachromatic**
- It is due to the interaction between the dye and the cell component, producing a different compound with a different color. e.g. the staining of **mucopolysaccharide** granules of mast cells by **toluidine blue** which changes to the **red** or **violet** colors.

## Orthochromatic stains

- These react with the contents of the cells and they give the same color of the stain.

## Preparation of tissues for electron microscope :

**Fixation:** very small piece of tissue (not exceed 3mm) is obtained and fixed immediately in **glutaraldehyde** followed by **osmium tetroxide**.

**Clearing:** in propylene oxide

**Embedding:** using epoxy resin as araldite or epon Resin is resistant to the damaging effects of electron beam.

- It is much harder than paraffin so very thin section can be obtained.

**Sectioning:** ultra-thin sections are prepared (0.005-0.1  $\mu\text{m}$ ) the epoxy resin block is cut by glass or diamond knives of the ultramicrotome.

**Mounting:** sections are mounted in copper grids.

**NB:** The presence of heavy metal salts as uranyl acetate **أسيتات الاليورانييل** and lead citrate **سيترات المريثان** enhance the contrast in EM

## Histochemistry and cytochemistry

- They are methods for localizing substances in tissue sections.
- These methods produce insoluble colored or electron-dense compounds that enable the localization of specific substances by means of light or electron microscopy.

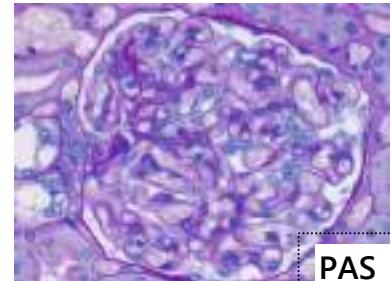
**Examples are:**

### Demonstration of nucleic acids:

- **Feulgen reaction:** DNA can be identified in cell nuclei using the Feulgen reaction producing a red color .
- **Methyl green pyronin:** DNA and RNA can be analyzed by staining cells or tissue sections with methyl green pyronin stain. DNA is stained green and **RNA is stained red**.

## 4 Demonstration of enzymes

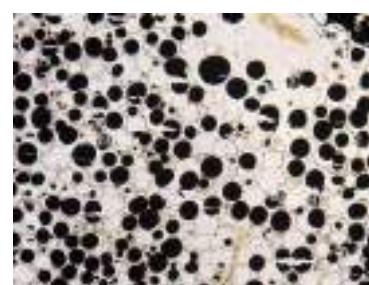
- a- Phosphatases enzymes as alkaline phosphatases which have activity at an alkaline pH and acid phosphatases.
- b- Dehydrogenases enzymes as succinate dehydrogenase which is an enzyme in the citric acid (Krebs) cycle present in mitochondria.
- c- Peroxidase is an enzyme present in several types of cells.



PAS

## 5 Demonstration of glycogen

- a- Best's carmine: It is a specific stain for glycogen which is stained red.
- b- Periodic acid-Schiff (PAS) reaction produces a purple or magenta color. Polysaccharides, oligosaccharides and glycoproteins can be demonstrated by the PAS reaction and they are PAS positive.



## 6 Demonstration of lipids

- a- Sudan III (orange color).
- b- Sudan black (black color).
- c- Osmic acid (black color).



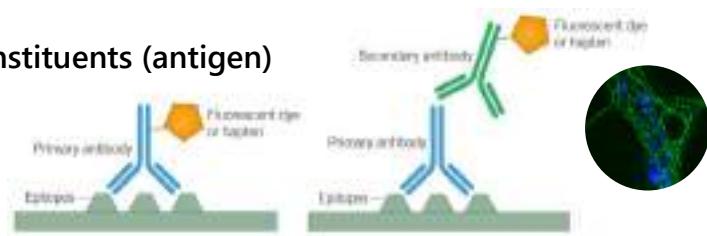
Sudan III

Sudan black

Osmic acid

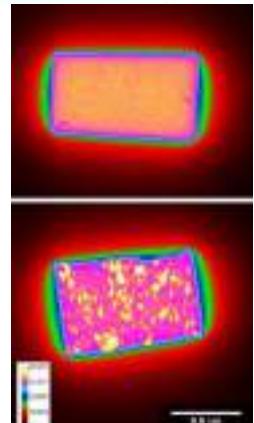
## immunocytochemistry

- It is a technique for identifying cellular or tissue constituents (antigen) by means of antigen antibody interactions.



## Autoradiography

- Autoradiography permits the localization of radioactive substances in tissues by means of the effect of emitted radiation on photographic emulsions.
- Silver bromide crystals present in the emulsion act as microdetectors of radioactivity.
- In autoradiography, tissue sections from animals previously treated with radioactive compounds are covered with photographic emulsion.
- After various exposure times the slides are developed photographically and examined.





# Microscopy



- **Microscopy :** It is the science of studying subjects through a microscope.
- **Microscope :** Micro (G. micros = small) + Scope (G. scope = to view).
- An instrument that gives an **enlarged detailed image** of an object or substance that is **minute** or **not visible** with the naked eye
- The human eye can recognize two objects if they are **not closer than 0.1 mm** at a **normal viewing distance of 25 cm**.
- This ability to optically **separate** two objects is called **resolving power**.
- Any finer detail than this can be resolved by the eye only if the object is enlarged by the use of optical instruments such as hand lenses, compound light microscopes and electron microscopes.
- The **resolving power** is the smallest distance between two particles at which they can be seen as separate objects.

## N.B:

- The resolving power improves as the wavelength of the illuminating light decreases.
- 1 millimeter (mm) = 1000 micrometers ( $\mu\text{m}$ ).
- 1  $\mu\text{m}$  = 1000 nanometers (nm).

## Types of microscopes



### Microscopes depend on :

A) ordinary visible light.	B) other than visible light.
1. Conventional light microscope. 2. Polarizing microscope. 3. Phase contrast microscope. 4. Dark-field microscope. 	1. Fluorescent microscope 2. X-ray microscope 3. Laser microscopes 4. Electron microscope

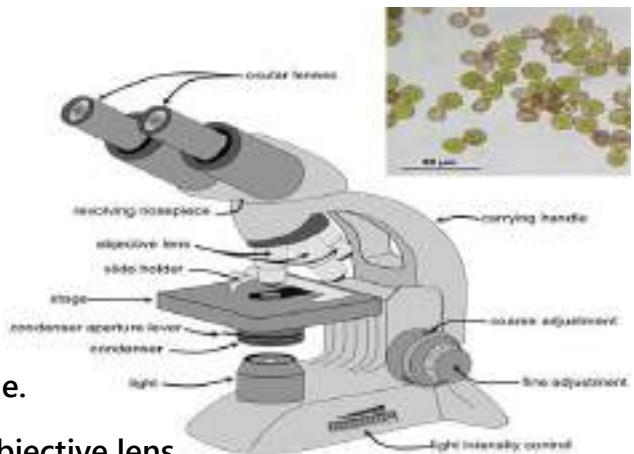
### • **Conventional light microscope :**

Basically the ordinary light microscope performs its function through 2 systems mainly, the optical and illuminating systems.

#### The illumination system

Light, from the illumination source (electrical lamp) is directed and focused onto the specimen (mounted on a glass slide) through the aperture in the stage.

This light then passes through the specimen and into the objective lens.



**The optical system** It consist of:

condenser	The objective lens	The ocular lens
<p>It <b>collects</b> and <b>focuses</b> the illumination to produce a cone of light that illuminates the object to be observed.</p> 	<p>It <b>enlarges</b> and <b>projects</b> the illuminated image of the object in the direction of the ocular lens.</p> <p>The magnifying power of objective lens may be <math>\times 10</math>, <math>\times 20</math>, <math>\times 40</math> or <math>\times 100</math> (oil immersion).</p> 	<p>It further <b>magnifies</b> this image and <b>projects</b> it onto the viewer's retina or a photographic plate.</p> <p>Its magnifying power may be <math>\times 5</math>, <math>\times 10</math> or <math>\times 15</math>.</p> 

- \* The **total magnification** is obtained by **multiplying** the magnifying power of the objective and ocular lenses.
- \* This power permits good images magnified **1000–1500 times**.
- \* Objects **smaller than  $0.2 \mu\text{m}$**  cannot be distinguished by this instrument.



Polarized Light Microscope Configuration

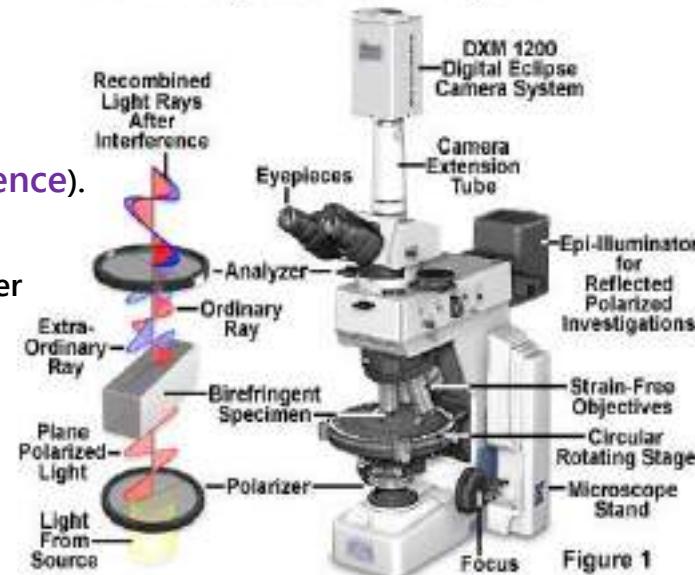


Figure 1

#### • Polarizing microscope :

- When light passes through certain substances e.g. crystals or body tissues as fibers it divides in a way that produce 2 light rays from one.
- This called double refraction or polarization(**birefringence**).
- In its simplest form, the polarizing microscope is a conventional microscope in what a Nicol prism or filter is interposed in the light path below the condenser and is **called polarizer** which converts all light passing through the instrument into plane polarized light.
- A similar second prism or filter termed the **analyzer** is placed within the parallel of the microscope above the objective lens
- When the analyzer oriented so that its polarizing direction is parallel to that of polarizer, regular image was seen. However, if the analyzer is rotated until its axis is perpendicular to that of the polarizer, no light can pass through the ocular lens and the field is black.
- The field will remain black if an isotropic or singly refractive object is placed on the stage.
- A birefringent object however will appear light upon a dark background when examined in this manner. Birefringent or anisotropy is exhibited by many biological structures e.g. **muscle fibers** and **collagen fibers**.





### • Dark-field microscope :

- For darkfield illumination, the **cone of light** illuminating the specimen must **not** enter the microscope objective lens.

- Only light that is **scattered** by the specimen is detected by the objective lens.

- This is achieved by use special dark-field substage condensers called **cardioid condensers**.

### • Fluorescence microscopy :

- When excited by radiation of **short wavelengths (nonvisible)**, some substances will emit light of a **longer wavelength (visible)**.

- This phenomenon is called **fluorescence**.

- The usual light source for excitation radiation is **ultraviolet (UV)**.

- The fluorescent images produced can be recorded on either black and white or color film.



Fluorescence

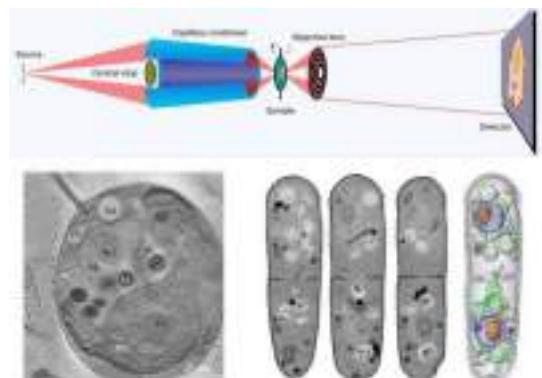
### • X-ray microscope :

- X-rays have a **shorter wave length** than visible or ultraviolet light so, it has a **higher resolving power**

(Resolution is not particularly high and with the instruments available is still far from theoretical limits).

- the specimen placed upon a photographic emulsion and exposed to soft X-irradiation.

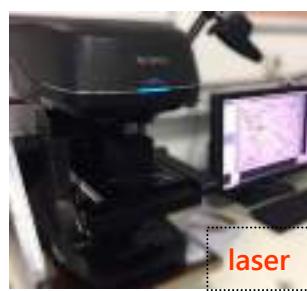
- The small X-ray picture obtained is subsequently magnified optically.



### • Laser microscopes :

- Confocal microscope.

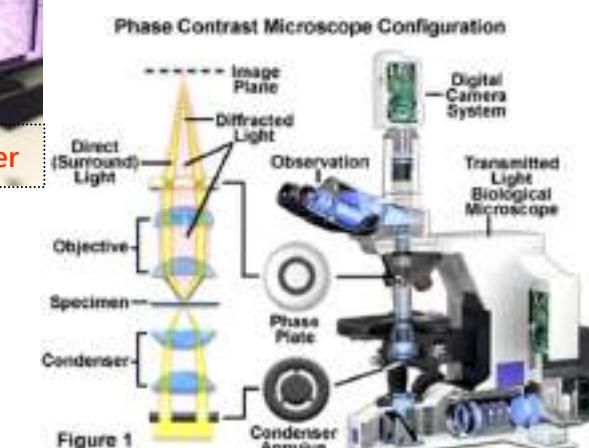
- Multiphoton (Femto-second) microscope.

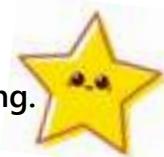


### • Phase contrast microscope :

- The principle is based upon the fact that the light changes its speed and direction when passing through cellular and extra-cellular (media of different refractive indices).

- These changes cause the structure to appear lighter or darker related to each other by using a phase contrast system (phase plate) that convert the difference in speed into difference in intensity.





• **Electron microscopes** : they are 2 types ; transmission and scanning.

Transmission electron microscope (TEM).	Scanning electron microscope (SEM).
<ul style="list-style-type: none"> <li>-In TEM the Specimens are examined by passing the <b>electron beam</b> through them, revealing more information of the internal structure of specimens.</li> <li>-The resolution is very <b>high</b>, reaching up to about 0.2 nm and it can magnify up to <u>500.000</u> times.</li> <li>- The image obtained is finally seen on a <b>fluorescent screen</b> or is projected onto photographic plates.</li> <li>- In <u>high-voltage</u> electron microscope <b>increased acceleration</b> of the electrons by a much greater potential difference (1000-3000 kilovolts) leads to <b>increase</b> their ability to <b>penetrate</b> the tissue thus thick sections up to 3 un can be examined, also it provides <b>better resolution</b> (0.2 nm).</li> </ul>	<ul style="list-style-type: none"> <li>-In SEM the specimen is scanned with a <b>focused beam of electrons</b> which produce "secondary" electrons as the beam hits the specimen.</li> <li>-These are detected and converted into an image <b>on a television screen</b>.</li> <li>-The resolution power of SEM is 10 nm.</li> </ul> 

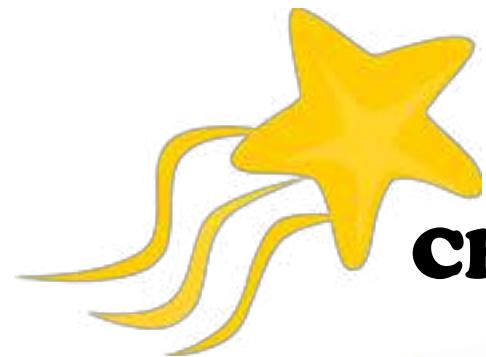




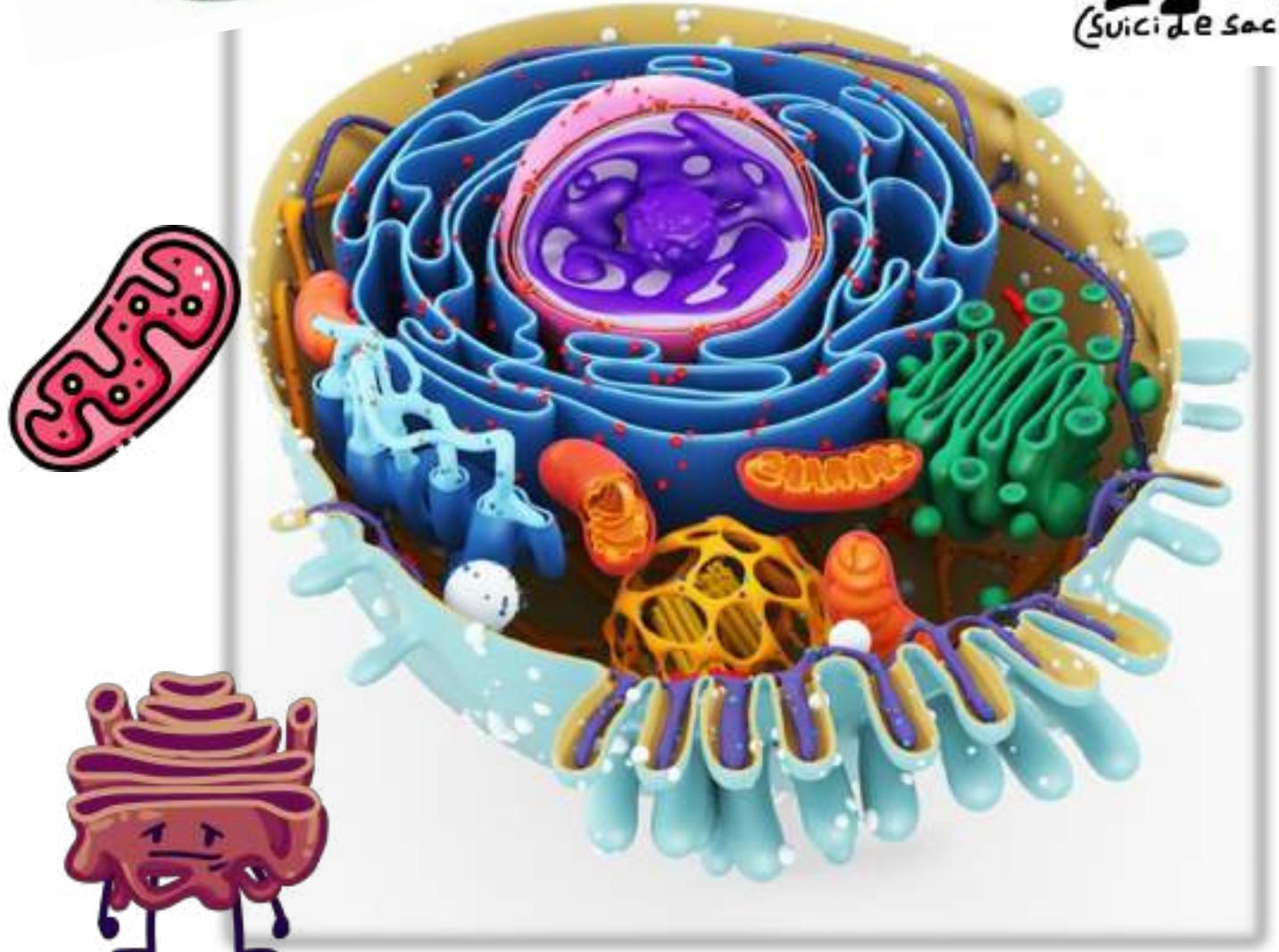
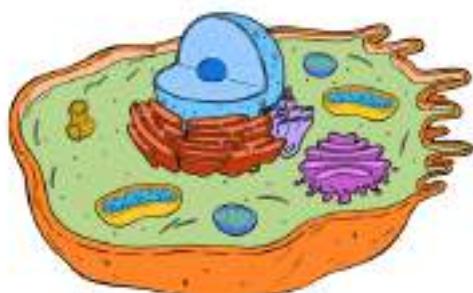
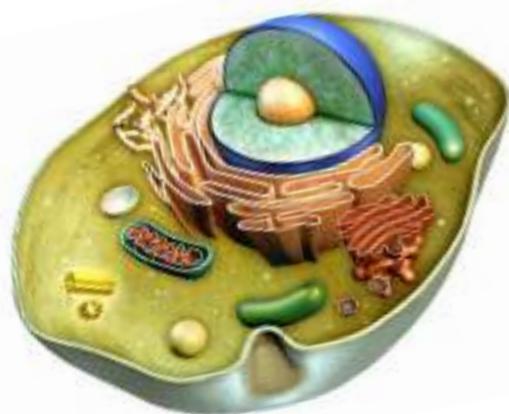
## Comparison between LM and EM

	Comparison	LM	EM
Machine:	resolution	0.2 $\mu\text{m}$ .	0.2mm.
	magnification	1000-1500 times.	Up to 500,000 times.
	Beam used	Light beam, so stained specimens can be seen colored.	Electron beam, so specimens never seen colored.
	Voltage used	Low(220 v) or no current when using mirror.	High(50-5000 kilovolts).
	tube	Contains air.	Vacuum.
	lenses	Glasses.	Electromagnetic coils.
	viewing	By eye.	Indirectly through fluorescent screen.
	Cooling system	Not needed.	Needed.
Technique:	fixation	In 10% formal saline.	In glutaraldehyde then osmium tetroxide.
	Clearing by	Xylol.	Propylene oxide.
	Embedding in	Paraffin.	Epoxy resin as araldite and epon.
	Cutting by	Metal knife by rotatory microtome.	Glass or diamond knife by ultra-microtome.
	thickness	Up to 4-10 $\mu\text{m}$ .	Up to 1/40 $\mu\text{m}$ .
	Staining by	H&E or other stains.	Uranyl acetate & lead citrate
	Mounting on	Glass slide.	Copper grids.





## Chapter 2 : Cytology



## ch 2 : CYTOLOGY

### Cell components:

Cells are the structural and functional units of all living organisms.

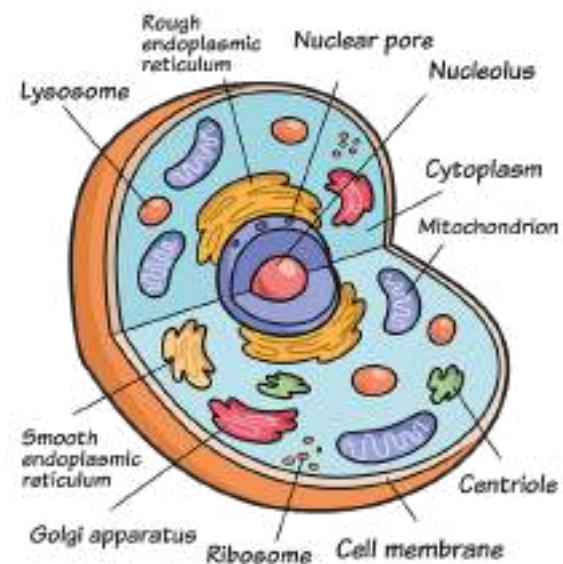
The cell is composed of protoplasm and is surrounded by cell membrane protoplasm

(the living substance of the cell) is composed of:

- 1- Cytoplasm.
- 2- Nucleus.



**CYTOPLASM**

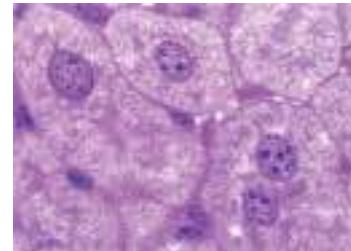


It is a specific kind of protoplasm consisting of matrix with suspended cytoplasmic contents; organoids and inclusions.

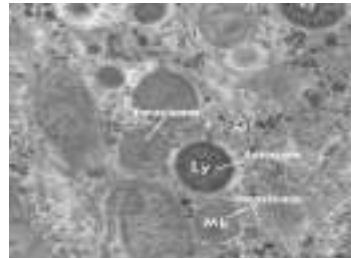
### Matrix (Cytosol, Cell SAP )

It is **colorless** watery fluid or semi fluid substance in between organelles and inclusions.

**LM:** it appears as homogenous or finely granular ground substance, commonly acidophilic in reaction, but may be basophilic or neutrophilic.



**EM:** appears as **amorphous** substance with a variety of electron densities.



**Function:** Provides a **suitable medium** for reactions occurring in the cytoplasm.

### Cytoplasmic Organelles:

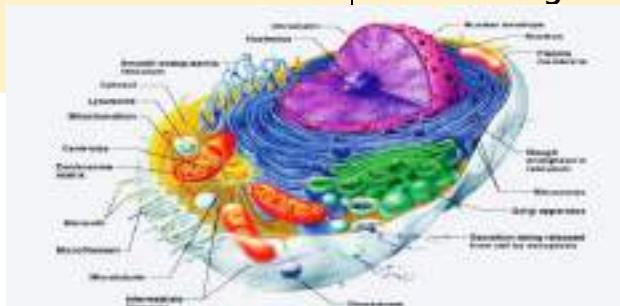
They are **metabolically active** structures performing distinctive functions. Organelles may be membranous or non-membranous.

#### Membranous organelles:

- 1- Cell membrane.
- 2- Endoplasmic reticulum
- 3- Golgi apparatus.
- 4- Lysosomes.
- 5- Peroxisomes.
- 6- Mitochondria.
- 7- Annulate lamellae

#### Non-membranous organelles:

- 1- Ribosomes.
- 2-proteosome
- 3- Microtubules.
- 4- Centrosomes
- 5-Cilia & flagella.
- 6-cell filaments.



# Membranous Organelles

## 1-Cell Membrane (Plasmalemma):

**Def:** It is the **envelope** of the cell that encloses its cytoplasmic compartments and preserves its shape.

**LM:** appears as a very thin limiting border line.

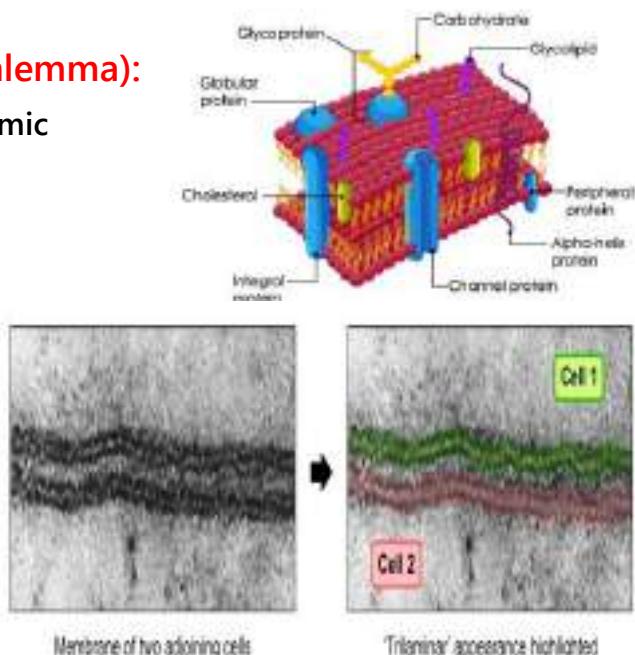
**EM:**

- appears as a 3-layered membrane (**tri-lamellar or unit-membrane**).
- usually about 7.5-10 nm. in thickness.
- two electron dense lines (2.5 nm each) separated by an electron lucent intermediate zone (2.5 - 3 nm).

**NB:** Cell membrane appears as a trilaminar structure (2 thin, dense lines with intervening light area) after fixation in **osmium tetroxide**

(the light layer is mostly non-polar lipid, the dark layers mostly the charged ends of the lipid molecules with attached protein) **due to the deposition of reduced osmium on the hydrophilic groups present on each side of the lipid bilayer.**

- Each layer is about 2.5 nm.
- The inner (cytoplasmic) dense line is its inner leaflet,
- The outer dense line is its outer leaflet.



## Components of Plasma Membrane:

### a) Lipids:

**-Phospholipids:** Phospholipids are the **primary membrane's material**

**-Cholesterol:** it folded between the hydrophobic tails of phospholipids

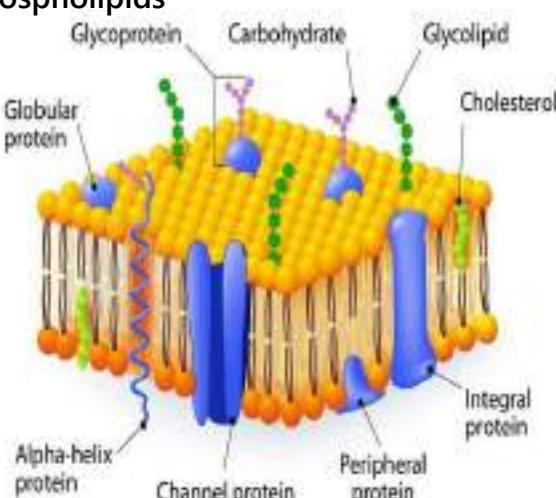
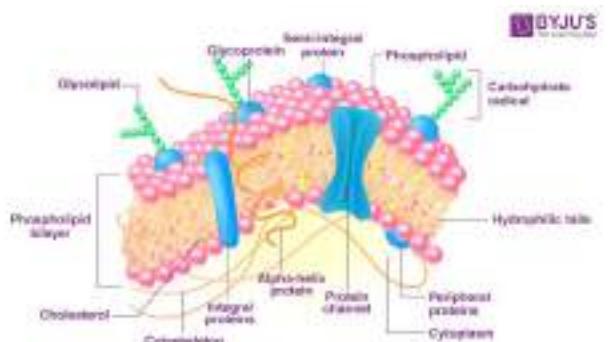
### b) Proteins:

**-Peripheral proteins:** Peripheral proteins are found on the inner or outer bilayer of phospholipids, but not incorporated into the hydrophobic core

**-Integral proteins:** Integral proteins have been discovered to be present within the bilayer of phospholipids.

### c) Carbohydrates:

found to be linked to the proteins (glycoproteins) or lipids on the extracellular surface (glycolipids)





## Functions :

### a) Selective Permeability:

- Membranes can be selectively permeable (or semi-permeable) this means they allow only specific molecules are able to traverse them.
- The oxygen, water carbon dioxide, and water can freely pass (passive diffusion).
- Ions (e.g. sodium or potassium) and polar molecules are unable to traverse the membrane.

### b) Physical Barrier:

- The plasma membrane covers every cell and physically divides the cytoplasm (which is the cell's material, the body of the cell) and the fluid that is outside the cell.

### c) Structural support for the cell.

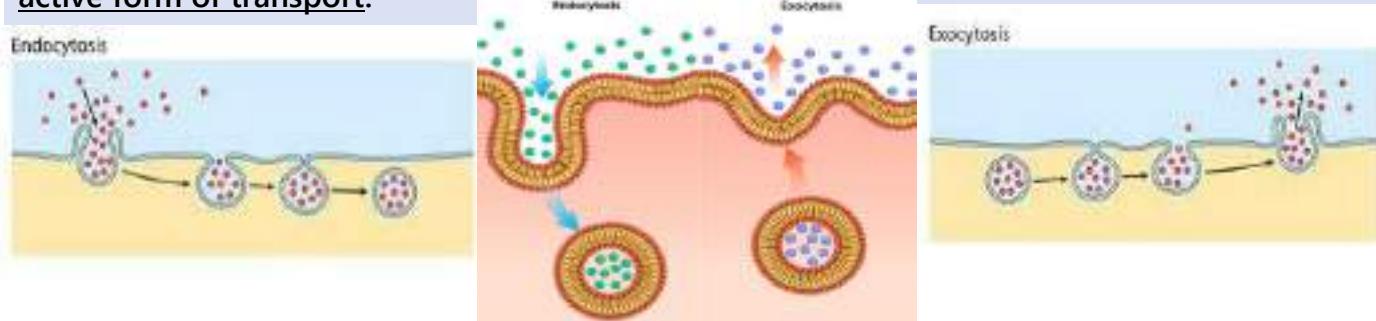
- It is the anchor for the cytoskeleton which is a system of protein filaments within the cell that holds all the components of the cell

### d) Cell Signaling

- The cell membrane serves to aid in communication and signals between cells.
- It accomplishes this through the use of different proteins and carbohydrates within the membrane.
- The membrane is also equipped with receptors that allow it to perform specific functions when substances like hormones or other hormones are bound to the receptors.

### e) Cellular transport

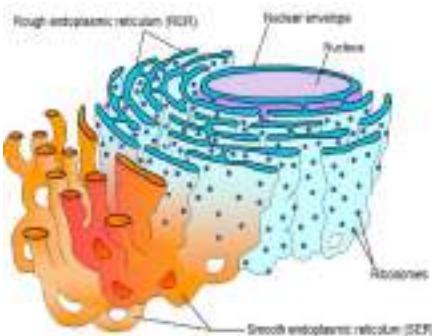
Endocytosis	Exocytosis
<p>It's a process by the cells absorb molecules by taking them and engulfing them. Either solid particles ("cell eating" or the process of phagocytosis or small molecules and ions ("cell drinking" or pinocytosis) and it is a process that requires energy, and thus is an <u>active form of transport</u>.</p>	<p>It's a process that occurs to clear the undigested residues of the substances brought in through endocytosis, and to release (excrete) substances such as hormones or enzymes</p>



## 2-Endoplasmic reticulum :

**Def:** It is the **largest membranous system** of the cell, present all over the cytoplasm extending between nuclear envelop and cell membrane.

**It exists in 2 forms:**



	Rough endoplasmic reticulum (rER)	Smooth endoplasmic reticulum (sER)
Origin	arises from nuclear membrane ( <b>internal</b> )	arises from rER by loss of its ribosomes ( <b>near cell membrane, peripheral</b> )
Well developed in	cells which synthesize proteins for internal use as fibroblasts and for export as glandular secretory cells, beta cells of pancreas	cells of the adrenal cortex and the interstitial cells of the testis, liver cells
LM	appears as a basophilia of the cytoplasm.	appears as a acidophilia of the cytoplasm
EM	present in the form of tubules, vesicles or cisternae. <u>Ribosomes</u> are attached to its cytoplasmic surface	present in the form of tortuous tubules, concentric or spiral arrays of highly fenestrated cisternae <u>with absence of ribosomes</u> from its cytoplasmic surface
		
Function	Protein and enzyme synthesis on the ribosomes - <b>No enzymes for detoxification</b>	1)Lipid synthesis e.g. steroid hormones in adrenal cortex 2) <b>liver detoxification</b> of metabolic waste products, drugs, and alcohol (enzymes present) 3) <b>muscle storage of Ca ions</b> 4) <b>Production</b> of HCl in gastric parietal cells. 5) <b>Glycogen synthesis</b>

## 3-Golgi complex (Golgi apparatus):

**Def:** It is one of the membranous organoids which is present in nearly all cells.

It is variable in size and shape.

**Site:** Its position **depends on cell activity** it is present at one side of the nucleus (basal or apical) as in glandular cells or surrounding the nucleus as in nerve cells.

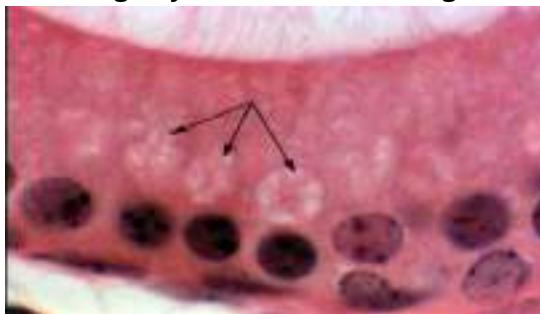


**LM:** In living cells: identified by phase contrast microscope or after vital staining.

In fixed cells: After **silver staining** or osmic acid fixation it appears as fibrillar or granular network (positive Golgi image).

In H&E stained sections:

it appears as lightly stained areas (negative Golgi image) as in plasma cells.



Negative Golgi image(H&E stain)

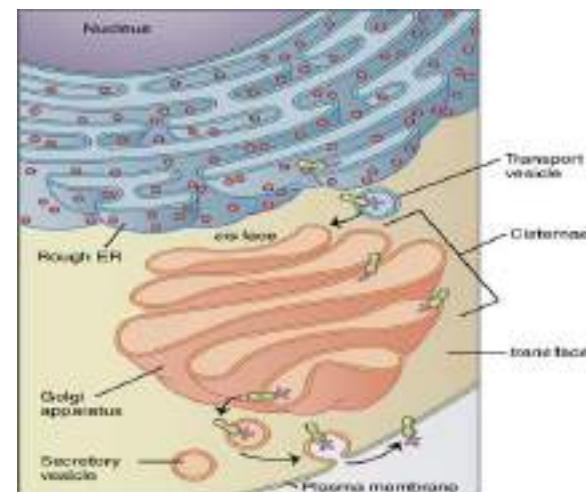


positive Golgi image (Silver stain)

**EM:** It appears to be formed of three components:

### 1) Flattened vesicles or saccules:

- These are 4-10 parallel elongated smooth surfaced double-walled membranous sacs or cisternae forming stacks.
- The cisternae have a convex face towards the base (immature or Cis face) and a concave face towards the cell membrane (mature or Trans face).
- These sacs or cisternae are continuous in their central regions while peripherally they often show dilatations and fenestrae or pores and may be connected with the ER.



### 2) Microvesicles or transfer vesicles:

- These are smooth-surfaced small spherical vesicles.
- Arising by budding from the RER.
- Migrating through the cytoplasm, fuse with the immature face of the Golgi where they discharge their contents thus causing expansion of the saccules.
- Some of the vesicles may be in the form of coated vesicles.

### 3) Macrovesicles or secretory vesicles:

- These are smooth-surfaced large spherical vesicles.
- Arising by budding from the periphery of the saccules of the mature face at one pole
- They contain formed substances.
- They either migrate to fuse with the cell membrane and discharge their contents through it to the outside as secretory granule or remain in the cytoplasm as lysosomes.

## Fate of molecules enter Golgi body take one of four paths:

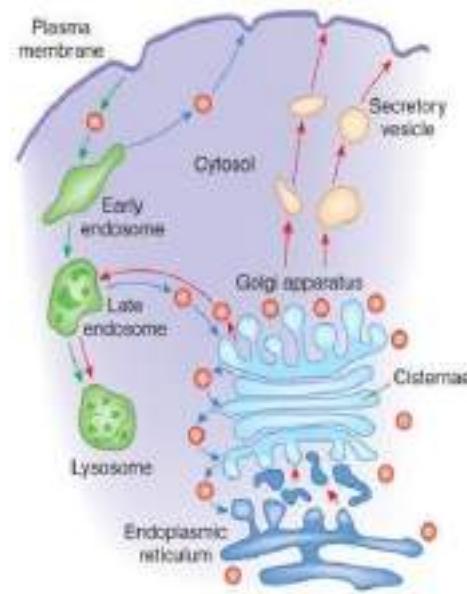


- The proteins that enter the Golgi by mistake are sent back into the cytosol

- Proteins destined for the cell membrane are processed continuously.
- Once the vesicle is made, it moves to the cell membrane and fuses with it (often protein channels).

- proteins are secreted from the cell to act on other parts of the body.

- The final destination for proteins coming through the Golgi is the lysosome. Vesicles sent to this acidic organelle contain enzymes that will hydrolyze the lysosome's content



### Functions:

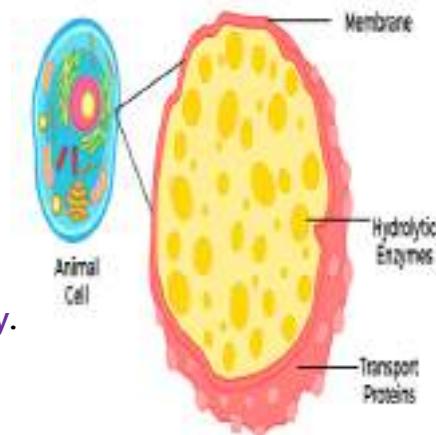
- Processing, concentration and packaging of secretory products e.g.
- Converting the inactive proinsulin, by enzymatic cleavage, into active insulin.
- Addition of carbohydrate fractions to proteins coming from RER to form glycoproteins.
- Formation of complex carbohydrates, glycoproteins , glycolipids.
- Modification** of the secretory products such as glycosylation and sulfation of proteins to form glycoproteins and sulfated glycoproteins (mucus).

### 4- Lysosomes:

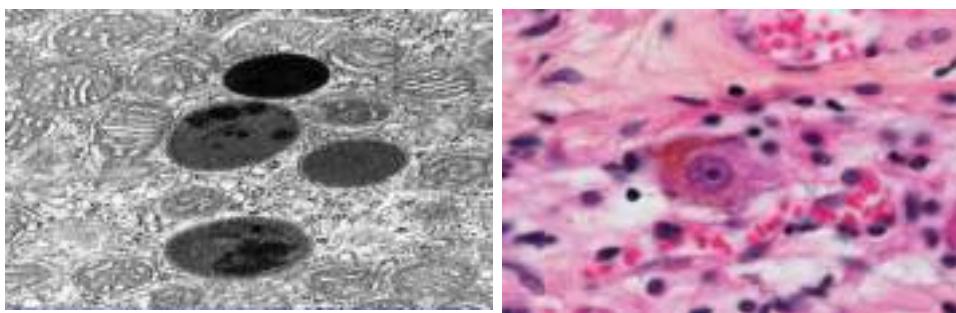
**Def:** Lysosomes are membranous vesicles containing hydrolytic enzymes which are active at an acid pH (5.0) such as proteases, lipases, nucleases, glycosidases and sulphatases among others which are at least 40 types of acid hydrolases. They are variable in number, size and shape.

**Site:** They are present in all cells specially those having phagocytic activity.

**LM:** Identified by special histochemical methods for their enzymes.



**EM:** They appear as homogenous membrane bound vesicles (trilaminar unit membrane).



- **The substrates that lysosomes act upon may be:**

- Heterophagosomes:** containing exogenous substrates entering into the cell by phagocytosis or pinocytosis and enclosed within a membrane.
- Autophagosomes:** containing endogenous substrates derived from cytoplasmic organelles (excess old organelles such as mitochondria or endoplasmic reticulum).

**Phagosomes:** They are membrane limited vesicles containing materials for lysosomal digestion

### Types:

- 1) **Prelysosomes :** They contain only substrates

- 2) **Primary lysosomes:**

Are freshly formed **lysosomes contain hydrolytic enzymes only.**

They are small, spherical and their contents are homogenous or finely granular.

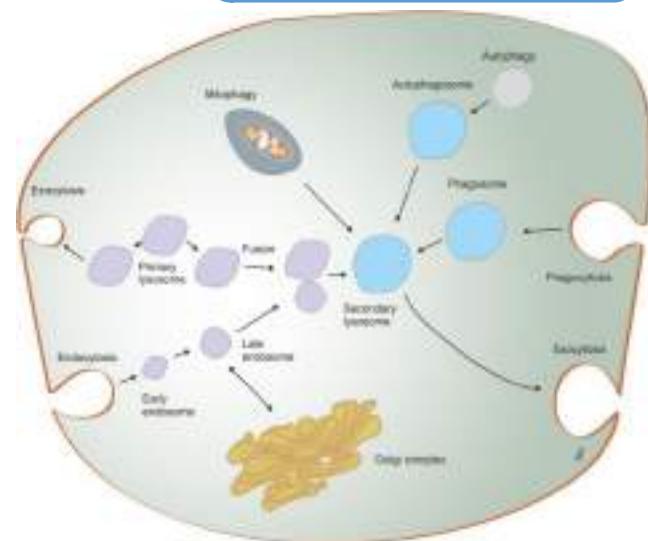
- 3) **Secondary lysosomes:**

Are formed by fusion of the primary lysosomes with the substrates and they may be:

a- **Heterolysosomes:** formed by fusion of primary lysosomes with heterophagosomes.

b-**Autolysosomes:** formed by fusion of primary lysosomes with autophagosomes.

c- **Multivesicular bodies:** formed by the fusion of primary lysosomes **with pinocytotic vesicles.**



### Functions:

- Defensive function against bacteria, viruses etc.
- Remodeling of tissues e.g. cartilage and bone.
- Intracellular digestion:** Lysosomes will fuse with the food vacuoles formed by phagocytosis, helping to breakdown the engulfed particle into their basic components.
- Normal replacement** and turnover of the cellular organelles : mitochondria.

### Post lysosomes (residual bodies):

The hydrolytic enzymes digest most of the contents of the phagosome especially the protein and carbohydrate components.

Lipids are **resistant** to complete digestion and they remain within the lysosome forming residual body.

They are of large size contain electron-dense pigments, granules and lipid like inclusions.

They have no enzymatic activity and are common to both hetero and autophagy.

**Fate:** either: a) excreted by exocytosis. b) Accumulate in cells as (lipofuscin pigment → age pigment)

### 5-Peroxisomes (Microbody)

**Def:** These are spherical or ovoid (0.2 to 1.0  $\mu\text{m}$  in diameter) membrane-limited organelles similar to lysosomes, but containing **oxidative enzymes** as oxidases and catalases.

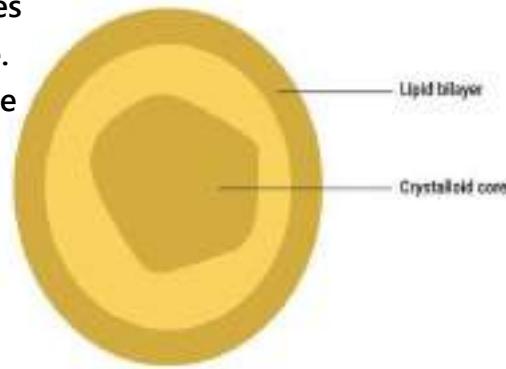
**Site:** present in almost all animal cells especially **hepatic cells** and those of the **proximal convoluted tubules of the kidney**.

**LM:** They appear after special cytochemical methods for their enzymes as e.g. **DAB** (3', 3-diaminobenzidine) reaction for the catalase.

- They appear as **spherical microbodies** bound by a single membrane (unit membrane) and with a finely granular matrix.

**EM:** They appear as spherical microbodies bound by a single membrane (unit membrane) and with a finely granular matrix.

Peroxisome



#### Functions:

- a) Degradation of purines by oxidases yielding **hydrogen peroxide** ( $\text{H}_2\text{O}_2$ ) then destroying it by the catalase thus protecting the cell against it.
  - b) **Breaking Down:** Peroxisomes contain at least three oxidase (D-amino acid oxidase, urate oxidase and catalase).
- The **D-amino acid oxidase**, urate oxidases are responsible for the production of hydrogen peroxide ( $\text{H}_2\text{O}_2$ ).
  - The **catalase** then utilizes the  $\text{H}_2\text{O}_2$  in oxidation (and therefore, detoxification) of various toxic substances such as phenol, alcohol and fatty acids.

- Peroxisomes can break:

Hydrogen peroxide(H <sub>2</sub> O <sub>2</sub> )	Chemicals and drugs:	Long-chain fatty acids (beta-oxidation of fatty acids):	Purines to Uric acid
This is the main chemical produced by oxidation in peroxisomes. Is very cytotoxic! Luckily, the enzyme catalase helps break down hydrogen peroxide into water and oxygen, thus making it harmless and further enhancing the oxygen rich internal environment.	Peroxisomes detoxifies chemicals primarily in liver cells	forming H <sub>2</sub> O <sub>2</sub> +Acetyl CoA (This is the major function of peroxisomes)	The enzyme <b>urate oxidase</b> helps breakdown uric acid and amino acid in mammals.



### Compare between Lysosomes & Peroxisomes?

Lysosomes	Peroxisomes
<ul style="list-style-type: none"> <li>- Membrane bound sacs performing a digestive function.</li> <li>- Contains enzymes to digest food, wastes, invading bacteria and breaks down old organelles.</li> <li>- Present in animal cells only.</li> </ul>	<ul style="list-style-type: none"> <li>- Membrane bound sacs performing a digestive function.</li> <li>- Enzymes in peroxisomes are oxidases that catalyze redox reaction.</li> <li>- Liver contains many peroxisomes to break down alcohol.</li> </ul>

## 6- Mitochondria



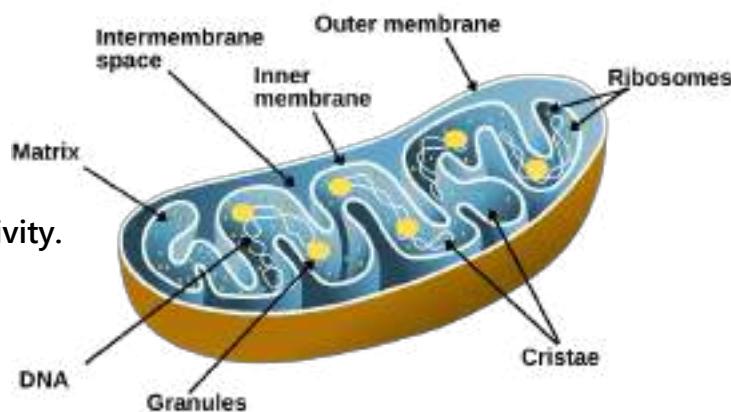
**Site:** They are distributed all over the cytoplasm in nearly all cells.

They tend to **accumulate in parts of intense metabolic activity** as the apical ends of ciliated cells, middle piece of spermatozoa and base of ion transferring cells.

**LM:**

**In living cells:** As cultured cells under the **phase contrast microscope** and **dark field microscope**, or after **supravital staining** as Janus green B stain, appear as spheres, rods, ovoids or thread like bodies.  
It can move, change shape and size, divide and fuse.

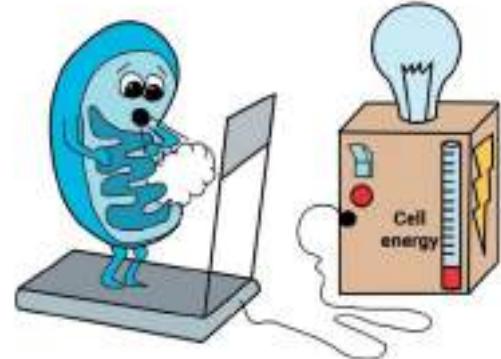
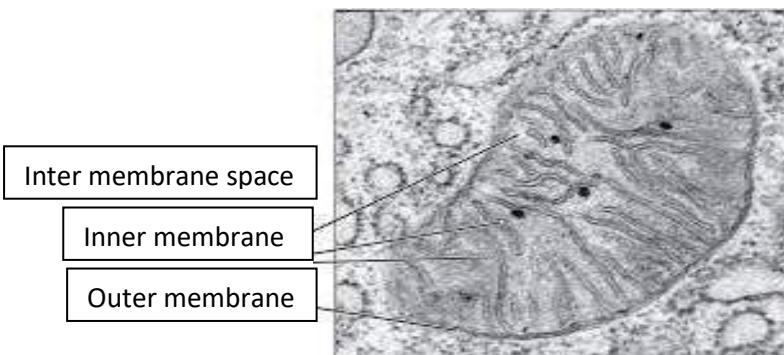
**In fixed cells:** After **iron haematoxylin** stain, they appear as granules, rods or filaments of variable number, length and size depending on cell activity.



**EM:** They appear as elongated or rounded structures, 0.5-1  $\mu\text{m}$  in width and up to 10  $\mu\text{m}$  in length. Each mitochondrion is formed of :

1)The outer membrane	2-The inner membrane	3) Intermembrane space
It is formed of the unit membrane and is smooth and permeable to water and ions	It is formed of a special type of the unit membrane known as the tripartite repeating unit membrane of 6 nm thickness	The narrow space (8nm) between the inner and outer membranes and contains a low-density fluid

4)Cristae	5)The matrix space (intercristal space)	6)Mitochondrial matrix
<p>The inner membrane is thrown into shelf-like projections known as cristae of which the following types can be observed:</p> <p>1-Septate (typical) :</p> <ul style="list-style-type: none"> <li>- Present in most cells.</li> <li>- Situated transversely, longitudinally or obliquely.</li> </ul> <p>2-Tubular (villous):</p> <ul style="list-style-type: none"> <li>- Present in the mitochondria of steroid secreting cell</li> </ul>	<p>It is enclosed by the inner membrane and filled with a fine granular material of variable electron density</p>	<ul style="list-style-type: none"> <li>- Contains a dense fluid which is viscous with occasional spherical or ovoid dense granules rich in cations as Ca and Mg.</li> <li>- The matrix rich in protein (at least 50%) and containing some DNA and the 3 types of RNA.</li> <li>- Enzymes for the citric acid (Krebs) cycle and fatty acid <math>\beta</math>-Oxidation are found to reside within the matrix space.</li> </ul>



**Functions:** Mitochondria are known as **the powerhouses of the cell**; being the site of Krebs cycle and oxidative phosphorylation thus providing the ATP which is an energy rich compound.



## 7-Annulate lamellae

**Def:** These are membrane- bounded cisternae, frequently near and resembling the nuclear membrane.

**Site:** They are found in many cells especially oocytes, spermatocytes and rapidly growing cells.

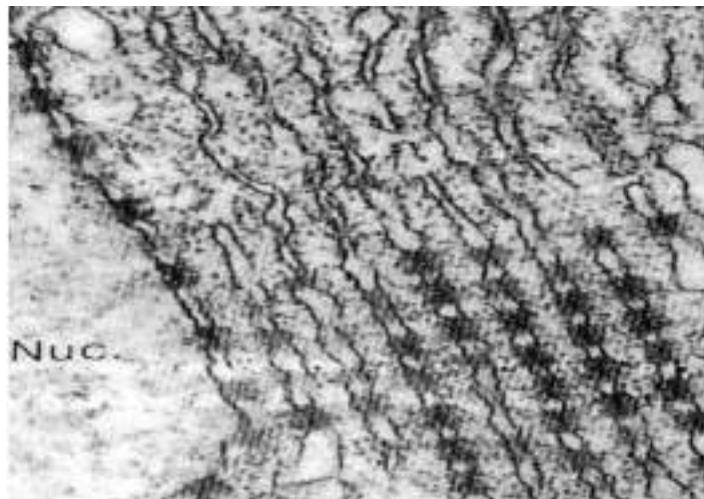
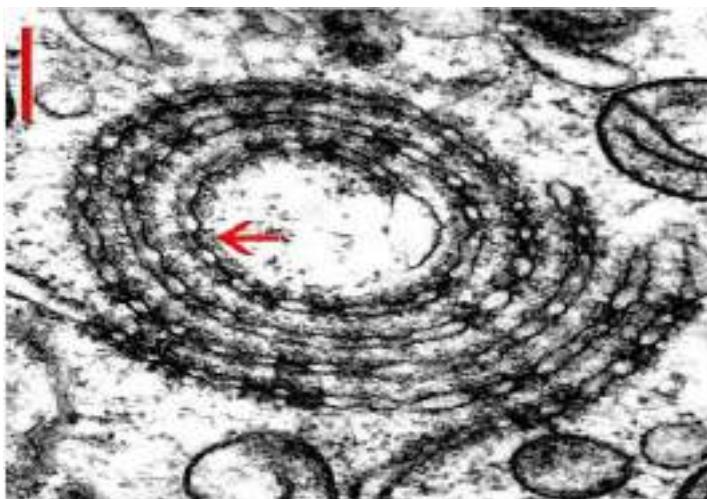
**L/M:** It appears as birefringent elements in the cytoplasm.

**EM:**

- They appear as single or stacks of pairs of parallel membranes enclosing a space traversed with circular pore complexes or annuli at regular intervals.
- The cisternae of annulate lamellae are continuous with rER.

**Function:**

May be a messenger function, carrying information from the nucleus to other cell regions.



## Non membranous organoids :

سمير  
3C +M+R

Ribosomes

Microtubules

Centrosomes

Cilia &  
Flagella

cell filaments

### Ribosomes

**Site:** They are found in all cells except the mature RBCs and sperms .

**Origin:** They are manufactured in the nucleolus and released into the cytosol through nuclear pores.

**Types:** They are either free or attached to the ER.

LM	EM
<ul style="list-style-type: none"> <li>They are very minute to be seen individually.</li> <li>They are detected as a basophilia of the cytoplasm which may be:           <ul style="list-style-type: none"> <li><b>Diffuse basophilia</b> as in actively growing and dividing embryonic cells.</li> <li><b>Localized basophilia</b> due to the attached ribosomes to the ER as in the basal basophilia of pancreatic acinar cells, Nissl granules in nerve cell.....etc.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>They appear as electron dense spherical or ellipsoidal granules, they may be either free in the cytoplasm (Fig. 2-19) or attached to the ER (Fig. 2-20).</li> <li>The free ribosomes may be:           <ul style="list-style-type: none"> <li><b>Single</b> representing the <b>inactive</b> form of ribosomes.</li> <li><b>Polysomes</b> are aggregations in clusters in the form of spiral chains linked by long molecules of mRNA. They represent the <b>active</b> form of the ribosomes e.g. in reticulocytes of the blood.</li> </ul> </li> </ul>

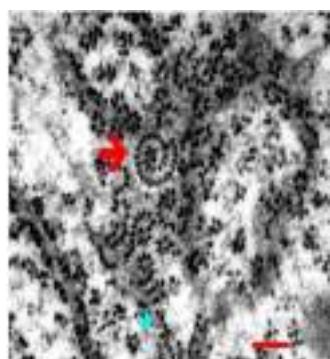


Fig. (2-19): polysomes.

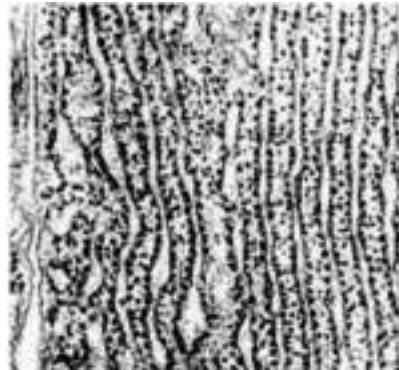


Fig. (2-20): Attached ribosomes.



-Each ribosome is formed of two subunits (large and small) that clamp together, leaving a central channel through which **mRNA is drawn**.

-Alongside the channel are three distinct sites formed by the 2 subunits.

a) **The P site (peptidyl):**

holds the tRNA carrying the growing polypeptide.

b) **The A site (aminoacyl):**

holds the tRNA carrying the next amino acid to be added to the chain.

c) **The E site (exit):**

discharged tRNA's leave the ribosome through this recently discovered site.

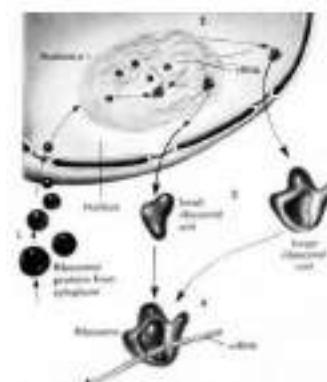
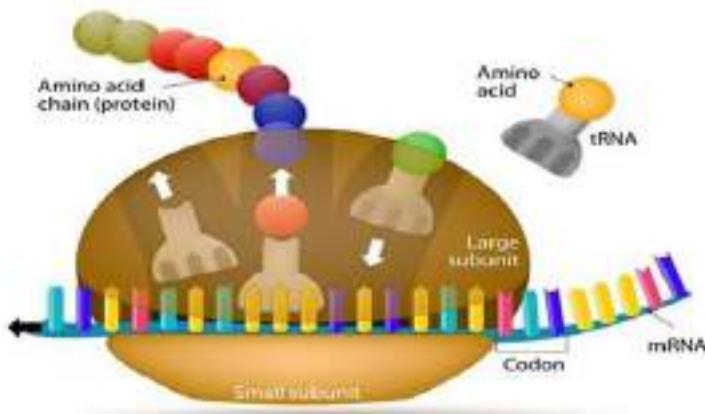


Fig. (2-21): 2 subunits of ribosome.

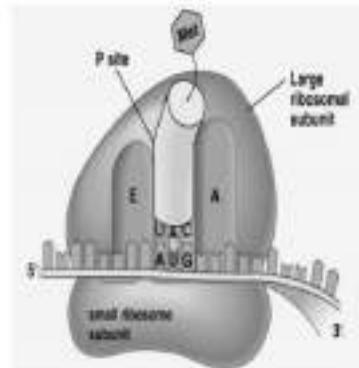
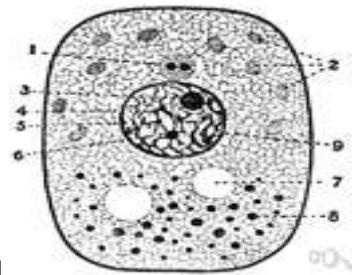


Fig. (2-22): 3 sites formed by the 2 subunits.

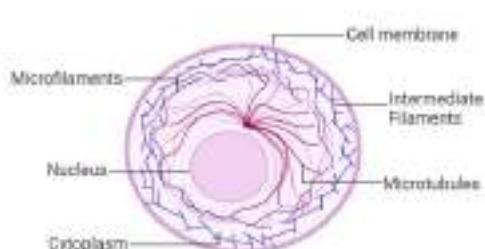
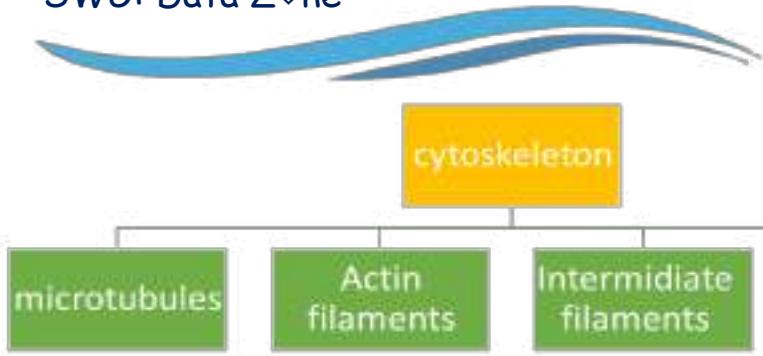
## Microsomes

**Def:** are ribosomes and fragments of the ER.

**Functions:** They are concerned with protein synthesis:



1. **The free ribosomes** are concerned with protein synthesis needed for growth and building up of the cell organoids and special proteins as haemoglobin.
2. **The attached ribosomes** are concerned with the synthesis of proteins for secretion as in pancreatic acinar cells, intracellular storage as in lysosomes and as a component of other membrane as integral proteins.



## Microtubules

**Site:** They are present in all cells especially where stiffness, shape or oriented motion are needed as in blood platelets, cilia, flagella, mitotic spindle,....

**LM:** They appear as filaments by immunofluorescent technique using antibody against tubulin.

**EM:**

LS	TS
<p>لسانی أقدر أطوله</p> <ul style="list-style-type: none"> <li>They appear (LS) as long, straight, slender, non-branched structures, of variable lengths and of uniform diameter; 24nm (Fig. 2-23).</li> </ul>	<p>TS</p> <ul style="list-style-type: none"> <li>Each one (TS) resembles a tubule with a less dense central core and a wall which is composed of 12-15 (13) globular subunits (<b>protofilaments</b>) arranged in a spiral fashion (Fig. 2-24).</li> <li>Formed of tubulin protein which occurs in two forms; <math>\alpha</math> and <math>\beta</math> tubulin.</li> </ul>

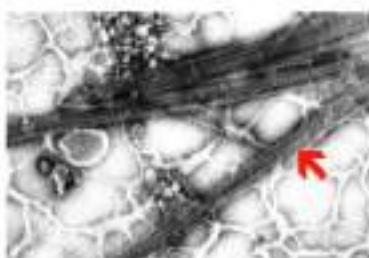


Fig. (2-23): LS of microtubules.

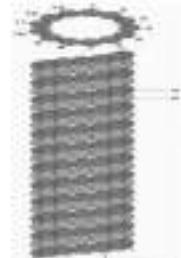
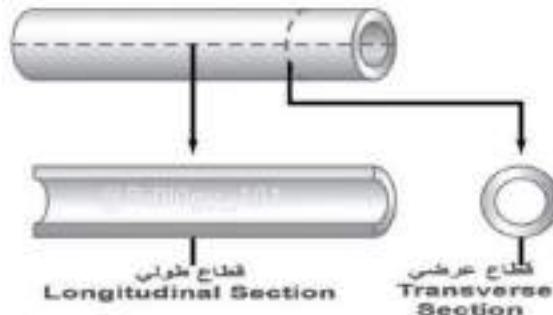
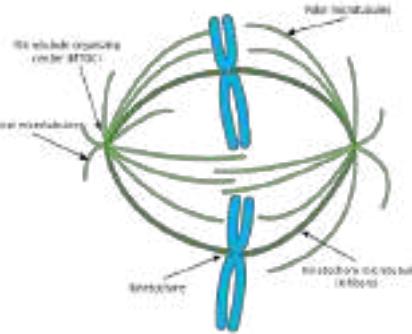


Fig. (2-24): TS of microtubule.



## Functions:

1. Cytoskeleton of cell: has a role in the development and maintenance of cell shape due to their rigidity.
2. Formation of **mitotic spindle**, necessary for chromosomal movement.
3. They form centrioles and the **axoneme of cilia and flagella**



## Centrosomes

### Site:

- They are present close to the nucleus and Golgi complex in all cells.
- Not found in mature nerve cells and RBCs as these cells do not divide.

### LM:

In living cells:	In fixed cells:
by phase-contrast microscope.	<ul style="list-style-type: none"> <li>• by using <b>iron haematoxylin stain</b>.</li> <li>• They appear as 2 cylindrical structures (<b>diplosomes</b>) perpendicular to each other forming a <b>T-shaped</b> configuration and embedded in a pale mass of cytoplasm known as <b>centrosome or centrosphere</b>.</li> </ul>

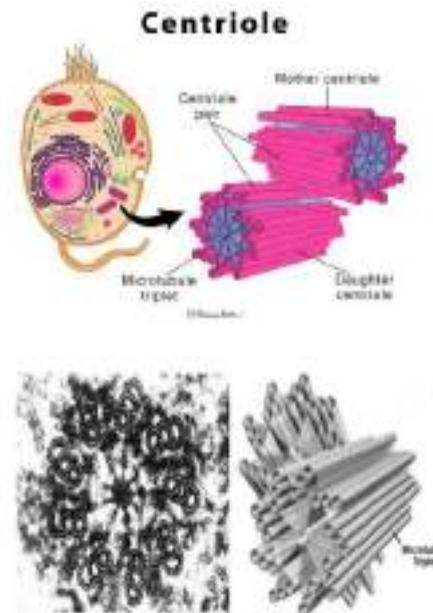


Fig. 2-25: Centrioles.

### EM:

They appear as parent and daughter centrioles.

Parent centriole: (fully formed)	Daughter centriole: (small partially formed)
<ul style="list-style-type: none"> <li>• Appears as a short cylinder.</li> <li>• The wall composed of 9 triplets of microtubules enclosing a central lumen (Fig. 2-25) containing a central vesicle and a spirally wound DNA strand .</li> <li>• The triplet microtubules formed of 3 microtubules a, b and c.</li> <li>• At the <b>proximal end</b> of the lumen, there is a <b>cart-wheel structure</b> formed of a central hub and 9 spokes radiating to the triplet base.</li> <li>• At the distal end of lumen, there is an <b>octagonal end structure</b>.</li> </ul>	<ul style="list-style-type: none"> <li>• Lies opposite the proximal end of the parent centriole and separated from it by a distance.</li> <li>• There is <b>neither</b> central lumen, cart-wheel nor octagonal end structures. ولا اي حاجة موجودة</li> </ul>  <p>The diagram illustrates a centriole's structure. It shows a 'Mother centriole' at the top and a 'Daughter centriole' below it. Labels include 'Distal ends', 'Proximal ends', 'Microtubule triplet', 'Intercalating fibers', 'Daughter centriole', 'Mother centriole', 'Distal appendages', 'Subdistal appendages', and 'Central lumen'.</p>



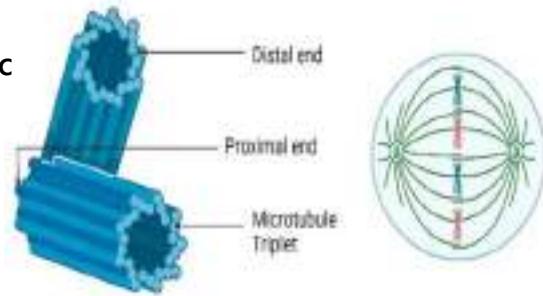
NB:

**Pericentriolar bodies:** are associated with the centrioles and from which microtubules arise. They represent the organizing center for microtubules.

### Functions:

1- Formation of mitotic spindle, they organize the cytoplasmic microtubular network in both normal and dividing cells.

2- They form motile structures as cilia and flagella.



## Cilia

- These are elongated motile structures forming outgrowths of the free cell surface.

### Site:

They are present in the ciliated epithelium in **respiratory and genital tracts.**

### LM:

- They appear as short, fine hair-like processes.
- Each cilium is connected with a deeply-stained basal body.

### EM:

Each cilium is formed of: (Fig. 2-26)

(Basal body (kinetosome) , Shaft(Axoneme), Rootlets, Basal foot)

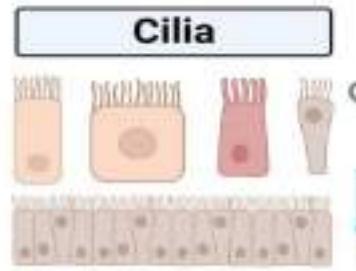


Figure: Cilia in ciliated epithelium

### Basal body (kinetosome):

This is a centriole which has migrated to near the cell surface and to which the cilium is anchored.

### Shaft (axoneme):

is formed of **5c**

- 2 single (singlets) microtubules:** in the **center**, each being **circular** in cross section, and both are joined together with a bridge and are surrounded with a solid **cylindrical sheath**.



From this sheath, extend 9 slender spokes to the subunit a of each doublet.

The spokes are important to convert the sliding of the tubules into bending.

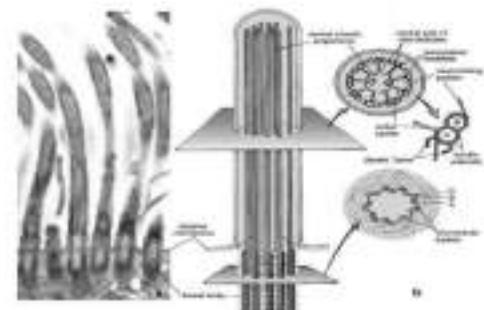
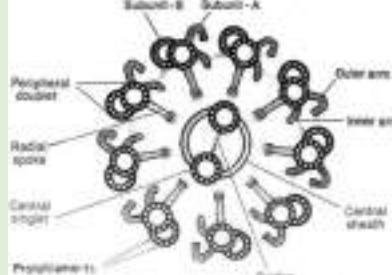


Fig. 2-26x: Structure of a cilium.





- b) **9 paired (doublets) microtubules:** circularly arranged around the periphery, each being formed of 2 subunits, a and b which are unequal in size.

Subunit a	Subunit b:
<ul style="list-style-type: none"><li>lies nearer the cilium axis</li><li>smaller in size</li><li>forms a <b>complete circle</b> in cross section.</li><li>Its wall is made of about 13 protofilaments.</li></ul> 	<ul style="list-style-type: none"><li>lies away from the axis,</li><li>larger in size</li><li>has a <b>C-shape</b> in cross section.</li><li>Its wall is made of about 11 protofilaments.</li></ul>

### c) Inter-doublet links:

- are present at periodic intervals, attaching the subunit a of one doublet to the subunit b of the adjacent doublet.
- They are made of an elastic substance known as **nexin**.

### 3- Rootlets: (Fig. 2-28)

They extend from the deep aspect of the basal body into the cytoplasm.

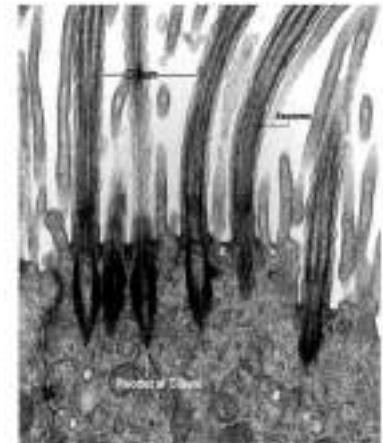


Fig. (2-28): Rootlet of a cilium.

### Functions:

- Spreading of a thin film of fluid or mucus across the cell surface through the rhythmic beating in **one direction**.
- Cilia are modified to receive stimuli as in **rods, cones** and **olfactory** epithelium.

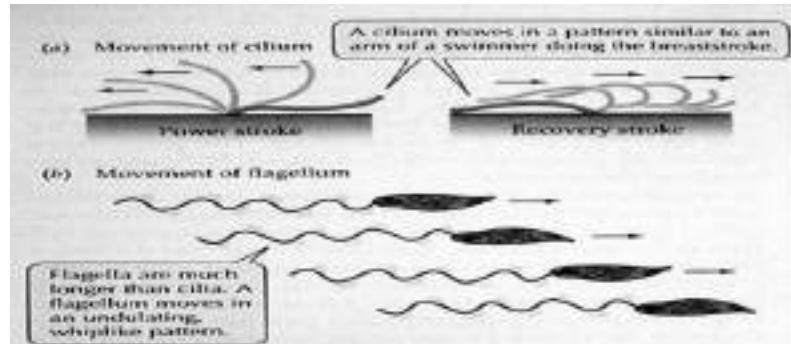
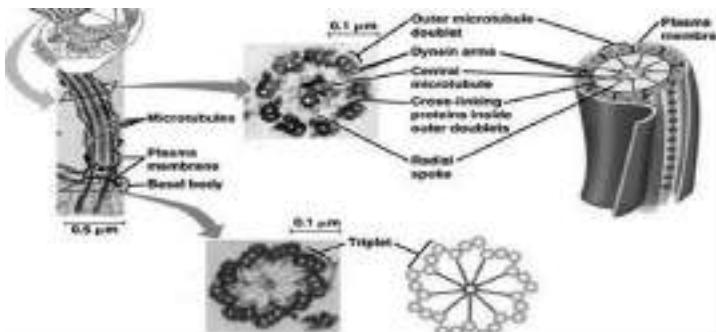


**NB:**

Absence of dynein arms in some inborn diseases leads to immotile cilia as in **Kartagener's syndrome** (presenting with sinusitis, bronchiectasis, dextrocardia or situs inversus totalis and male infertility).

# Flagella

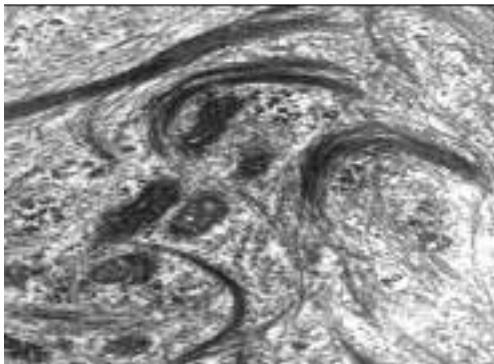
They resemble the cilia but are rather longer and usually single as in the tail of spermatozoa. They are used **for movement** through exhibition of an undulating motion resulting from propagation of successive waves of bending from the base to the tip.



# Cell Filaments

They are non-membranous organoids.

- Site**
  - They are widely spread in various cells as myofilaments in muscle cells, neurofilaments in nerve cells, tonofilaments in epithelial cells, ....
  
- L/M**
  - They appear as filaments by immunofluorescent technique by using fluoresceinlabelled anti-actin antibody.
  
- E/M**
  - They appear as thread-like structures forming either network within the cytoplasm, bundles or sheets under the cell membrane.



Actin filaments forming bundles



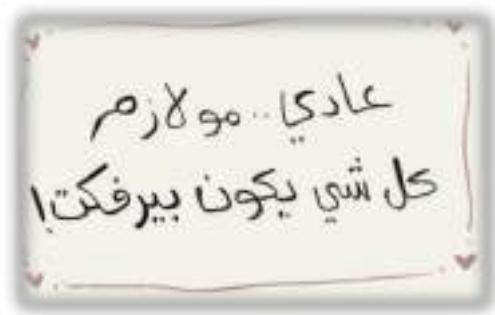
Actin filaments forming sheets

- **Thick filaments:** 10-15nm as the myosin filaments in the muscle fibers.
- **Thin filaments (microfilament):** 6-8nm as the actin filaments in the muscle fibers and other cells.
- **Intermediate filaments:** 8-10nm as in neurofilaments in nerve cells, glial filaments in glial cells of the nervous system,...etc.

Types: According to the diameter		
Thick filaments (myosin)	Thin actin filaments (microfilaments)	Intermediate filaments
10-15nm as the myosin filaments in the muscle fibers.	6-8nm as the actin filaments in the muscle fibers and other cells.	8-10nm as in neurofilaments in nerve cells, glial filaments in glial cells of the nervous system,...etc.

### Functions of cell filaments:

- 1- Formation of the cytoskeleton of the cell.
- 2- Contraction of muscle fibers and non muscular cells.
- 3- Movement of microvilli.
- 4- Retraction of the blood clot.
- 5- Separation of cells in cell division.
- 6- Mobility of the cell membrane in the free cells and macrophages for phago and pinocytosis.



**N.B.** Cytoskeleton is formed of:

- |                            |                        |
|----------------------------|------------------------|
| 1- Microtubules.           | 2- Actin filaments.    |
| 3- Intermediate filaments. | 4- Accessory proteins. |

## Cell Inclusions

They are temporary constituents of the cell.

They may be: Nutritive substances, Pigments & Crystalloids.

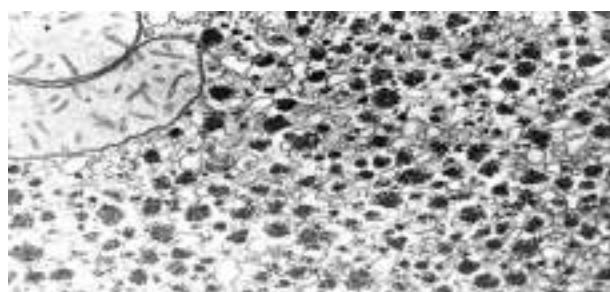
ابعد عن أي حد بيخرجك  
من المستقبل أو بيجعلك



A) Nutritive Substances			
	Proteins	Glycogen	Lipids
	These are present in all cells, either free as insulin or bound to other substances as lipoproteins.	is present in muscle and liver cells as granules.	are present in most cells.
L/M		They appear as red granules after staining by Best's carmine and purple after staining by periodic acid-Schiff (PAS).	After freezing or after special stains as osmic acid, Sudan III and Sudan black they appear as small round droplets or as large globules. <b>(أسامة جاب دهون من السودان)</b>
E/M		They appear in 2 forms: <ul style="list-style-type: none"> <li>• <b>Alpha granules:</b> which are clusters or rosettes of very electron dense beta granules and is present in liver.</li> <li>• <b>Beta granules:</b> are single irregularly spherical electron dense granules and is present in muscle fibers.</li> </ul>	They appear as non-membranous drop. The droplets may appear very dense throughout or with a dense core surrounded by a less dense rim.



LM for Glycogen



Alpha glycogen granules forming rosettes in liver



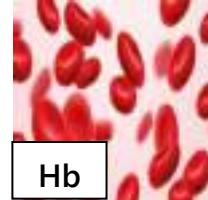
Lipid Droplets



## b- Pigments:

They are membrane-bounded substances which are present in only special types of cells.

They can be divided into:

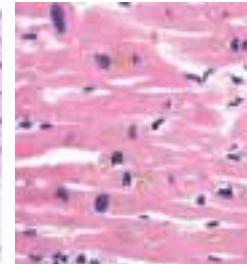
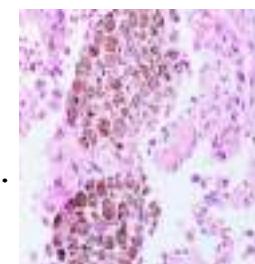


A) **Endogenous pigments** : are made up inside the body,

- **Melanin:** present in the epidermal cells of the skin and nerve cells of the substantia nigra of the midbrain and pigment cells of retina.

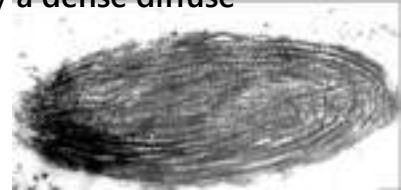
LM: The granules appear brownish-black.

EM: They appear as small lozenge-shaped granules of 2 types:

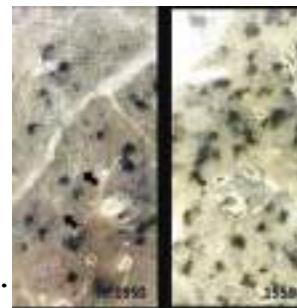


- **Light granules:** with a crystalline lattice structure of tyrosinase enzyme and dense granules with special pattern of spacing.
- **Dark granules:** as the light type but the lattice structure is masked by a dense diffuse substance around it.

**Melanosomes:** found in melanocytes and are bounded with a membrane



- **Haemoglobin (Hb):** is present in RBCs.
- **Hb derivatives:** as haemosiderin, bilirubin and biliverdin which are present in the phagocytic cells.
- **Lipofuscin:** is present in nerve cells, heart and steroid secreting cells of the endocrine glands in aged animals and human.



B) **Exogenous pigments** : are taken into the body from outside.

- **Dust and carbon particles:** are inhaled then phagocytosed by the dust cells of the lungs. & They appear black.
- **Tattoo particles:** are particles of inorganic pigment, introduced by needles into the skin then phagocytosed by the histiocytes.
- **Lipochromes:** as carotenes ingested with food of carotenecontaining substances as carrots, then stored in fat cells.
- **Minerals:** are due to intoxication with silver appears in the C.T. cells of the skin or lead which appears in the C.T. cells of gums.



## C- Crystalloids:

- a) **Charcot-Bottcher** crystalloids in Sertoli cells.
- b) Crystals of **Reinke** in interstitial cells of Leydig in the testis

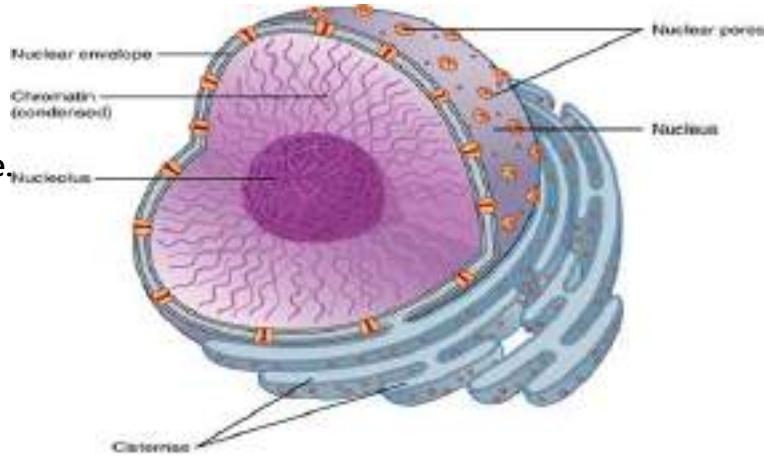


# Nucleus

- It is the largest single membrane-bound compartment in the cell that controls its functions.
- Essential for the life of the cell.

## Site:

Lies in the region which is metabolically, most active.  
usually central, but may be **eccentric** e.g. fat cells.



## Number:

It is usually single (mononuclear), but may be;

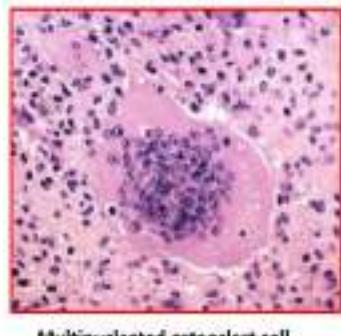
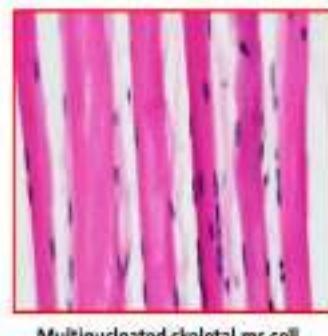
- binucleate e.g. hepatocytes (liver cells) and cells of autonomic ganglia,
- multinuclear e.g. osteoclasts, skeletal muscle fibers and syncytiotrophoblast,
- Anuclear e.g. erythrocytes ( RBCs),some lens fibers, keratinized cells of epidermis,nail and hair .

## Size:

Varies between 5-10  $\mu\text{m}$ .

## Shape:

Follow the shape of the cell . May be (rounded, flat, oval, kidney shaped, segmented, bilobulated,..)



## Movement:

It may rotate clock or anti-clock wise or even change its site.

Binucleated cell →



## Appearance:

It is basophilic in reaction and it appears more refractile than the cytoplasm.

It may be either:

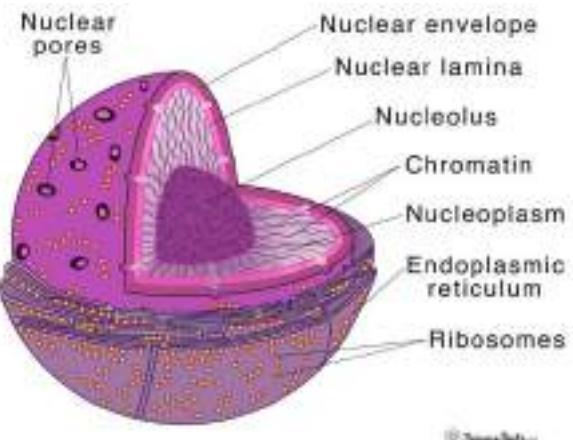
1- **Lightly stained (vesicular nucleus ):** The details of its components are well seen inside it  
e.g. plasma cell, liver and nerve cells. **Active cells**

2- **Deeply stained (condensed nucleus):** The details are not seen  
e.g. the nucleus of lymphocytes. **Inactive cells**



## Structure:

- 1- Nuclear envelope (nuclear membrane) .
- 2- Chromatin (DNA) (the genetic material) .
- 3- Nucleolus.
- 4- Nuclear skeleton .
- 5- Nuclear matrix= nuclear sap = nucleoplasm.



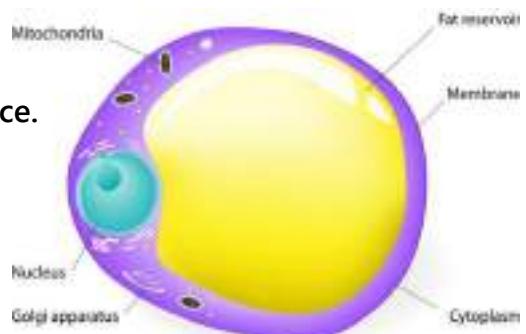
## Nuclear Envelope

### LM:

It appears as a single **basophilic line** surrounding the nucleus .  
This basophilia is due to the chromatin attached to the inner surface.

### EM:

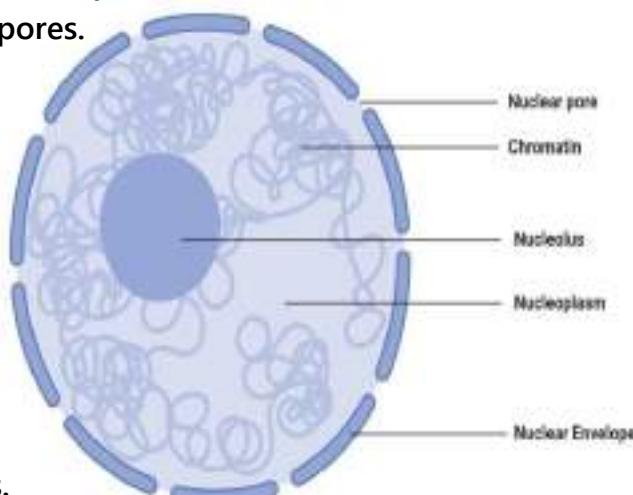
- It appears as a double-walled membrane
  - outer membrane facing the cytoplasm
  - inner membrane facing the nucleoplasm
- each is formed of a unit membrane with a space (peri-nuclear space ) in between perforated at regular intervals by nuclear pores and with pores.



**NB :** Polyribosomes and ribosomes adhere to the outer surface of the outer membrane and sometimes it is continuous with rough endoplasmic reticulum .

### Nuclear pores:

- They interrupt the nuclear membrane **at regular intervals**.
- Their number is **variable**.
- At each pore, the outer and inner membranes fuse together forming a diaphragm with a **low electrical conductivity** (Fig. 2-38).



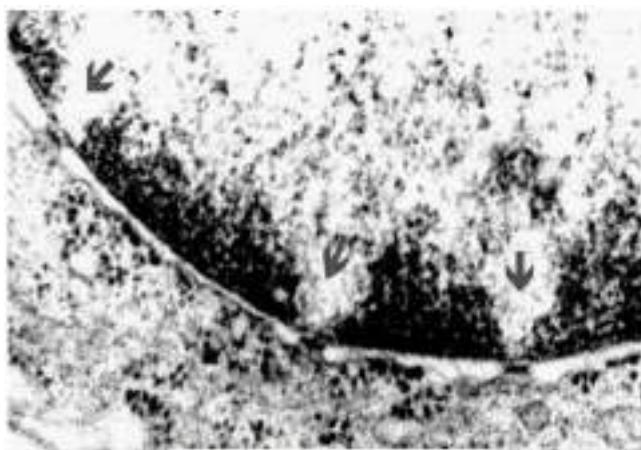
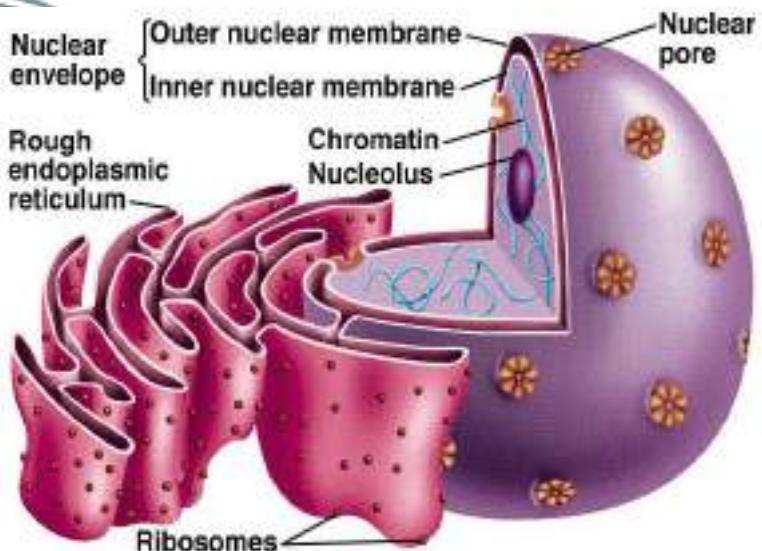


Fig. (2-38): Nuclear pores.



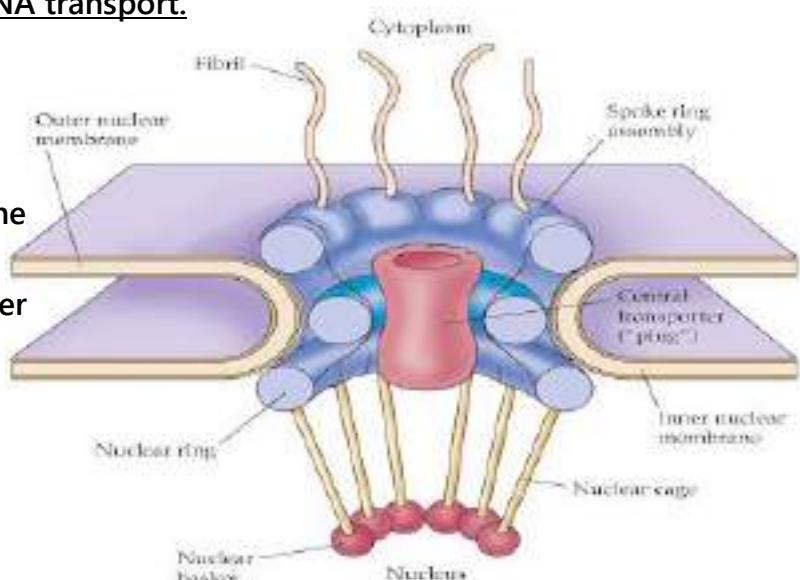
## Nuclear pore complex (NPC)

The NPC is composed of four protein elements:

- 1- **The scaffold** : surrounds the pore and supports the other elements. It maintains the pore and simple diffusion channels.
- 2- **The transporter (central hub)** is the central protein ring responsible for transporting proteins into and out of the nucleus via receptor-mediated transport.
- 3- **Thick filaments (cytoplasmic filaments)** : (about 3 nm in diameter) project from the scaffold ring into the cytoplasm and may serve as a staging area prior to protein transport.
- 4- **The basket (nuclear basket)** is projecting from the scaffold ring into the nucleoplasm, its function is RNA transport.

### Function:

- The NPC permits passive movement across the nuclear envelope via a 9 nm open channel.
- **Most proteins**, regardless of size, pass in either direction only by active transport
- Allow the passage of all types of RNA.



## Chromatin

It is composed mainly of coiled strands of DNA bound to basic proteins (histones).

**LM:**

It appears as basophilic granules which may be coarse or fine according to their size.

They represent the coiled parts of the chromosomes as the extended parts are very thin to be visible.

They give + ve Feulgen reaction.

**EM:**

It appears as a mass of fine fibrils.

The fibrils attach to the inner side of the nuclear membrane and to the annuli of the pores. (annular subunit)

**Types:**

1- **Heterochromatin (condensed or coiled or inactive):**

**LM:** appears as basophilic clumps.



Heterochromatin

**EM:** appears as aggregations of electron dense granules distributed within the nucleus as:

a- **Peripheral or marginal chromatin:** lies close to the inner nuclear membrane.

b- **Nucleolus-associated chromatin:** lies around the nucleolus, in the form of a crust.

c- **Chromatin islands or karyosomes:** lie in the nuclear sap in the form of clumps

or discrete bodies of irregular size and shape.

2- **Euchromatin (extended or uncoiled or active):**

**LM:** Invisible

**EM:** It appears as very thin uncoiled threads .

Their genes are active and direct protein synthesis.

3- **Perichromatin:** appears as dense granules.



Euchromatin

## Molecular biology:

- The basic structural unit of chromatin is **nucleosome** (4 histone proteins around which wrapped double-stranded DNA).
- Chromatin is a nucleoprotein formed of: nucleic acid (DNA), basic proteins (histones) and acidic protein.

### Note :

- During cell division, DNA contracts and folds to form distinct structures called chromosomes.
- The chromosomes are formed at the start of cell division.



## Nucleolus

- Present within the nucleus.
- it is a dense, membrane-less structure composed of RNA and proteins .

### LM:

- It appears as ( one or more , rounded , Variable in size , basophilic bodies. )
- It is deeply stained due to its content of ribonucleoprotein.
- It is Feulgen -ve.

### EM:

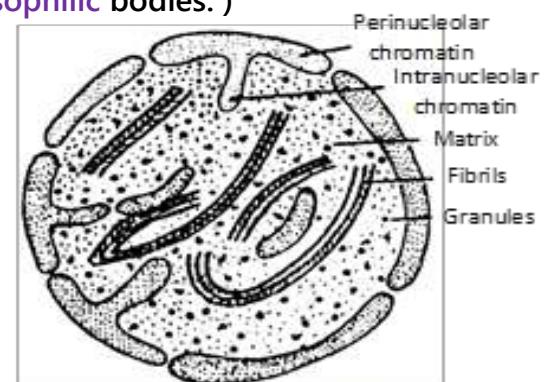
It appears to be formed of :

#### 1- Pars fibrosa (PF) :

- is composed of a fine filamentous material
- representing newly transcribed precursor rRNA

#### 2- Pars granulosa (PG):

- (surrounds the pars fibrosa)
- consists of 15-20 nm ribonucleoprotein granules
- representing maturing ribosomal subunit particles.



3- **Pars amorpha** : is a structureless proteinaceous material of variable amount and density.

4- **Pars chromosoma** : which lies in and around the nucleolar parts being attached to the chromatin masses. (NAC)

5- **Temporary components** : are proteins or lipids.





## 6- Nucleolar organizer regions (NO) :

- they are the secondary constrictions of acrocentric (satellite ) chromosomes 13, 14, 15, 21 and 22.
- They have the genes coding for rRNA .
- They stain with silver salts.
- Nucleolus is formed of: rRNA, proteins, lipids, lipoprotein and DNA/RNA hybrids.
- Function: It is the site of production of the rRNA . The nucleolus is organized from the "nucleolar organizing regions" on different chromosomes.
- A number of chromosomes get together and transcribe ribosomal RNA at this site.
- The nuclear organizing (NO) regions are seen as circular areas ( pale ) surrounded by a rim of electron dense filaments ( pars fibrosa )

## Nuclear Matrix

It is the component that fills the space between the chromatin and the nucleoli in the nucleus.

L/M: As a colorless medium.

E/M: As fine randomly distributed granular areas.

## Molecular biology:

-It is composed mainly of protein; some of which have enzymatic activity, metabolites, nucleic acids, sugars, enzymes and ions.

-When its nucleic acids and other soluble components are removed, a continuous fibrillar sponge like proteinaceous structure remains, forming the nucleoskeleton.

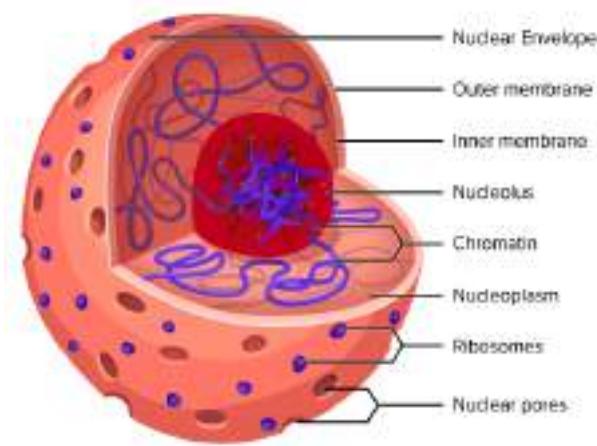
## Nuclear skeleton

A sponge like proteinaceous structural framework of nucleus visible after extraction of chromatin and karyoplasm

The lamina of the nuclear envelope is part of nucleoskeleton

## ❖ General functions of the nucleus :

1. Synthesis and storage of rRNA.
2. Reproduction of the cell (cell division).
3. It is the origin of the RER.
4. Formation of annulate lamellae.
5. Protection of the mRNA from the RN-ases in the nucleus.



## Cell death

**Apoptosis (physiologic), (programmed cell death):**

Pathway of cell death induced by a tightly regulated **suicide** program

- It is **physiological** process.
- Removal of damaged or unnecessary cells
- ✓ Fragmentation of DNA.
- ✓ Fragmentation of nucleus.
- ✓ Blebs form and apoptotic bodies are released
- ✓ Apoptotic bodies are phagocytized.
- ✓ No neutrophils

زنادل ضياء ألسنة  
الدراسية بنشاط  
وميلحق يخلع  
كل الذي وراءه ...  
دول مأخذ ووش غير...



نصن المنفع  
بس ..



**Necrosis (pathologic):**

- Morphologic expression of **pathological cell death** Loss of functional tissue, Impaired organ function, transient or permanent
- Progressive disintegration of cell structure
- Initiated by **overwhelming stress**
- Usually elicits an acute inflammatory cell response (neutrophils may be present)

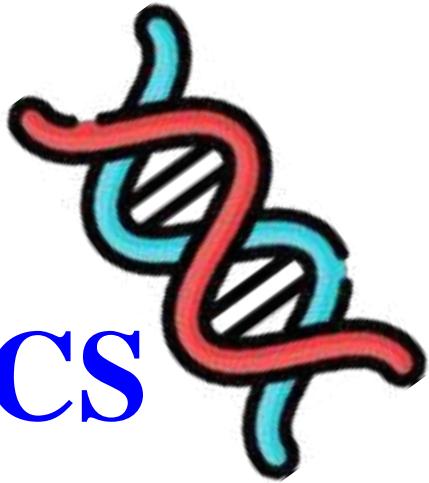
	Necrosis ( uncontrolled cell death )	Apoptosis ( programmed cell death )
Size	Cellular swelling	Cellular shrinkage
	Many cells affected	One cell affected
Uptake	Cell content ingested by macrophages	Cell content ingested by neighbouring cells
	Significant inflammation	No inflammatory response
Membrane	Loss of membrane integrity	Membrane blebbing but integrity maintained.
	Cell lysis occurs	Apoptotic bodies form
Organelles	Organelle swelling and lysosomal leakage	Mitochondria release pro-apoptotic proteins
	Random degradation of DNA	Chromatin condensation and Non-Random degradation of DNA





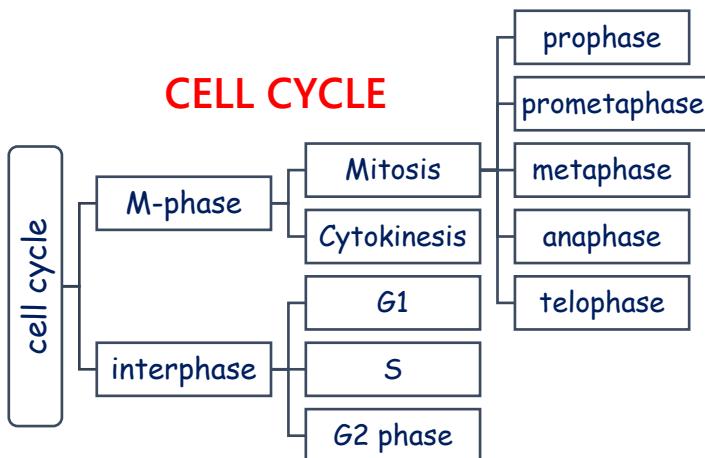
# Chapter 3 :

## CYTOGENETICS



## Ch3 : CYTOGENETICS

**Cytogenetics:** is the study of heredity at the cellular level through cytological techniques and chromosomal preparations.



**Objectives:** At the end of this chapter the student should be able to know:

- The stages of cell cycle and cell divisions.
- The structure, types and classification of chromosomes.
- Methods used to study chromosomes.
- The clinical importance of chromosomal study.

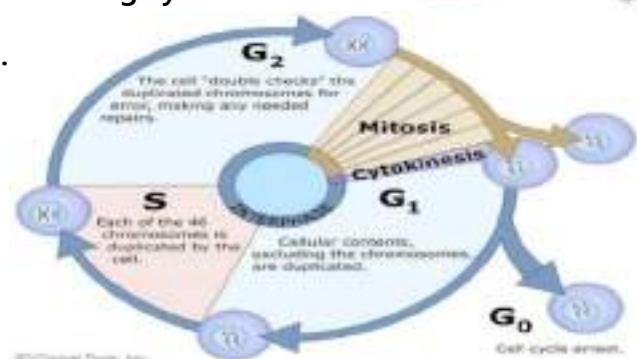


**Definition:** The term cycle is used to denote the repetition of a sequence of events during a given time period , with final event terminating at the same point from which the cycle has begun .

The repeating pattern of cell growth (an increase in size) followed by division (splitting of one cell into two) is called the cell cycle.

**Purposes of cell cycle:**

- **Process of expansion:** through which cells of most tissues of the body undergo a series of divisions in order to grow in size.
- **Process of renewal:** through which the lost cells as a result of wear and tear are restored.
- The length of the cell cycle in different cell types varies.  
In cell of the early embryo it may less than 24 hours.  
In adult, some cells have a very short cycles and others have long cycles.
- Stages of the cell cycle: is formed of two main stages.
  - 1) Interphase.
  - 2) Mitosis.



## Interphase

- It is a preparatory stage for the subsequent cell division.
  - The chromosomes are invisible.
  - Interphase chromosomes are called chromatin.
  - Cells perform its function, prepare itself for next cell division
- It is formed of:

### 1) Gap 1(G1) phase:

- It is post-mitotic period between the end of mitosis and the beginning of S phase.
- During this phase, the cells synthesize RNA, regulatory proteins essential to DNA replication, and enzymes necessary to carry out these synthetic activities.

Thus, the cell volume, reduced by dividing the cell in half during mitosis, is restored to normal.

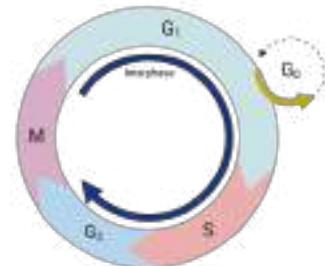
Additionally, the nucleoli are reestablished during the G1 phase.

During this time the centrioles begin to duplicate themselves, a process that is completed by the G2 phase.

- It is of varied duration. In rapidly dividing cells of the human embryo is few hours.  
The faster the cell turnover, the shorter the G1.

NB:

In mature brain, cells become arrested in a resting form of G1 known as G0 and do not normally divide again during a person's lifetime.



### 2) Synthesis (S) phase:

- This period follows the G1 phase.
- During the S phase, the synthetic phase of the cell cycle, the genome is duplicated. All of the requisite nucleoproteins, including the histones, are imported and incorporated into the DNA molecule, forming the chromatin material.

The cell now contains twice the normal complement of its DNA.

The amount of DNA present in autosomal and germ cells also varies.

Autosomal cells contain the diploid ( $2n$ ) amount of DNA before the synthetic (S) phase of the cell cycle when the diploid ( $2n$ ) amount of DNA is doubled ( $4n$ ) in preparation for cell division. In contrast, germ cells produced by meiosis possess the haploid ( $1n$ ) number of chromosomes and also the haploid ( $1n$ ) amount of DNA.

### 3) Gap 2(G2) phase:

- It is premitotic phase.
  - During the G2 phase, the RNA and proteins essential to cell division are synthesized, the energy for mitosis is stored, tubulin is synthesized for assembly into microtubules required for mitosis,
- DNA replication is analyzed for possible errors, and any of these errors is corrected.
- It lasts about 4 hours.

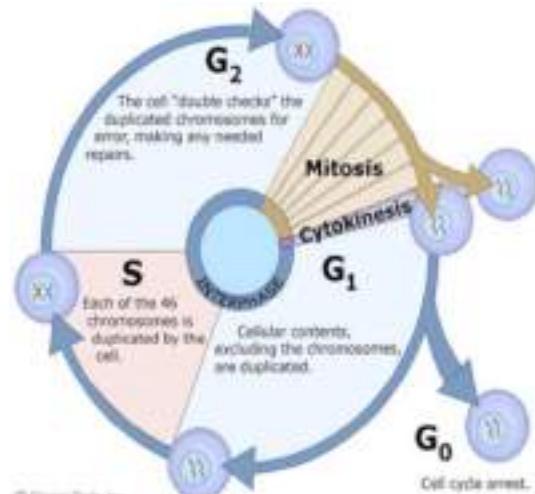
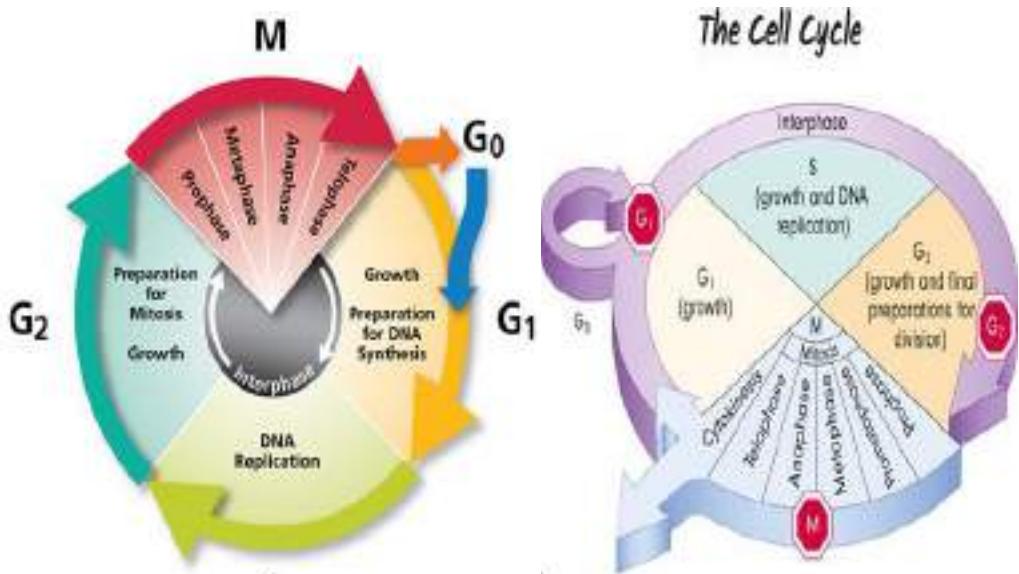
## Types of cells in relation to their cell cycles:

There are three types of cells in the body classified according to their capacity for regeneration and renewal as follow:

- **Cells of type one** (terminally differentiated):  
These cells can not divide and replacement of the worn cells is impossible  
e.g. nerve cells and cardiocytes.
- **Cells of type two:** these cells are unable to divide but when they die, they are replaced by daughter cells arising from stem cells, mother cells or progenitor cells of the same family.  
Stem cells may be:
  - **Unipotential** which produce one type of cells as spermatozoa.
  - **Multipotent** which produce many cells as blood mother cells.
- **Cells of type three:** these cells are normally not divide but at time of need, they can divide and renew their kinds of cells e.g. liver cells and the hormone secreting cells of the endocrine glands.

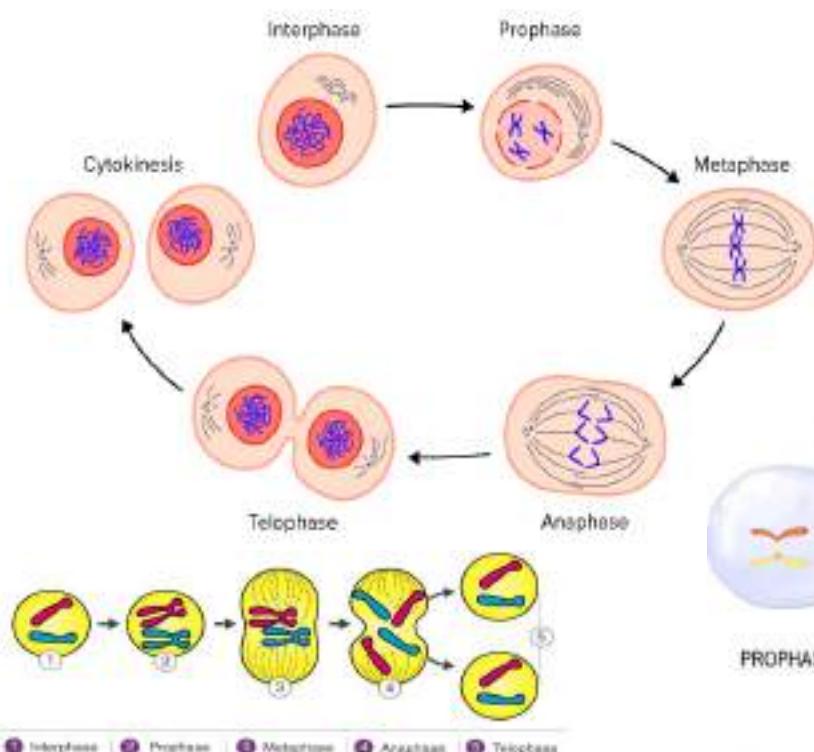
↙ بحص بحصه سريعة على المقارنة

<b>G1 phase</b>	<p>between the end of mitosis and the beginning of S phase. <b>(post mitotic period)</b></p> <ul style="list-style-type: none"> <li>• <b>Prepare for DNA replication</b></li> <li>• Cell synthesis RNA, protein, enzymes requir for DNA replication</li> <li>• Cell volume increase which decreased during mitosis,</li> <li>• <b>Nuclei reestablish</b></li> <li>• Centriole start duplicate that is completed by G2</li> </ul>
<b>S phase</b>	<p>follows the G1 phase <b>DNA replication</b> occur</p> <ul style="list-style-type: none"> <li>• Cell double dna by synthesis new strand of dna (DNA duplicated)</li> <li>• Cell contain now twice amount of DNA</li> <li>• Autosomal cell contain diploid amount (<math>2n</math>) but after s phase diploid become doubled (<math>4n</math>)</li> <li>.....in contrast germ cell.....</li> </ul> <p>Produced by meiosis posses haploid (<math>1n</math>)</p>
<b>G2 phase</b>	<p><b>Pre-mitotic phase</b></p> <ul style="list-style-type: none"> <li>• Cell accumulate rna enzymes , protein need for Mitosis</li> <li>• Energy stored for mitosis by mitochondri</li> <li>• <b>Tubulin synthesis for mitosis</b></li> <li>• DNA analyzed for possible errors and any of these errors is corrected</li> </ul>

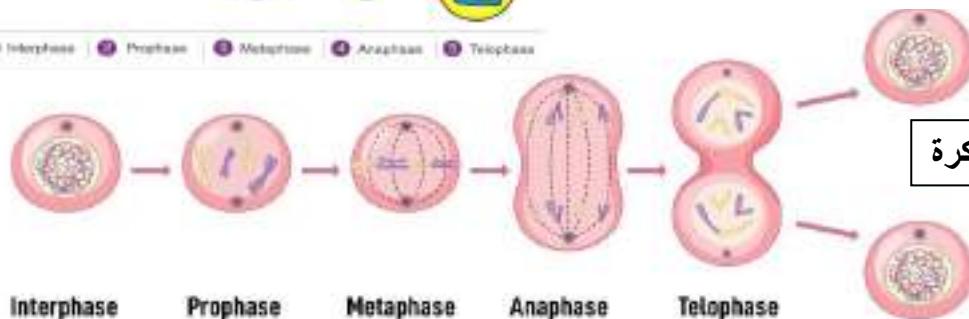
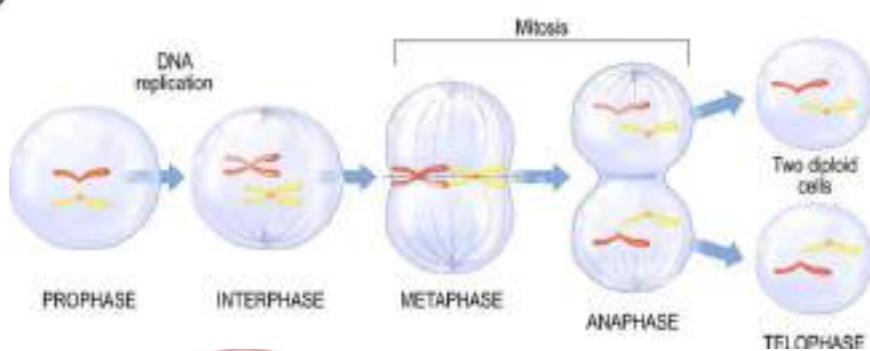


## Mitosis

- After DNA replication, the nucleus contains double amount of chromatin and protein
- The (s) chromosomes become (d) chromosomes
- In human, each cell begin mitosis with 46 d chromosomes.



يعني لو جبت برتقانة وقسمتها نصين



متنساش ترجع للديجرامات بعد ما تخلص مذاكرة

P Prophase	M Metaphase	A Anaphase	T Telophase
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## Stages of mitosis:

### 1- prophase.

- One pair of centriole move towards one pole of cell and other move towards the other pole.
- Microtubule (continuous and astral) begin to form from each pair of Centrioles from a small area called microtubule organizing center.

The Continuous or interpolar microtubules are termed so because they extend From one pole of the cell to the other.

They form a shape of spindle and Thus are termed mitotic spindle

- The chromosomes contact and shorten.
- The nucleus disappear.

### 2- prometaphase.

- It begins with **breakdown** of nuclear envelope due to phosphorylation of Nuclear lamins.

There are Three different types of microtubules are present:

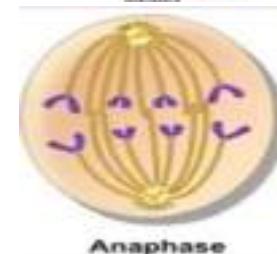
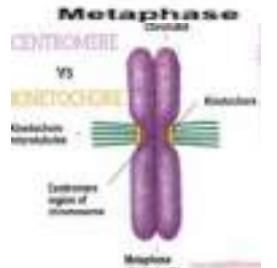
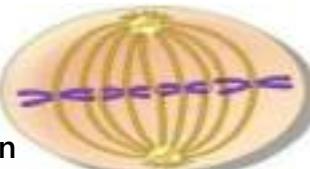
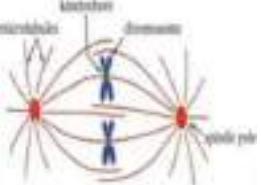
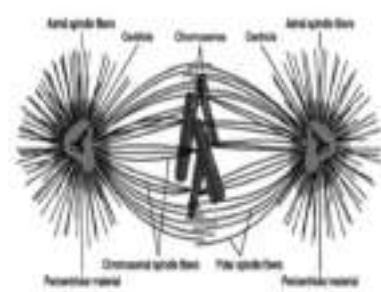
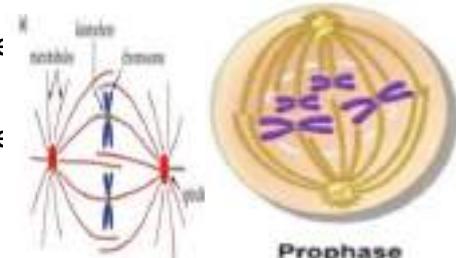
1. **Kinetochores (chromosomal) microtubules:** the centromeres of d-chromosomes are formed of two organs of movement known as kinetochores from which other sets of microtubules diverge toward either pole of the cell to be attached to mitotic spindle.
2. **Polar microtubules:** arise from each centrosome and extend from one pole of the cell to the other.
3. **Astral microtubules:** are short microtubules extend out from the centrosome toward the periphery of the cell.

### 3- Metaphase

- The chromosomes become arrange in the **equatorial plane** ( midway position between the two poles of the cell).
- The chromosomal microtubule **interdigitate with** and are bonded to the continuous microtubule.
- Each pair of sister chromatids is attached to the mitotic spindle at the kinetochore

### 4 – Anaphase

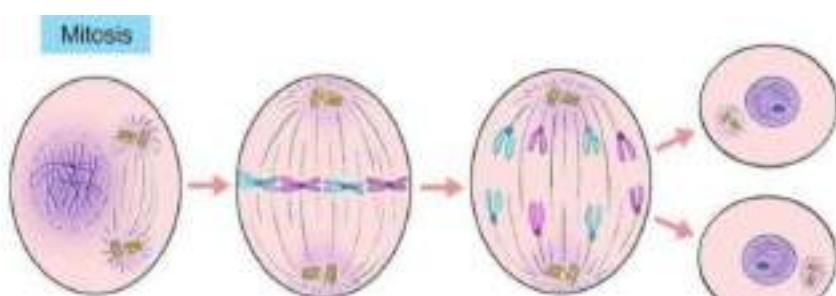
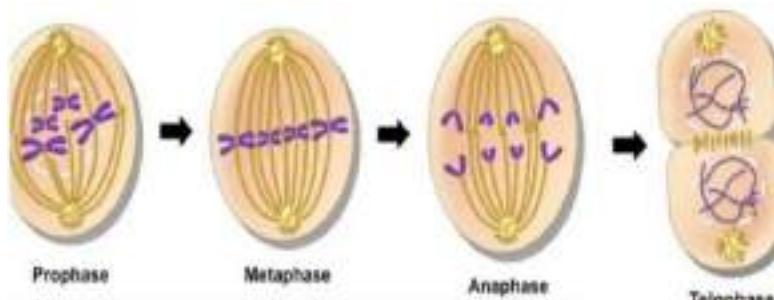
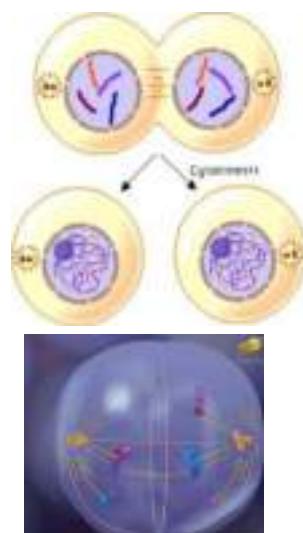
- The centromere of each d chromosomes **split longitudinally** as a result of the dragging power of continuous microtubule .
- Each **d chromosomes** become completely sperate into **two s chromosomes** .
- Each set of **s chromosomes** **is pulled towards a pole** of the cell by the dragging of continuous microtubule



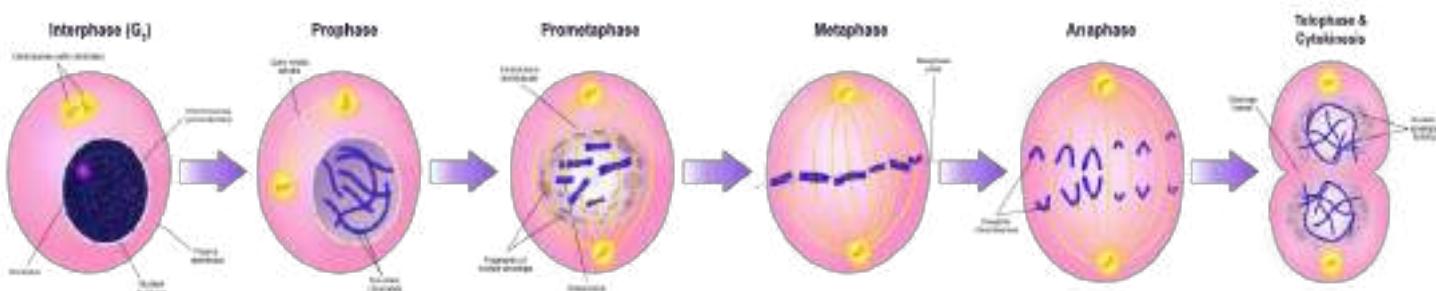
## 5 -Telophase

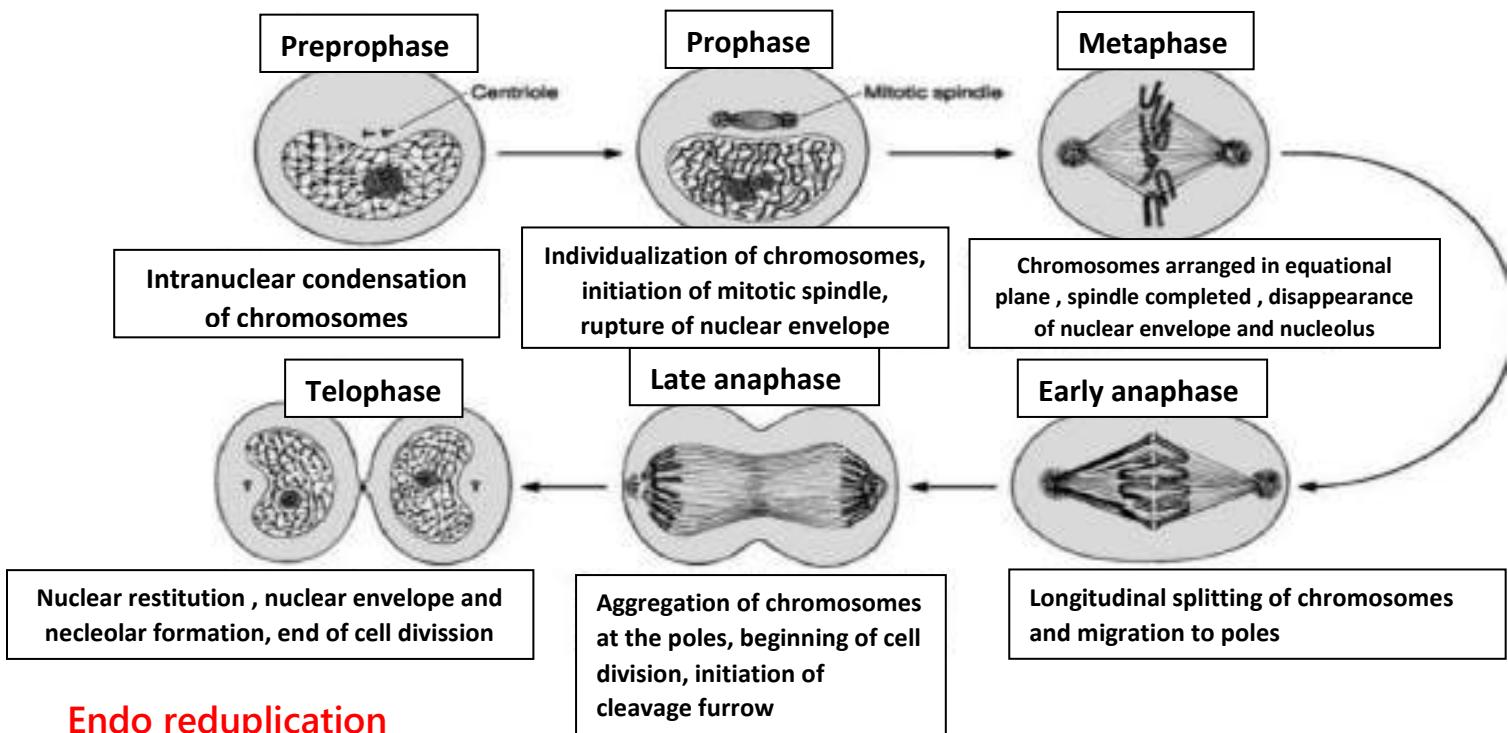
- Each set of chromosomes has reached its respective pole, the nuclear lamins are **dephosphorylated** and the **nuclear envelope** is **reconstituted**.
- The chromosomes uncoil and become organized into heterochromatin And euchromatin of the interphase cell.
- Nucleolus** is reformed.
- A constriction begins to develop in the middle of the cell in the region of equatorial plane. This constriction encircles the cell and deepens to form **cleavage furrow**.
- At the site of constriction there is an accumulation of actin filaments. These filaments make the cleavage furrow deeper and deeper and the cleavage becomes complete.

Finally the cytoplasm is divided (**cytokinesis**) into two approximately equal halves giving **two daughter cells**.



- Centrioles move toward poles
- Chromatin begins to form into chromosomes
- Nuclear envelope disintegrates
- Chromosomes align along cell equator to form metaphase plate
- Sister chromatids separate and move toward poles
- Daughter cells form
- Nuclei are genetically identical to parent cell





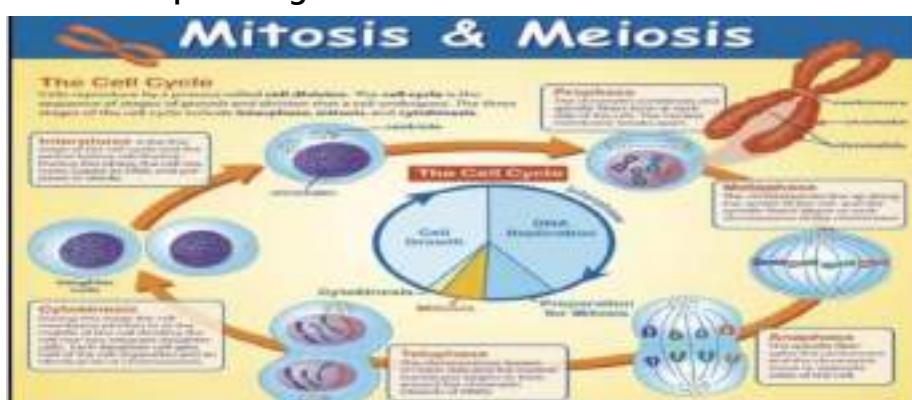
Is a special case of **tetraploidy** in which the chromosomes undergo 2 squent DNA Replication and enter prophase and metaphase a cell contains **2d chromosomes**. It appears in leukemia cell.

### Clinical Correlation

The understanding of mitosis and the cell cycle has greatly aided cancer chemotherapy, making it possible to use drugs at the time when the cells are in a particular stage of the cell cycle.

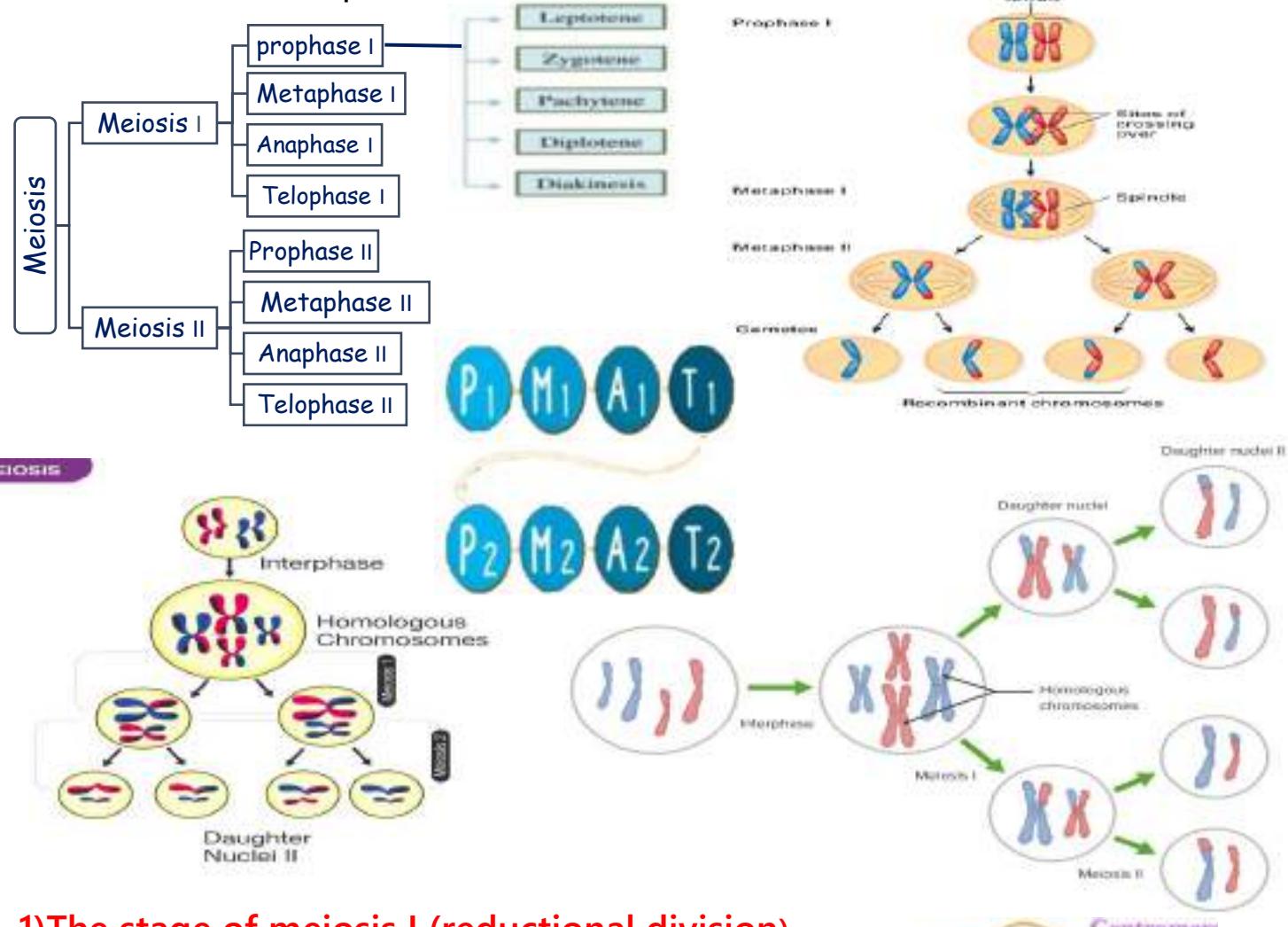
For example,

- **Vincristine** and similar drugs, **Colchicine**, another plant alkaloid disrupt the mitotic spindle, arresting the cell in mitosis.
- **Methotrexate**, which inhibits purine synthesis, and **5-fluorouracil**, which inhibits pyrimidine synthesis, both stop the cell cycle in the S phase, preventing cell division; both are common chemotherapeutic agents.



# Meiosis

- Occurs only in germinal cells of the testis and ovary.
- Each mother cell gives rise to 4 cells each has only haploid number of chromosomes(23).
- Meiosis consists of meiosis I and meiosis II without an intervening s phase.
- Genetic recombination by means of crossing over and reduction to the haploid chromosomal complement occur in meiosis I.



## 1) The stage of meiosis I (reductional division).

### A) Prophase I

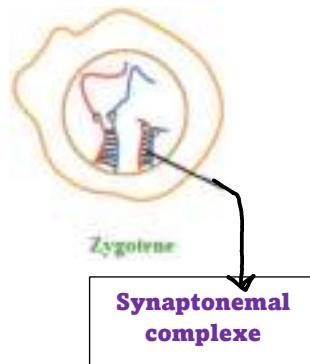
It is divided into the following stages:

#### 1-Leptotene stage (thin thread stage):

- Chromosomes are visible as fine thread like structure.
- Each chromosome appear as two sister chromatod.

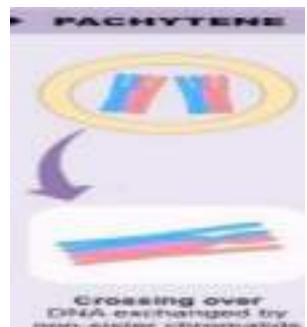
## 2-Zygotene stage (joined thread stage):

- The chromosomes continue to shorten and thicken, they are visible as paired structures.
- Homologous** chromosomes align directly opposite each other, a process known as **synapsis**, and are held together at several points along their length by filamentous structures known as **synaptonemal complexes**.
- Two homologous chromosomes that have paired are referred to as a **bivalent** (two homologous chromosomes in intimate contact). In the male pairing occurs between homologous segments of the X and Y chromosomes **at the tip of their short arms**, with this portion of each chromosome being known as the **pseudoautosomal region**.



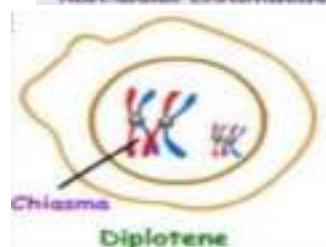
## 3-Pachytene: (thick thread stage):

- The bivalent becomes thicker and shorter.
- Each bivalent contains 4 strands DNA and now it called **tetrad (quadrivalent)**.
- Begin **crossing over** means exchange between two homologues chromatids thus **increasing genetic diversity**



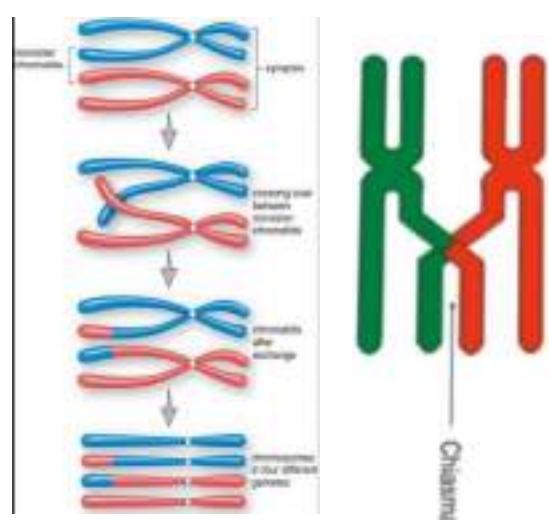
## 4-Diplotene (double thread stage):

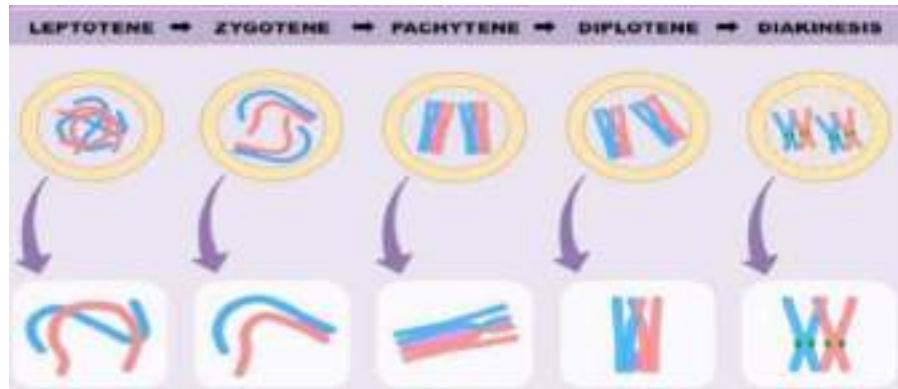
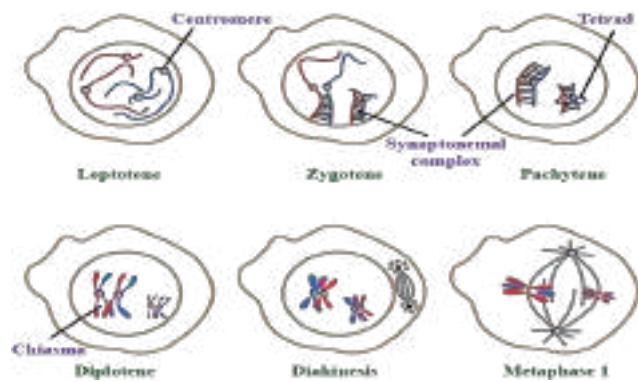
- The two homologous chromosomes begin to **separate** but **remain attached** at the points where crossing over has occurred (**chiasmata**).
- On average small, medium and large chromosomes have one, two and three chiasmata, respectively, giving an overall total of approximately 40 recombination events per meiosis per gamete.



## 5-Diakinesis (double movement):

- Each of the chromosome pairs separates extensively, but not yet at one or more distally located points of attachment (**chiasma**).  
(chiasmata move down the chromosome to its end).
- At the end of diakinesis the nucleoli and the nuclear membrane disappear and the cell enters metaphase I.





## B) Metaphase I

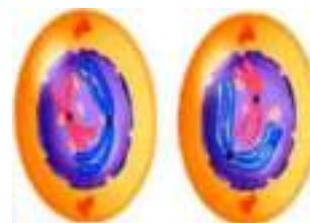
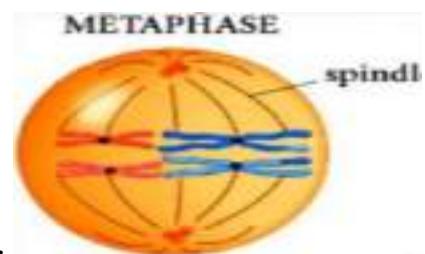
- Spindle apparatus is organized.
- Tetrads start moving and are aligned at the equatorial plane.

## C) Anaphase I

- Tetrads move apart from each other as a result of repulsion force.
- The total number of chromosomes moving to either pole of the cell is 23 d chromosomes.
- The chromosome number is haploid number.
- The centromeres do not divide

## D) Telophase I

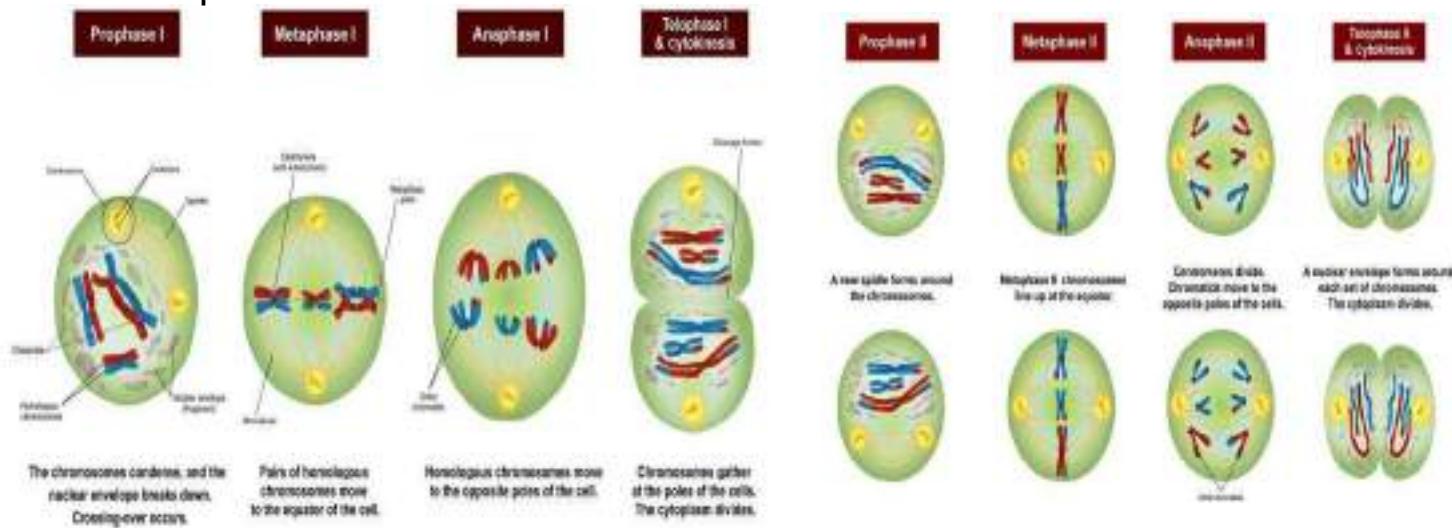
- By the completion of the cleavage furrow
- two daughter cells separate from each other.
- Nuclear membrane reformed.



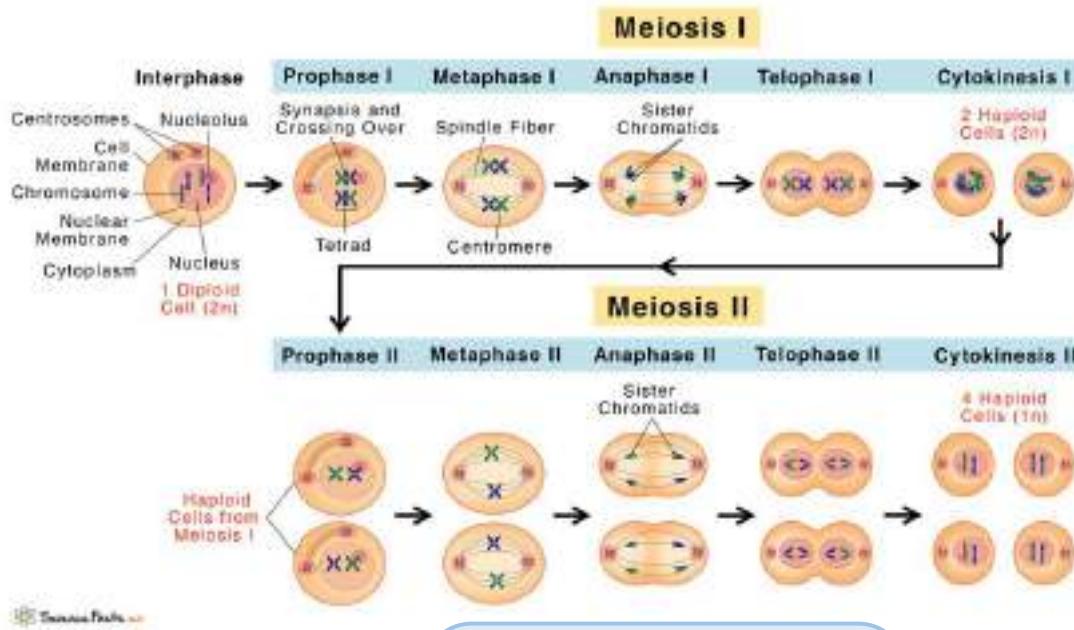
## Meiosis II (second meiotic division):

It is similar to mitotic division but differs in the followings:

- It is not preceded by DNA synthesis.
- Cells enter the division with a complement of 23 d chromosomes (haploid number).
- In prophase sister chromatids are not identical due to crossing over.
- Prophase II is of shorter duration and no nucleoli are observed.



	Meiosis I	Meiosis II
1- Preceded S phase	Present (the cell enter the prophase with 46 d chromosomes).	Absent (the cell enter the prophase w 23 d chromosomes).
2- Prophase	Pairing of homologous chromosomes result in 23 tetrad. Crossing over occurs between each tetrad.	No pairing No crossing over.
2- Metaphase	23 tetrad arranged at the equatorial plane of the cells.	23 d chromosomes arranged individual at the equatorial plane of the cells.
3- 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.
4- Telophase	Cytokinesis results in 2 daughter cells each with 23 d chromosomes.	Cytokinesis results in 4 daughter cells each with 23 s chromosomes.

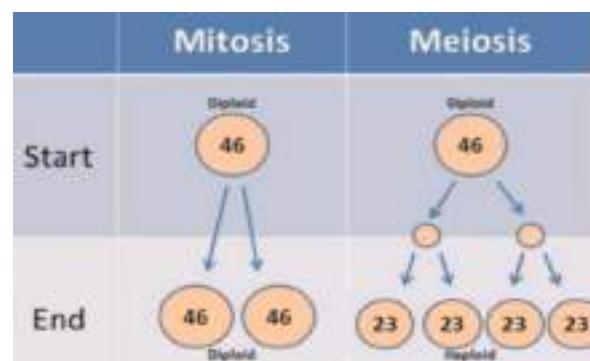


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	Mitosis	Meiosis
1- Types of cells	Somatic cells	Germ cells of testis & ovaries
2- Number of division	Single division	2 successive divisions: Meiosis I & Meiosis II.
3- Interphase	Preceded by interphase with S phase	Meiosis I preceded by interphase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

Mitosis	Meiosis
One division	Two divisions
Number of chromosomes remains the same	Number of chromosomes is halved
Homologous chromosomes line up separately on the metaphase plate	Homologous chromosomes line up in pairs at the metaphase plate
Chiasmata do not form and crossingover never occurs	Chiasmata form and crossingover occurs



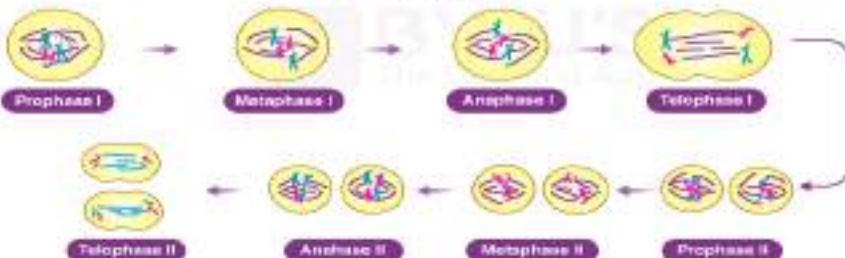
### TYPES OF CELL DIVISION

BYJU'S  
The Learning App

#### MITOSIS

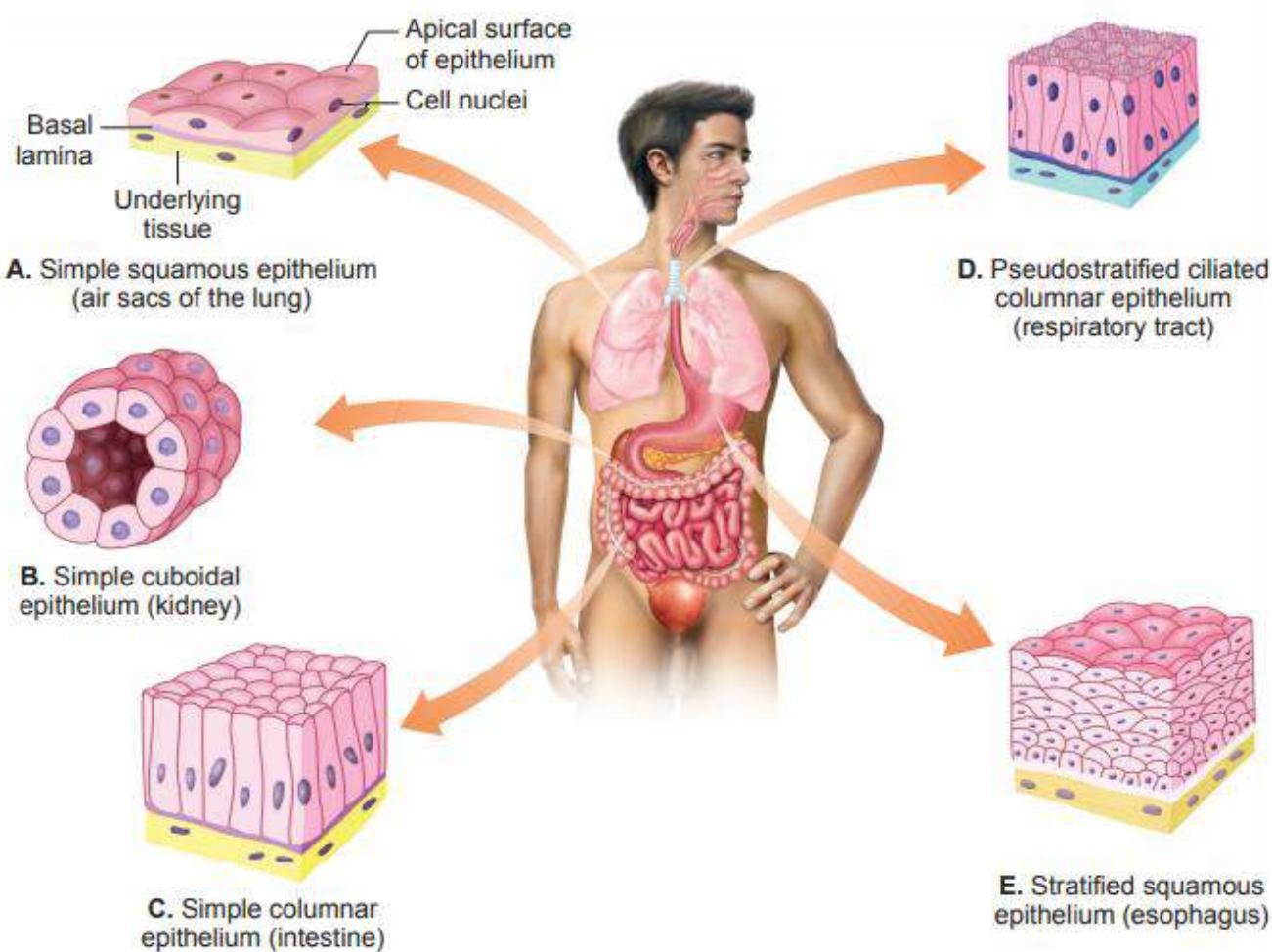


#### MEIOSIS





# Chapter 4 : EPITHELIAL TISSUE





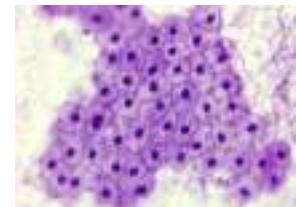
## Ch4 : EPITHELIAL TISSUE

The human body is composed of only four basic types of tissue:

1. Epithelial Tissue.
2. Connective Tissue.
3. Muscular Tissue.
4. Nervous Tissue.

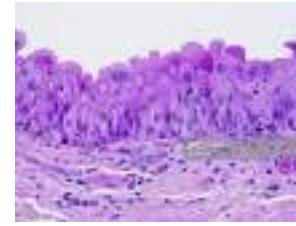
### Epithelial Tissue (epi, on + thelium, surface)

It covers a surface, lines a cavity or forms a gland. Epithelial tissue consists of cells attached to one another to form an uninterrupted layer of cells that separates the underlying tissues from the outside world.



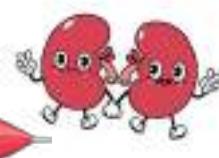
#### General characteristics:

- 1- No blood vessels (**avascular**) or lymphatic in between its cells and are nourished by **diffusion** from the vessels in the underlying connective tissue (C.T).
- 2- Nerve fibers can penetrate between the epithelial cells.
- 3- Epithelium can degenerate (destroyed) and can rapidly regenerate (**renewed**).



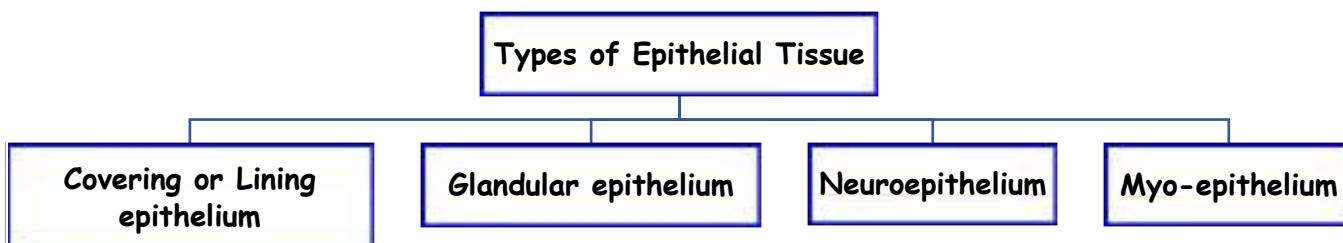
#### Principal functions: (MCASSEP)

1. **P**rotection against injuries, bacteria and chemicals as epithelial of skin.
2. **S**ecretion as glandular epithelial of pancreas, endocrine glands, ....
3. **A**sorption as the intestinal epithelium.
4. **S**ensation as the neuro- epithelium.
5. **E**xcretion as the cells of kidney and sweat glands.
6. **C**ontractility as the myoepithelial cells.
7. **M**ovement of fluid upon surface (cilia)



#### Types of Epithelial Tissue :

Epithelia are divided into four main groups according to their **structure** and **function**:



## A- Covering or lining epithelium

They can be classified according to the number of cell layers and the morphological features of the cells in the surface layer into:

**I. Simple epithelium:** contains only **one** layer of cells.



**I. Simple Epithelium :**  
Based on cell shape, simple epithelia can be:

- a- Simple squamous
- b- simple cubical
- c- simple columnar
- d- Pseudo-stratified columnar

(a) Squamous

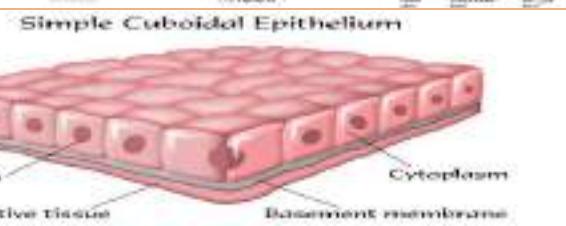
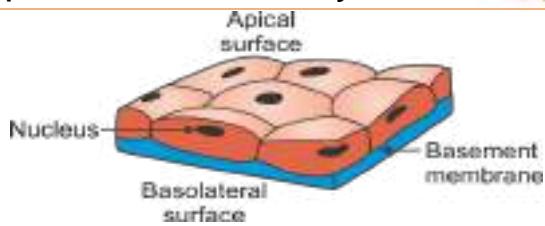
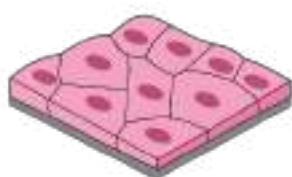
(b) Cuboidal



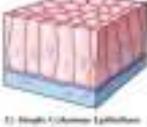
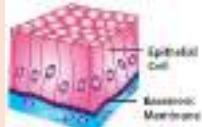
(c) Columnar (Ciliated)

(d) Stratified squamous

Simple squamous		Simple cubical
Origin	Single layer of <b>flat</b> cells with <b>flat</b> nuclei.	Single layer of <b>cube-like</b> cells with <b>central rounded</b> nuclei.
Sites	Lining of heart, blood vessels, lymph vessels ( <b>endothelium</b> ), pleura, pericardium and peritoneum ( <b>mesothelium</b> ), certain cells in the lung alveoli, Bowman's capsule and loop of Henle in the kidney.	Lining of thyroid follicles, acini of salivary glands and pancreas, convoluted tubules of kidney and small ducts of glands.



Simple columnar		Pseudo-stratified columnar
Origin	Single layer of <b>tall</b> columnar cells with <b>basal oval</b> nuclei.	Single layer of columnar cells. The cells are <b>crowded</b> over each other. All cells rest on the basement membrane. Some cells do not reach the surface; therefore their nuclei are present at different levels forming <b>false rows</b> .
Sites	Stomach and cervical canal of uterus ( <b>secretory</b> ), intestine, convoluted and collecting tubules of kidney ( <b>absorptive</b> ), fallopian tube, uterus and small bronchioles of lung ( <b>ciliated</b> ).	Nose, nasal sinuses, nasopharynx, trachea and bronchi ( <b>ciliated</b> with goblet cells), epididymis (with <b>stereocilia</b> ), large ducts of salivary glands and upper part of male urethra ( <b>non-</b> ciliated).



## II. Stratified Epithelium

It is formed of many layers of cells .

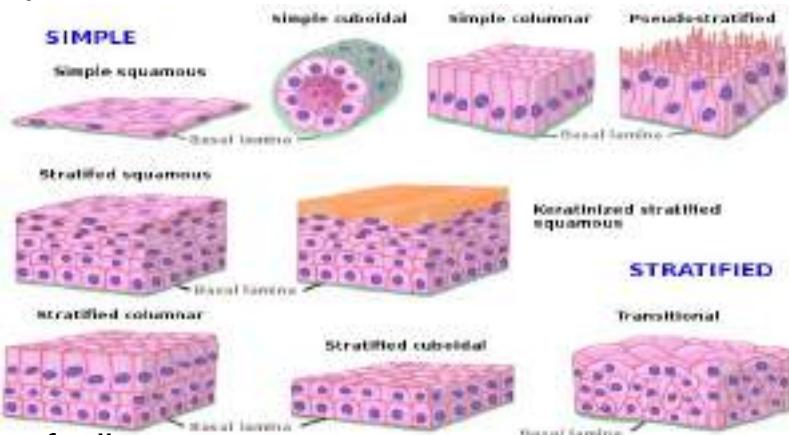
It is classified according to the type of the most superficial cells into:

- a-Stratified Squamous Epithelium
- b- Stratified cubical epithelium
- c- Straified Columnar Epithelium
- d- Uroepithelium (Transitional Epithelium)

### a- Stratified Squamous Epithelium:

- It is a thick type of stratified epithelium formed of many layers of cells one above the other.

The number of layers ranges from **5 to 30** layers of cells.



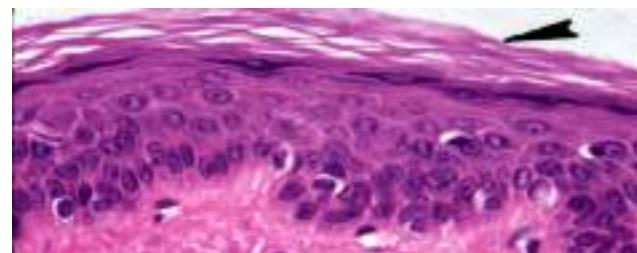
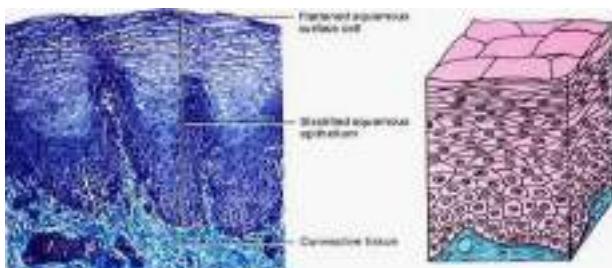
- The basal cells are well nourished and are formed of columnar cells with oval basal nuclei, from these basal cells, the other layers **germinate**.

**Hemidesmosomes** are present between these cells and the basement membrane

- The intermediate layers are polygonal cells with **desmosomal junction** between their cell boundaries.

-The superficial layers of cells are flat squamous cells which may be **nucleated** or **not**.

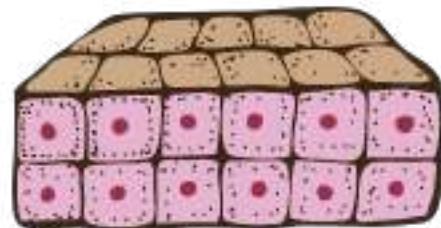
Stratified Squamous non-keratinized	Stratified Squamous keratinized
Cells in the superficial layers are flattened (squamous) and <b>nucleated</b> .	Cells in the superficial layers are <b>not nucleated</b> . The nucleus and cytoplasm get replaced by protein called keratin and this makes it water proof and protective in nature.
<b>Sites:</b> Oral cavity, inner surface of the lip, tongue, gums and palatine tonsils, esophagus, oropharynx, vocal cords, cornea, vagina, terminal parts of male and female urethra and anal canal.	<b>Sites:</b> Epidermis of skin and opening upon the skin (external ear, external nose, outer surface of the lip and anal orifice).



### b- Stratified cubical epithelium:

Usually is formed of 2 layers of cuboidal cells.

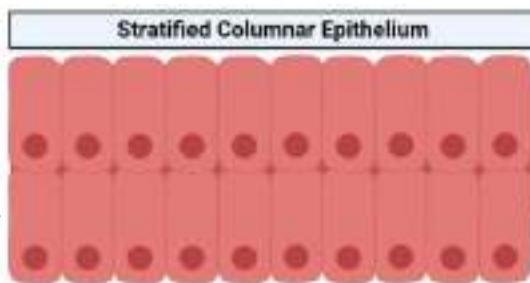
**Sites:** Ducts of sweat gland, sebaceous and mammary gland.



### c- Stratified Columnar Epithelium:

It is similar in structure to stratified squamous epithelium but its layers are **less in number** and the superficial cells are columnar cells.

**Sites:** Fornices of conjunctiva of the eye, penile part of male urethra, large ducts of glands, recto-anal junction (**non ciliated**), fetal esophagus, nasal surface of soft palate and laryngeal surface of epiglottis (**ciliated**).



### d- Uroepithelium (Transitional Epithelium):

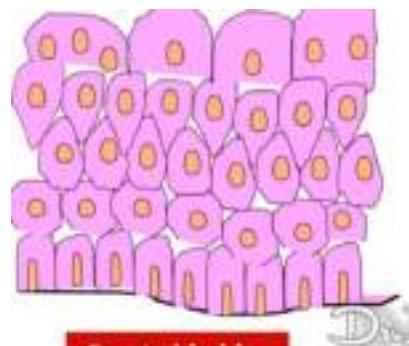
- It is a special type of stratified epithelium.
- It is present in the urinary tract.
- The epithelium rests on thin and corrugated basement membrane.
- Its superficial cells are **cuboidal** or **dome** shape with convex outer surfaces and concave base.



Some of the superficial cells may contain **two** nuclei.

The superficial cells are covered with a **mucus-like substance** which acts as an osmotic barrier between urine and tissue fluids.

- The basal cell layer is formed of high cuboidal cells.
- The intermediate cells are **polyhedral** and are separated from each other by mucus-like substance in their intercellular spaces.
- The presence of mucous substance between the cells facilitates gliding of cells on each other.



#### Stretching qualities:

The number of cell layers **decrease** with distension of the organ and relatively increase when the organ is contracted or empty.

In full distended urinary bladder, the transitional epithelium is formed of **3 to 4 layers** only while in an empty bladder is formed of **6 to 8 layers**.



**Sites:** Minor and major calyces of the kidney, pelvis of the ureter, ureter, urinary bladder and prostatic part of male urethra.





## B- Glandular Epithelium

It is formed by cells specialized to produce a fluid secretion that differs in composition from blood or intercellular fluid.

The different glands in our body are classified according to the following classifications:

### 1. According to number of cells:

- a) **Unicellular gland**, as goblet cell in respiratory and intestinal tract.
- b) **Multicellular glands** as the salivary glands.

### 2. According to presence or absence of ducts:

- a) **Endocrine or ductless glands**: secreting hormones **directly** in the blood as Thyroid, parathyroid, pituitary, suprarenal, .....
- b) **Exocrine glands**: have **ducts** to carry their secretions as salivary glands, sweat and sebaceous glands,...
- c) **Mixed glands**: possess the exocrine and endocrine functions as pancreas, testis, ovary, .....

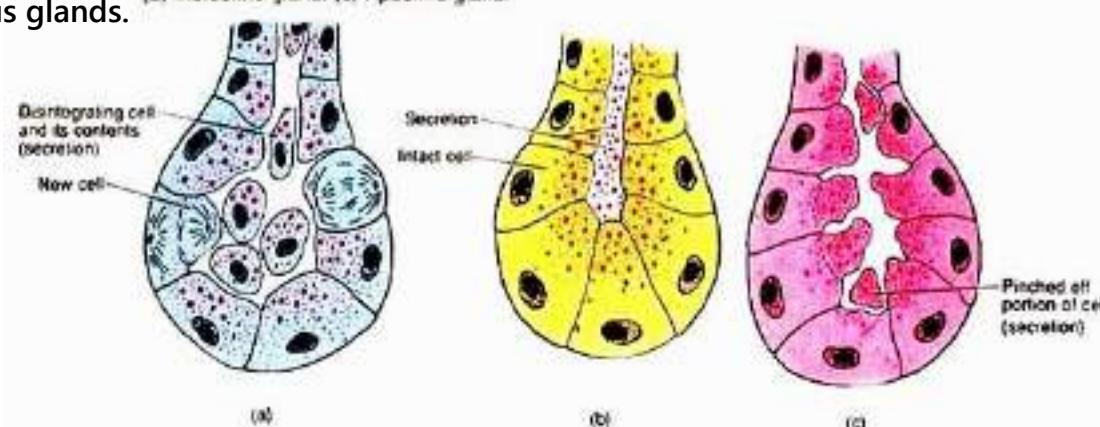
According to the shape of the secretory units: exocrine glands may be **simple** or **compound**



### 3. According to the mode of release:

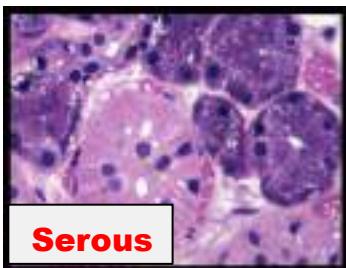
- a) **Merocrine gland**: there are **no cellular changes** in their secretory parts as salivary glands.
- b) **Apocrine gland**: in which the tips of the secretory cells are **detached** and **come out** with the secretory products of the gland as mammary glands and the axillary sweat glands.
- c) **Holocrine gland**: the whole secretory cells are **destroyed** and come out with the secretion as the cells of the sebaceous glands.

Functional classification of multicellular exocrine glands: (a) Holocrine gland.  
(b) Merocrine gland. (c) Apocrine gland.



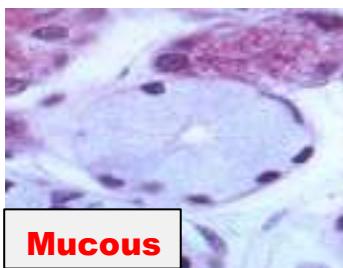
#### 4. According to the nature of secretion:

a) Serous secretory glands:  
as parotid gland and von Ebner gland of the tongue.



**Serous**

b) Mucous secretory glands:  
as Brunner's gland and goblet cells.



**Mucous**

c) Mucoserous secretory glands:  
as submandibular and sublingual glands.



**Seromucous**

d) Fatty secretory glands:  
as sebaceous glands.

e) Waxy secretory glands:  
as glands of external ear.

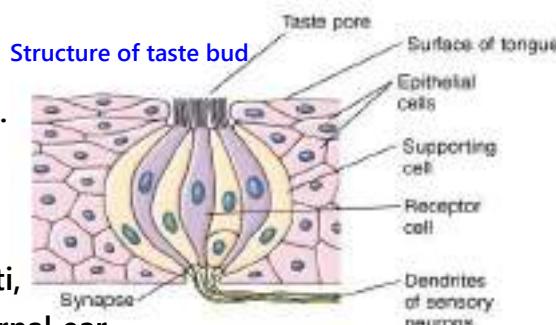
f) Cellular secretory glands:  
as testis and ovary.

Serous acinus	Mucous acinus
Smaller in size and rounded	Larger in size and variable in shape
Lining cells are pyramidal in shape	Lining cells are columnar in shape
More in number	Few in number
Nucleus is rounded and basal	Nucleus is flattened and peripheral
Cytoplasm is basal basophilic and apical acidophilic	Cytoplasm is pale and vacuolated

#### C- Neuro-Epithelium

They are cells of epithelial origin with specialized sensory function.  
The cells are provided with small hairs (**hairlets**) on their free ends while their bases are surrounded with sensory nerves.

**Sites:** taste buds in the tongue, retina of the eye and organ of Corti, crista ampularis, macula of the utricle and saccule in the internal ear



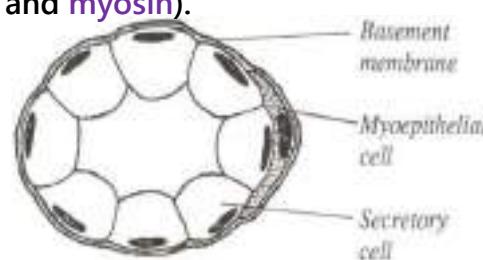
#### D-The Myoepithelial or Basket Cells

They are branched cells that arrange more longitudinally along the ducts of several glands (salivary, mammary,...).

The cytoplasm contains numerous microfilaments (**actin, tropomyosin and myosin**). It also contains intermediate filaments.

##### Function:

It contracts around the secretory or conducting portion of the gland and thus helps propel secretory products toward the exterior.





## Specializations (modifications) of the Epithelial Surface (tutorials)

### A) Apical (free) surface :

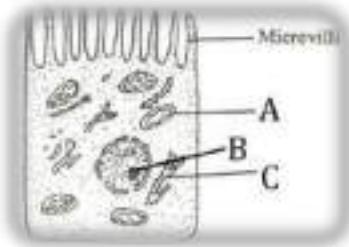
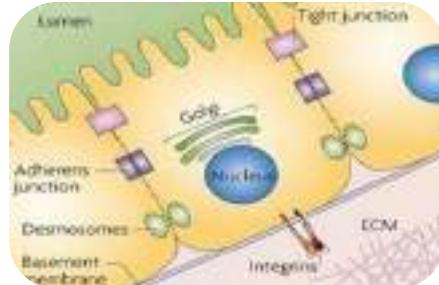
- striated border (microvilli)
- stereocilia
- Kinocilia
- flagella.

### B) Lateral surfaces :

- zonula occludens (tight junction)
- zonula adherens (belt desmosomes)
- macula adherens (desmosomes)
- gap junction (nexus)
- microvilli and microplicae and inter cellular cement

### C) Basal surface :

- basal lamina
- basal infoldings (basal striations)
- hemidesmosomes



### ❖ Specializations of the free surface:-

#### 1- Striated border (microvilli):

**Site:** small intestine (columnar absorptive cells), kidney, liver,...

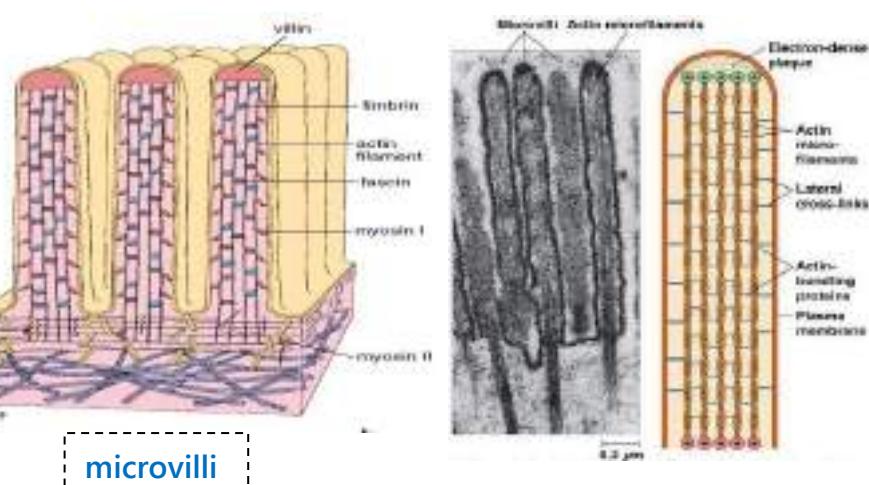
**L/M:** appears as acidophilic refractile free border (brush border) that exhibits fine vertical striation.

**E/M:** Each villous appears as:

A core of cytoplasm covered with plasma membrane with or without glycocalyx (act as a barrier to the large particles).



Contains parallel actin microfilaments attached to the tip and sides of the plasma membrane and extend down into the cytoplasm to join a horizontal network of filaments (terminal web) just below the base of the microvillus.



#### Function:

1- Increase the absorbing surface.

2- Share in the terminal digestion of carbohydrate, lipids and proteins.

## 2- Stereocilia: (long no motile microvilli):-

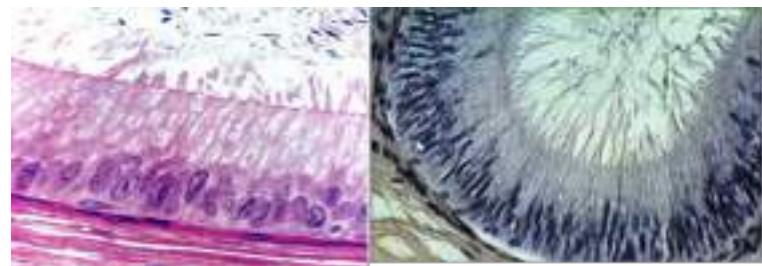
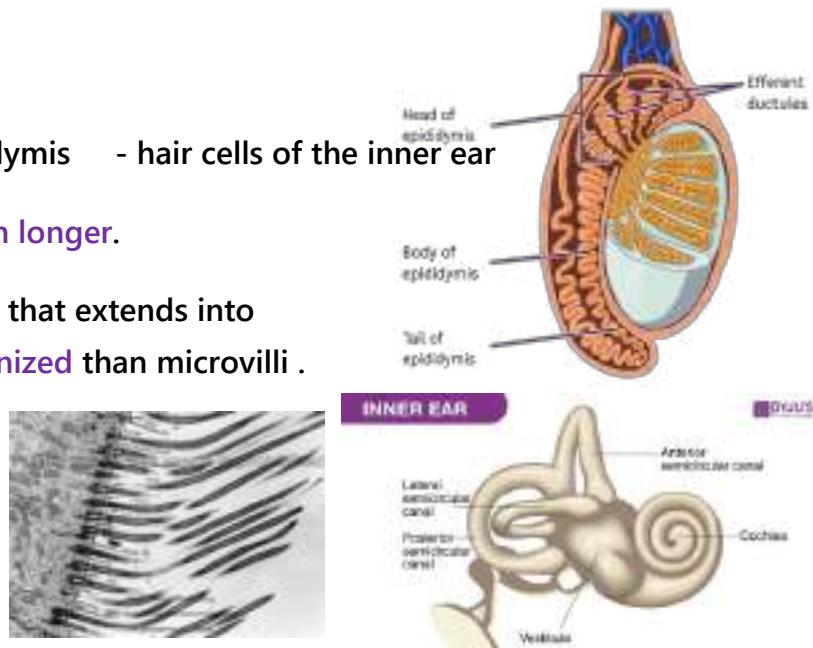
**Site:** In **pseudostratified epithelium** of - epididymis - hair cells of the inner ear

**L/M:** Resemble microvilli but they are very **much longer**.

**E/M:** They have a core bundle of **actin** filaments that extends into the apical cytoplasm, but it is **less well organized** than microvilli .

### Function:

- 1- **Eliminating** secretion in epididymis.
- 2- **Receiving** vibratory stimuli in the internal ear
- 3- **Kinocilia & Flagella** (see cytology).



**Stereocilia of epididymis**

### ❖ Specializations of the lateral surface :

#### 1- Zonula occludens (tight junction):

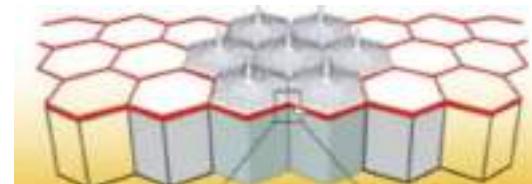
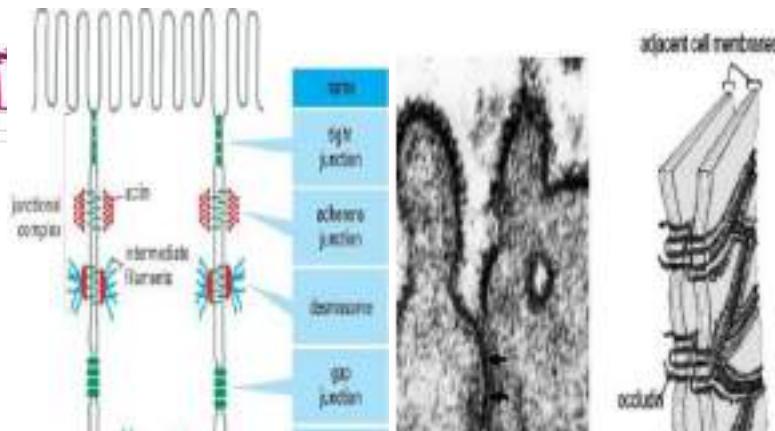
**Site:** In **columnar** cells of small intestine, cells of kidney tubules and urinary bladder.

**L/M:** It appears as a **fusiform** dark spot seen just below the free surface (terminal bar).

**E/M:** Formed of **5 layers**.

The middle dense layer is formed by the fusion of the 2 outer layers of the **trilaminar** membranes and on either sides by a **light** which is the middle layer of the trilaminar membrane and **dense** which is the inner layers of the trilaminar membrane.

**Function:** It acts as a **permeability barrier**, blocking the paracellular passage of large and small molecules.



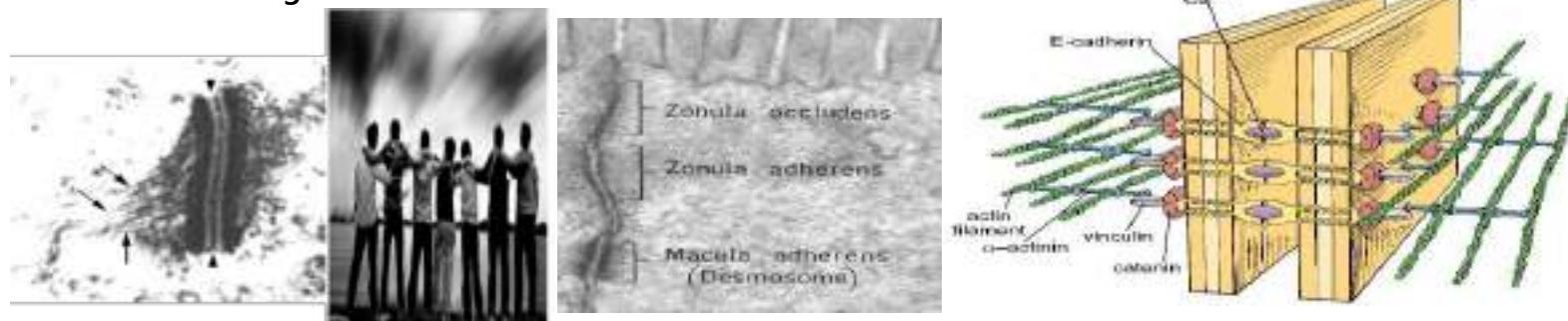
## 2- Zonula adherens (belt desmosomes):

**Site:** Columnar cells of small intestine - cells of kidney tubules and urinary bladder.

**L/M:** It is a **band-like** specialization of the membrane and subjacent cytoplasm below the tight junction and strongly bonds the cell together.

**E/M:** The opposing membranes are 15-20 nm apart and the intercellular space is occupied by material of low electron density that may exhibit an exceedingly fine transverse striation. In sections, the most conspicuous feature is a **plaque like dense area** (mat of fine filaments) of cytoplasm closely applied to the junctional membrane of the adjacent

**Function:** Strong attachment.



## 3- Macula adherens (desmosomes):

**Site:** In intestinal epithelium, cardiac muscle and **deep layers** of epidermis.

**L/M:** They are **separate plaques** (dots or fusiform thickenings of the cell boundaries) arranged in a **row** around the cell, just below the zonula adherens

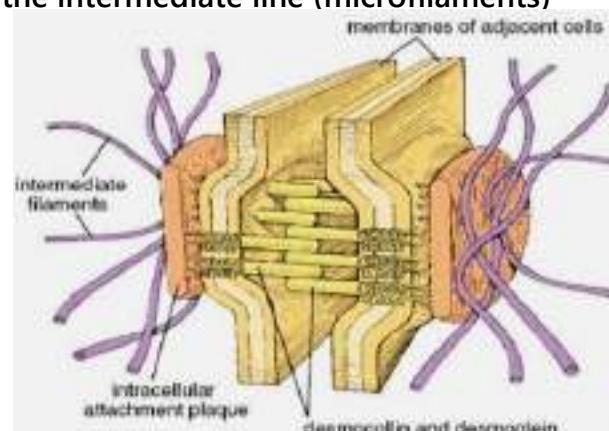
**E/M:** They are consisting of a **sub-plasmalemmal dens plaque** 10-15 nm thick on the cytoplasmic side of the opposing membranes.

The intercellular space of the macula adherens is wider (up to 30 nm) than that of the zonula adherens and is occupied by a dense medial band, the intermediate line (microfilaments)

**Function:**

1- Strong attachment.

2- Help the **structural stability** of the epithelium by linking the cytoskeleton of adjacent cells.



#### 4- Gap junction (nexus) :

It is a region of intimate cell contact that went undetected with the light microscope.

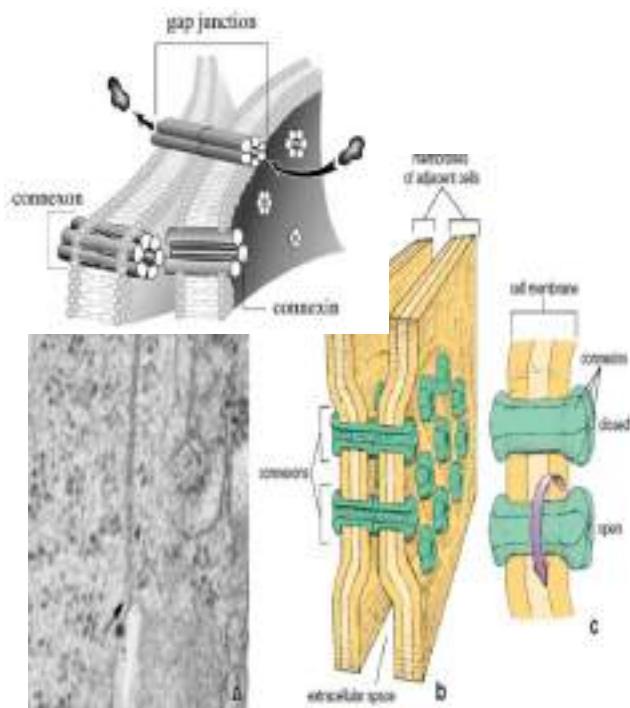
**Site:** Gastro intestinal tract, cardiac and smooth muscle and nervous tissue.

**E/M:** The intercellular cleft is narrowed to 3 nm and is of **constant** width throughout but there is no actual fusion of the membranes .

In favorable sections, minute structures; called **connexons**, can be seen bridging the gap.

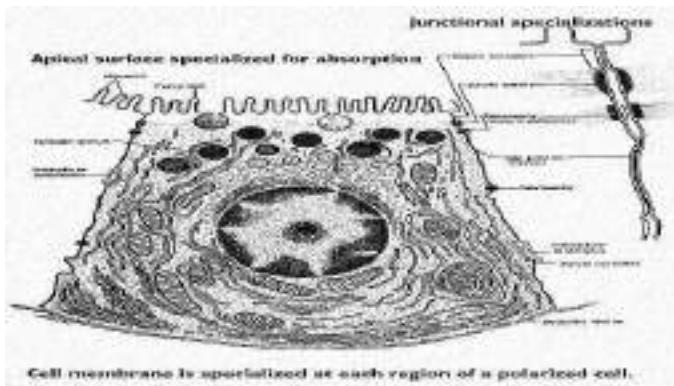
**Function:**

The junction permits **passage** of small molecules (smaller than 2nm in diameter) between cells.



#### 5- Microvilli and Microplica :

The lateral surfaces of certain epithelial cells show a tortuous boundary due to **infoldings** or **plicae** along the border of each cell with its neighbor that **increase** the lateral surface area of the cell (such as the intestinal and gallbladder epithelium)

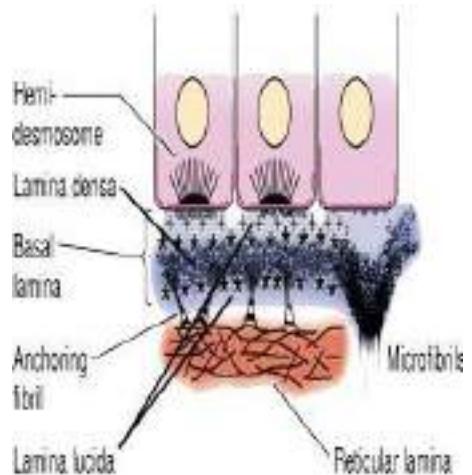
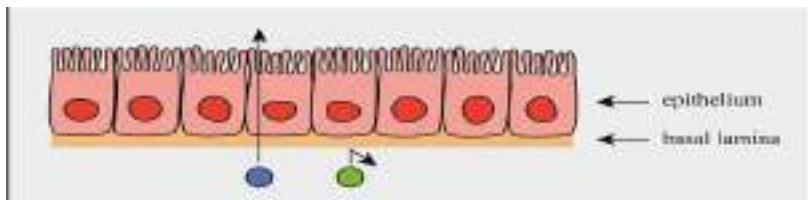


Infoldings of the lateral surface.

## ❖ Basal surface specializations:-

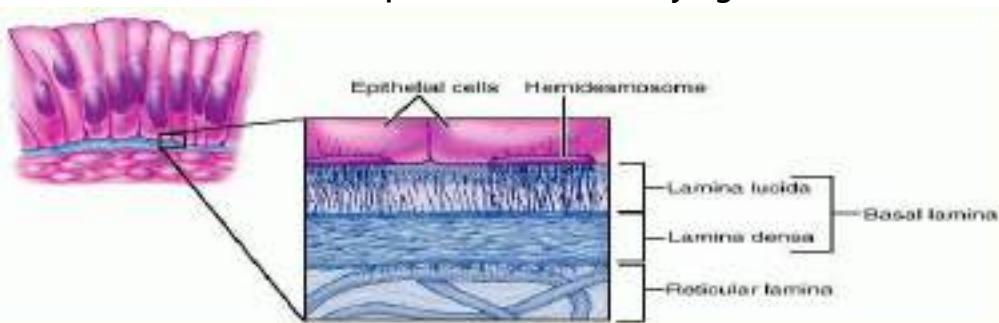
### 1- Basal lamina:

- A **thin** supporting layer at the boundary between the epithelium and the underlying C.T.
- Because it is **not** a lipid bilayers like the membrane of the cells, the term basement membrane is replaced by the term basal lamina.
- The principal chemical constituents of the basal lamina are **type- IV collagen, laminin and proteoglycans**.



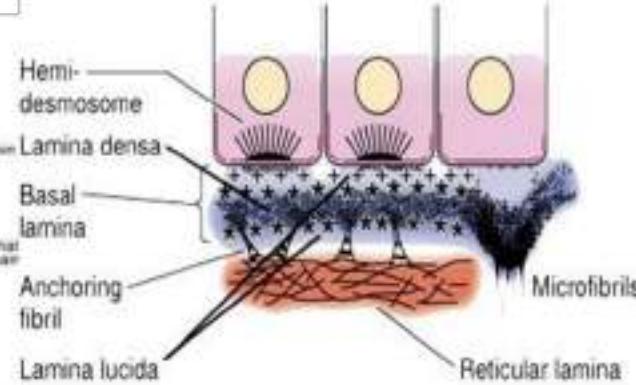
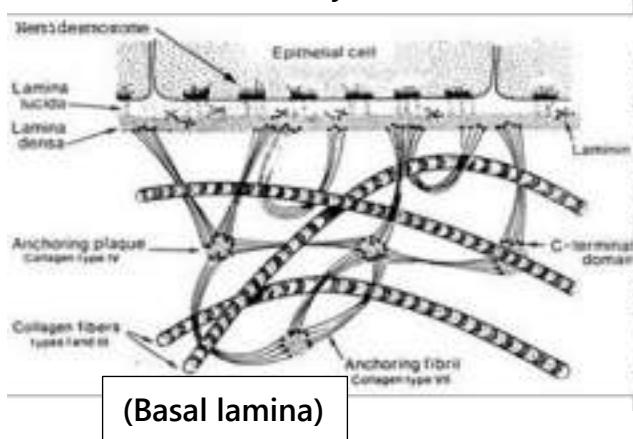
### 3 zones are distinguishable within the basal lamina:-

- 1) The **lamina rara interna (lucida)**: a **pale** zone of **very low density** immediately adjacent to the basal cell membranes of the epithelium.
- 2) The **lamina densa**: a central zone of **greater density**
- 3) The **lamina rara externa (reticular)**: exposed to the underlying C.T.



### Functions:

- 1- **Elastic Support** the epithelium.
- 2- **Repair after injury** to an epithelium.
- 3- **Ultrafilter** as in the kidney.
- 4- Around muscle cell and nerve cell is called **external lamina**.



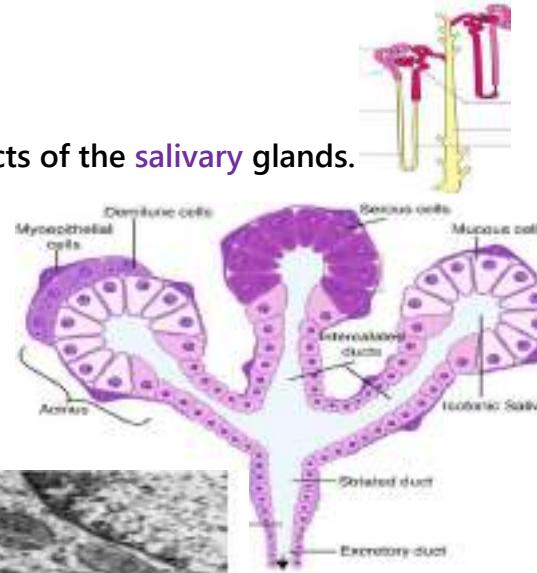
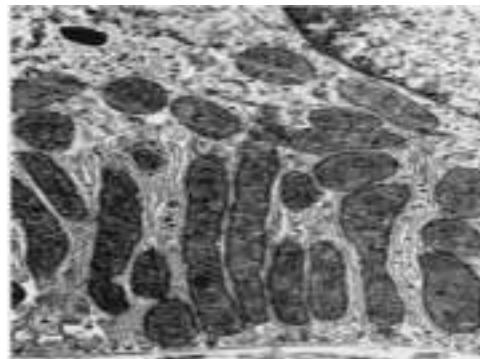
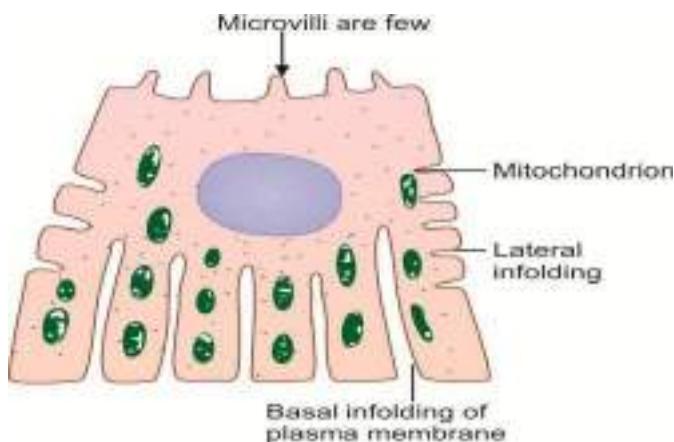
## 2- Basal infolding (basal striations):

**Site:** In proximal and distal tubules of the kidney and in striated ducts of the salivary glands.

**LM:** Basal acidophilic striation

**EM:** Mitochondria are typically concentrated at this basal site to provide the energy requirements for active transport.

**Function:** Increase the basal surface for rapid ion transport

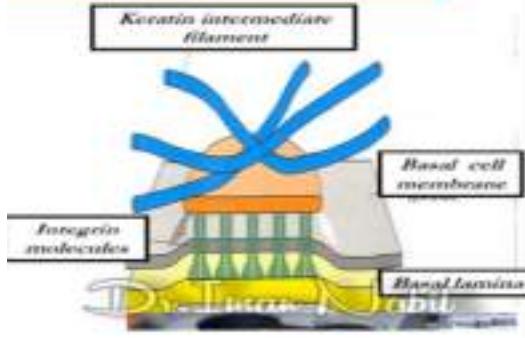


(Basal infolding.)

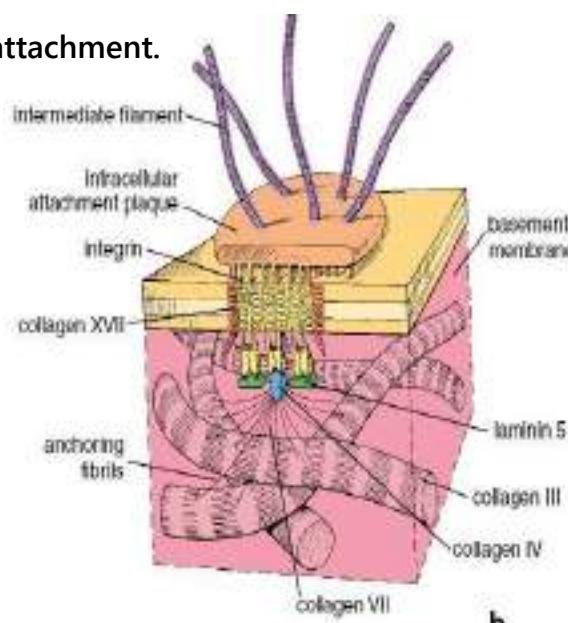
## 3- Hemidesmosomes:

They are found in certain epithelia subject to **abrasion** and mechanical **shearing forces** that would tend to separate the epithelium from the underlying connective tissue (cornea, skin, mucosa of the oral cavity, esophagus, and vagina). In these locations, only **half** the desmosome is present, hence the name hemidesmosome .

**Functions:** Act as points of **strong** attachment.



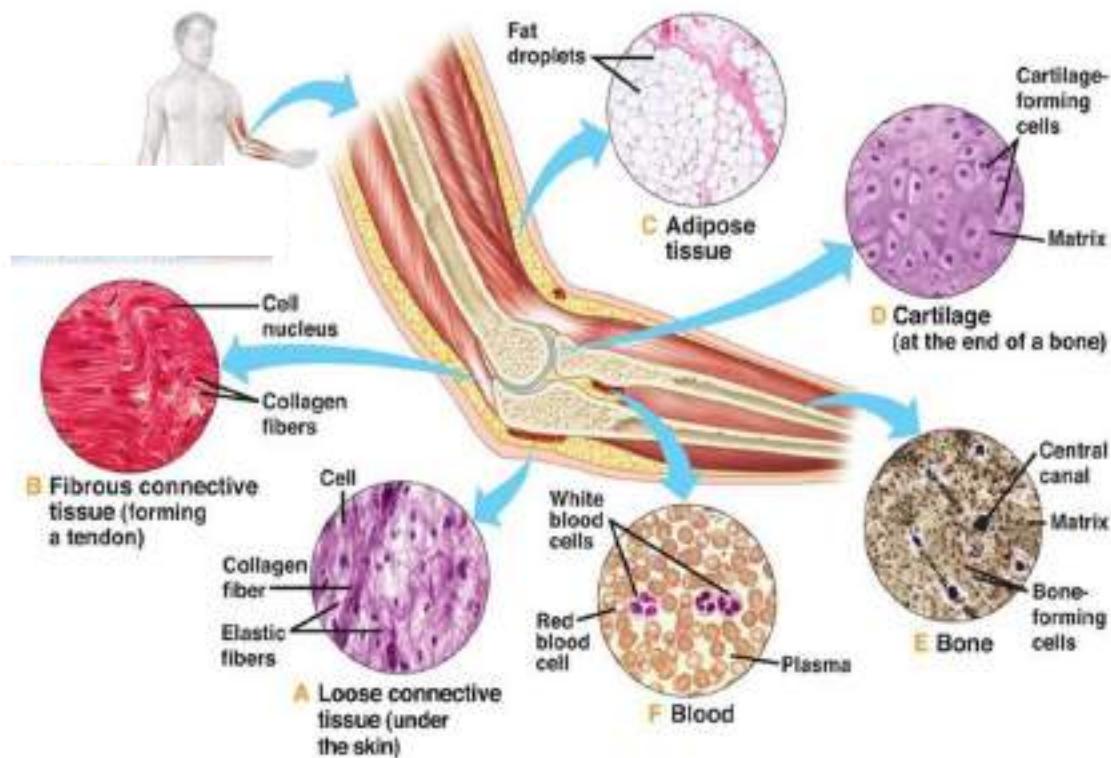
Hemidesmosomes



b



# Chapter 5 : CONNECTIVE TISSUE



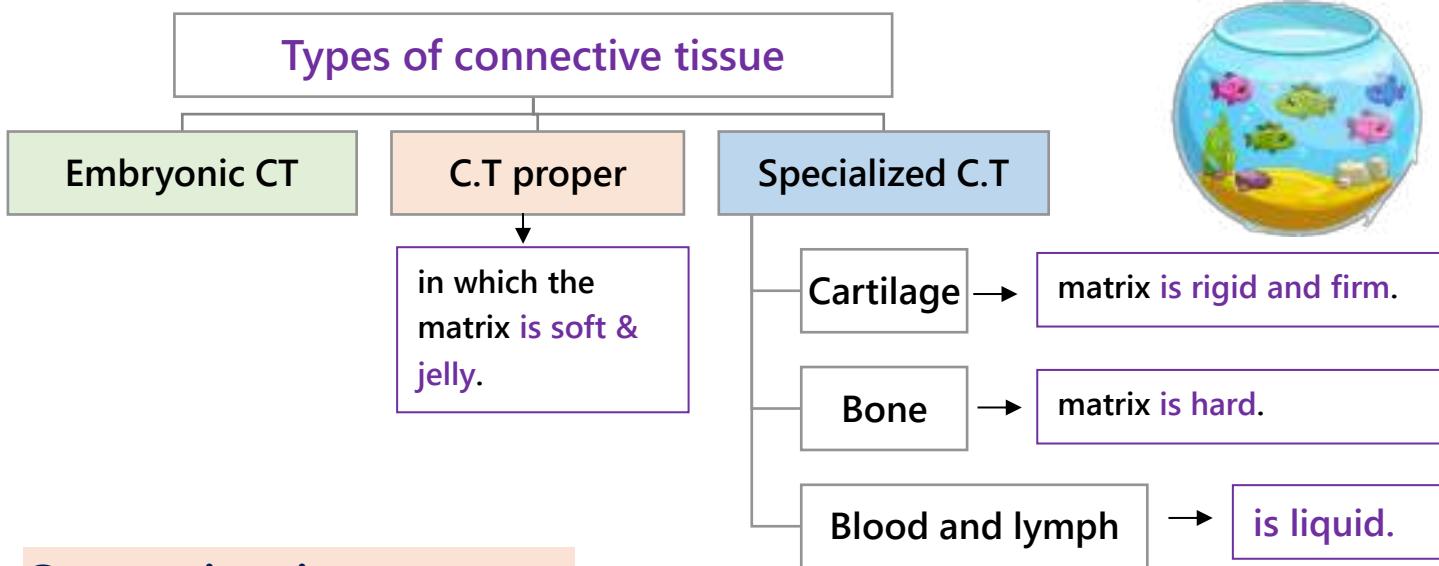
# CONNECTIVE TISSUE



## Objectives

By the end of this chapter the student should be able to know:

- Types of connective tissue.
- Site, origin, histological structure (LM & EM) and function of the cells of connective tissue proper.
- Site, origin, histological structure (LM & EM) and function of the connective tissue fibers.
- Structure and function of ground substances (matrix).
- Site, structure and function of each type of connective tissue proper.



## Connective tissue proper:

It is formed of many types of cells, fibers and jelly like ground substance(matrix)



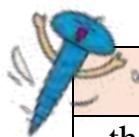
## General function:

- 1- It provides a mechanical **support**, packing and connection for body tissues and organs 🤝
- 2- Its fat cells within the connective tissue provide a **store** for energy. ❤️
- 3- The role of connective tissue in **defending** the organism is related to its content of phagocytic 😊 and immunocompetent cells as well as cells that produce pharmacologically active substances 💊 that are important in modulating inflammation. 🔥





## Cells of connective tissue proper




Fixed cells	Transient cells
<ul style="list-style-type: none"> <li>- they are resident and stable cells that are formed and remain in the connective tissue.</li> <li>ثابتة في مكانها ميتاحركش.</li> <li>عمرها طويل.</li> </ul>	<p>they are free or wandering cells that originate from <b>common stem cell</b> خلية جذعية مشتركة in the bone marrow, circulate in the blood and at proper signal, they leave the blood stream by migrating through the <b>endothelium</b> جدر الأوعية الدموية of blood capillaries or venules into the connective tissue where they are activated. They are <b>motile</b> بتحرك and have short life span عمرها قصير and continually replaced from stem cells.</p>
<p>They include:-</p> <ol style="list-style-type: none"> <li>1. Undifferentiated mesenchymal cells (pericytes in adults).</li> <li>2. Fibroblast.</li> <li>3. Some macrophages (Kuppfer cell).</li> <li>4. Mast cells.</li> <li>5. Adipocytes.</li> </ol>	<p>They include:-</p> <ol style="list-style-type: none"> <li>1. Plasma cell.</li> <li>2. Macrophages.</li> <li>3. Leucocytes خلايا الدم البيضاء (basophils, oesinophils, neutrophils, monocytes and lymphocytes).</li> </ol>

- كل السيتوبلازم اللي هنتكلم عنه بيكون basophilic ما عدا الـ fibrocyte

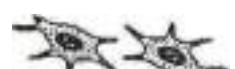
- كل الـ nucleus اللي هنتكلم عنها بتكون oval او قريبه من الماء

أى خلية من دول لازم نعرف عنها ٣ حاجات:

- structure
- function
- origin & site

### 1-The undifferentiated mesenchymal cell (UMC):

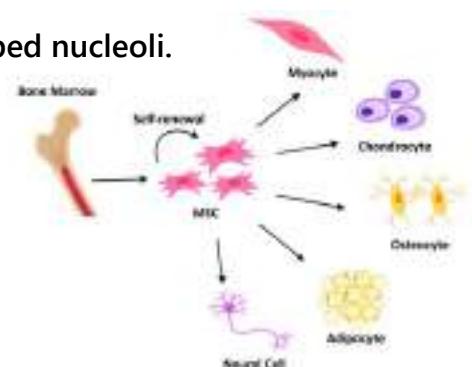
Site and origin: it is present mainly in C.T along the blood vessels. In adult, it is known as **pericyte** along the blood capillaries. It is derived from the **mesoderm**.



#### Structure:

L/M: it appears as a small branching cell with scanty cytoplasm and relatively large, oval and pale nucleus with well developed nucleoli.

E/M: the undifferentiated cell shows few amount of cytoplasmic organelles and the nucleus contains coarse chromatin pattern, any ribosomes. Pericytes have actin, myosin and tropomyosin.

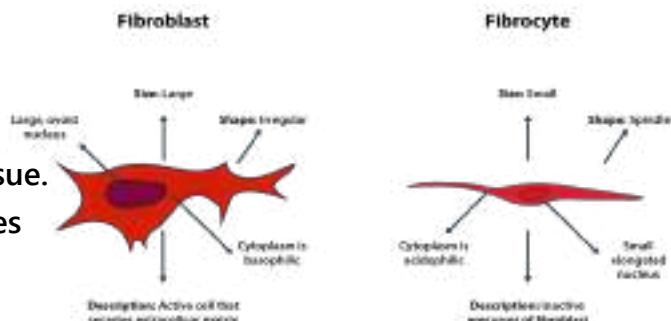


Function: Formation of other connective tissue cells.

## 2- The fibroblast:

Site and origin: It is present in all types connective tissue.

It is derived either from the UMC or from the pericytes



### Structure:

L/M: lies parallel to the long axis of collagen fibers. the shape of fibroblast is large, irregular branching cell with abundant, clear **basophilic** cytoplasm and large, oval and pale nucleus with distinct nucleolus.

E/M: The cytoplasm is rich in organelles responsible for **protein synthesis** (i.e. well developed rough endoplasmic reticulum, a plenty of ribosomes, a well developed Golgi apparatus and many slender rod-shaped mitochondria). The nucleus contains **pale euchromatin**.

Function: It forms all types of connective tissue fibers (collagen and elastic fibers) and secretes the amorphous part of the ground substance.

	Fibrocyte	Myofibroblast
L/M	A smaller cell than the fibroblast tends to be <b>spindle shaped</b> . It has a fewer processes than the fibroblast; a smaller darker, <b>elongated nucleus</b> ; an <b>acidophilic cytoplasm</b> .	A cell with features of both fibroblasts and smooth muscle is observed during wound healing <b>these cells have the morphologic characteristics of both fibroblast and smooth muscle cell</b> . L/M → similar to fibroblasts and it is difficult to differentiate between them.
E/M	It contains a small amount of rough endoplasmic reticulum, few Golgi, few mitochondria and many free ribosomes. When it is adequately stimulated, the fibrocyte may revert to fibroblast state, and its synthetic activities are reactivated .This occurs during wound healing.	Contains increased amount of <b>actin and myosin microfilaments</b> . Their activity is responsible for wound closure following tissue injury (wound contraction).

### 3- Macrophages: the mononuclear phagocytic system.

Site and origin: They originate from common stem cell in the bone marrow then migrate to the connective tissue.



#### Structure:

L/M: they are rounded or oval in shape, having finger like processes, dark and eccentric nucleus which may be **oval or kidney shaped**.

Their cytoplasm is **basophilic** containing vacuoles and phagocytosed particles which can be stained with **vital staining**. When a vital dye such as **trypan blue or India ink** is injected into the body, these cells engulf and accumulate the dye in their cytoplasm in the form of granules.

E/M: they appear irregular in outlines with their surfaces covered with short folds and microvilli. They generally have a well developed Golgi complex, plenty of lysosomes and phagosomes, prominent rough endoplasmic reticulum (Fig. 5-3). In process of stem cell to macrophage transformation, there is an increase in protein synthesis and cell size.

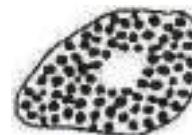
Function: Phagocytosis and digestion of foreign particles.



**NB** Macrophages which are distributed through the body were given specific names before discovery of mononuclear phagocytic system such as:

- Kupffer cells in the liver.
- Monocyte in blood.
- Langerhans cells in the skin.
- Microglia in C.N.S.
- Osteoclast in bone tissue.
- Dust cells in the lung.

### 4- Mast cell:



Site and origin: It is concentrated along the blood vessels especially in digestive and respiratory systems. It is derived from UMC or from the pericyte.

#### Structure:

L/M: it is oval to round in shape, its cytoplasm is filled with basophilic granules which can be stained **metachromatically** (they take a different color than that of the dye used e.g. they are stained reddish purple with **toluidine blue**, this is because it enters into chemical reaction with the dye, producing another compound having a different color. Central rounded nucleus that may be masked by the cytoplasmic granules.

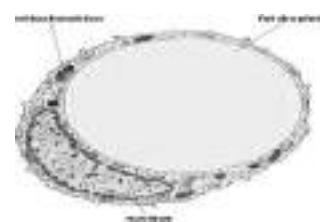
E/M: its cytoplasm contains a few small special mitochondria, short cisternae of rough endoplasmic reticulum, a well developed Golgi complex and many dense granules which are heterogeneous and surrounded by a unit membrane containing either particles or lamellar structure.

Function: mast cell acts in mediating inflammatory response and immediate hypersensitivity reaction.

## 5- Fat cell (adipocyte):

Site and origin: They are present in the ordinary C.T. mainly in the adipose connective tissue along the blood vessels. It is derived most probably from UMC or the pericyte.

- They are **fully differentiated** cell (**cannot divide**).
- They are of two types; unilocular and multilocular adipocytes.



### Unilocular adipocytes:

more abundant and form white adiposeconnective tissue.

#### Structure:

L/M: it appears large oval or rounded in shape with oval or flat peripheral nucleus.

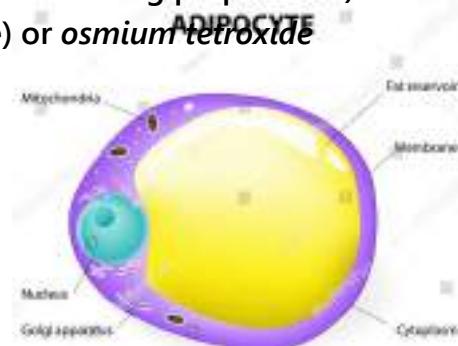
Its cytoplasm contains **single fat globule** filling most of the cell thus giving a signet-ring appearance.



In H & E sections, fat cells appear as **empty** spaces (because fat is dissolved during preparation). Films, smears or frozen sections can be stained with *sudan III* (orange) or *osmium tetroxide* (black).

E/M: The cytoplasm appears to contain a small number of ovoid mitochondria, a small filamentous Golgi complex, poorly developed cisternae of /rough endoplasmic reticulum, some free ribosomes, some vesicles of smooth endoplasmic reticulum and occasional microtubules.

The fat droplets are not surrounded by a membrane



### Multilocular adipocytes:

less abundant and form brown adiposeconnective tissue

#### Structure:

L/M and E/M: The same as unilocular adipocytes but they appear smaller with rounded nucleus. Its cytoplasm contains multiple small fat globules filling most of the cell and more mitochondria.

Function: Synthesis, storage and release of triglycerides.

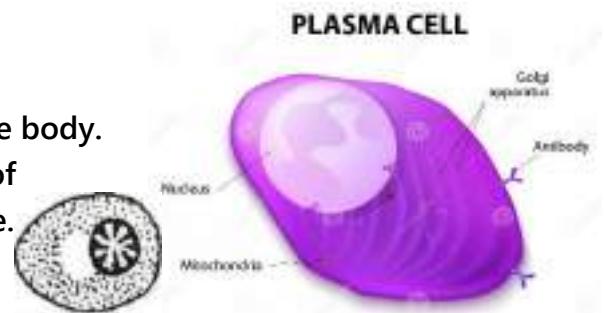


## 6- Plasma cell:

### Site and origin:

Plasma cells are few in number in C.T. in most areas of the body.

They are numerous in the lymphatic tissue and the C.T. of the alimentary tract and it is derived from B lymphocyte.



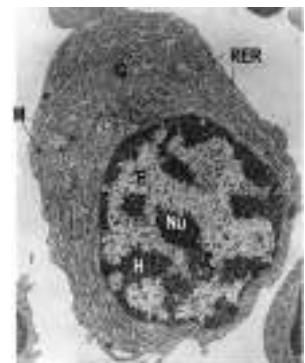
### Structure:

L/M: it appears large oval or rounded cell with well defined border.

Its cytoplasm is deeply **basophilic** with a pale unstained area near to the nucleus which is the site of the Golgi. ([\(Negative Golgi image?\)](#))

- Its nucleus is **eccentric, rounded** with coarse chromatin which may have a **cart-wheel appearance** with a prominent nucleolus.

E/M: Its cytoplasm contains well developed R.E.R. with enlarged cisternae, a well developed Golgi apparatus and secretory vesicles



**Function:** They are immunologically functioning cell, capable of synthesizing and secretion of specific protein (immunoglobulin or antibodies).

## The leucocytes (white blood cells):

Site and origin: They are frequently found in C.T.

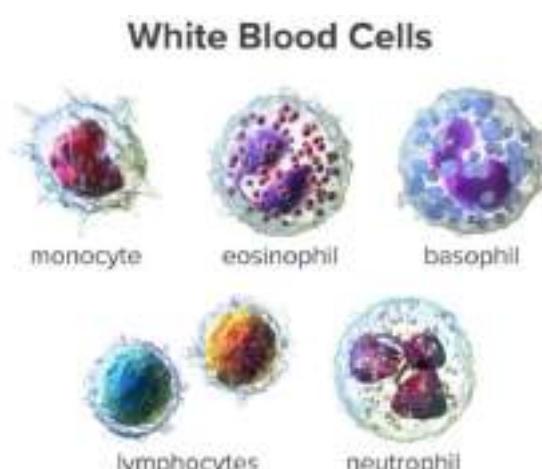
They are migrating across capillary and venule walls from the blood especially during inflammation. Their origin from the bone marrow and are described in details with the blood.

Types: there are two types

1- Granular which are neutrophil, eosinophil and basophil.

2- Non granular which are lymphocyte and monocyte.

Structure and function: described in details with the blood.



## Connective tissue fibers

### 1-The collagenous (white) fibers:

Site and origin: They are tough, firm inelastic fibers that resist tensile forces.

- They are present in most types of connective tissue.
- They are secreted by the fibroblasts, chondroblasts, osteoblasts and odontoblasts.



#### Structure:

L/M: The single fresh fiber appear colorless, however in bundles, they appear white and opaque. The fibers are thick of 1-20  $\mu\text{m}$  in diameter depend on the number of fibrils, with each fiber formed of finer fibrils (75nm) held together by a cementing substance.

These fibrils give the fiber its longitudinal striation.

The fibers do not branch, while the bundle can.

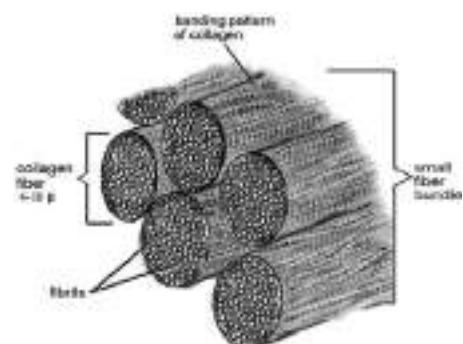
By H&E, they appear as wavy pink (acidophilic).

They appear red by van Gieson's stain; blue by Mallory's stain and green by Masson's trichrome.

E/M: Each collagen fiber is formed of fibrils.

Each fibril is formed of parallel microfibrils.

Each microfibrils is composed of elongated macro-molecules lying end to end in parallel rows.



#### Types of collagen fibers:

According to the **sequence of amino acids** in the alpha chains, 12 types of collagen are recognized, the most common are:

Type I: Which is present in ordinary C.T. and bone.

Type II: Which is present in hyaline cartilage.

Type III: Which is present in fetal dermis, loose C.T., blood vessels, uterus and stroma of various glands.

Type IV: Which is present in basal lamina of epithelia.

Type V: Which is present in basal lamina of epithelia and external lamina of smooth and striated muscles.

Type VII: Present in epithelium.

Type IX: Present in cartilage and vitreous body.

Type XI: Present in cartilage.

Type XII: Present in embryonic tendon and skin

## Function:

The collagen fibers have a **mechanical** importance in loose C.T. They strongly **resist a pulling force** and they are **flexible** but not **elastic**.

### 2- The elastic (yellow) fibers:

**Site and origin:** They are present in sheets in blood vessels and bundles in ligaments such as ligamentum flavum. They are secreted by the fibroblasts and the smooth muscle.



## Structure:

**L/M:** They are straight, thin and long which branch to form network.

The single fresh fiber appears colorless, however when old or inmass, they appear yellow with high refractive index.

They stain **pale pink** in H&E and **brown** with **orcein dye**.

**E/M:** Each fiber is formed of a central core of elastin protein surrounded by sheath of microfibrils.

They are homogenous with no periodicity.

## Function:

They are elastic so they **stretch easily** but **return** to their original shape when the forces are removed.

### 3- Reticular (argyrophil) fibers:

**type III collagen:**



**Site and origin:** Present in stroma of many organs. They are secreted by the fibroblasts and reticular cells.

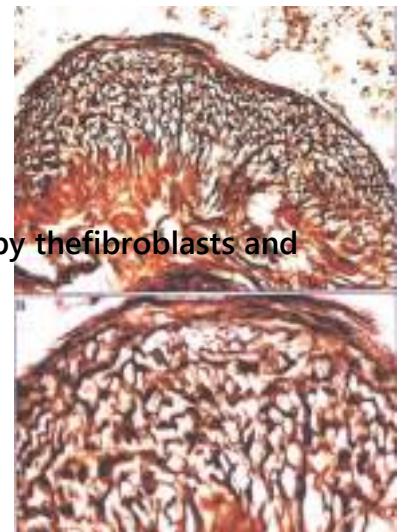
## Structure:

**L/M:** They are very thin, appear colorless.

They run straight or a wavy course.

They branch and anastomose forming a network.

They **cannot** be seen by H & E; however they appear as **dark brown fine network** by silver staining, also can be stained with PAS.



**E/M:** Each fiber is formed of parallel microfibrils with transverse striation at a periodicity of 64 nm as the collagen fibers.

**Function:** Reticular fibers form delicate network in the stroma of the glands and solid organs.

## Ground substance (Matrix)

It is homogenous transparent soft or jelly like substance in which the cells and fibers are embedded.

**It is composed of 2 components:**



- (1) Amorphous component (long unbranched disaccharides): **secreted by the fibroblasts**  
It is a viscid, colorless, transparent substance secreted by the fibroblasts.  
It is formed of protein core to which glycosamino-glycans (hyaluronic acid and chondroitin sulphate) are linked and adhesive glycoproteins that are responsible for adhesion of various components of extracellular matrix together.
- (2) Tissue fluid component:  
- **It is derived from the capillaries.**  
- It is formed of the crystalloid of the plasma and few colloids (protein of low molecular weight).

**Function:** It provides strength and support.

## Types of connective tissue

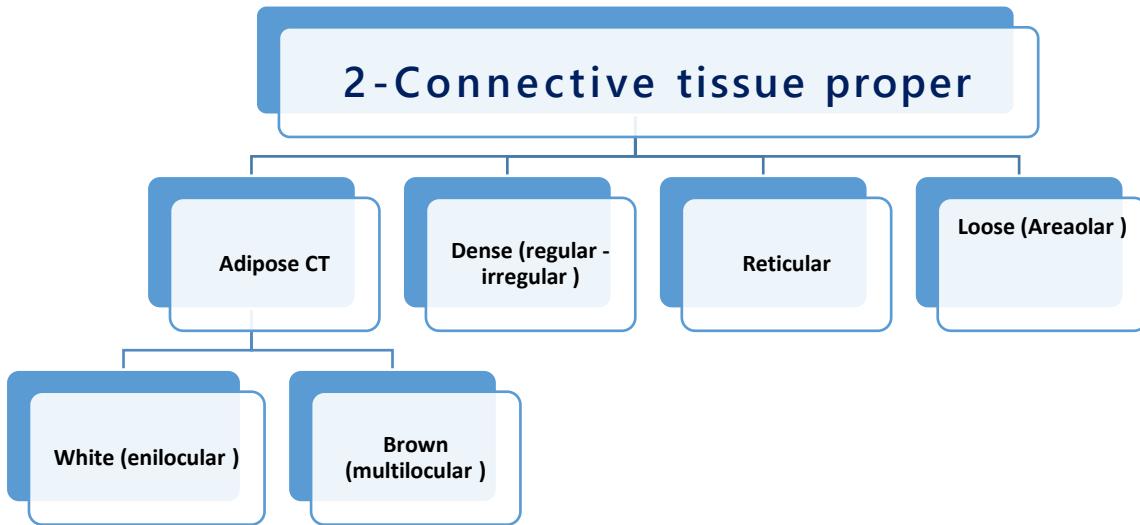
### 1- Embryonic connective

#### (1) Mesenchymal connective tissue.

It is present only in embryo, consisting of UMC, reticular fibers and amorphous ground substance. UMC are scattered through the embryo and in adults present only in tooth bulb and vitreous body of the eye and replaced by perivascular pericytes in adults.

#### (2) Mucous (mucoid) connective tissue.

It is present in the umbilical cord, consisting of fibroblasts and type I & III collagen fibers and jelly like matrix, so called Wharton's jelly connective tissue



### 1. The loose (Areolar) connective tissue:

It is present all over the body; filling the spaces, supports epithelial, forms a layer that ensheathes the lymphatic and blood vessels and also binding tissue and organs e.g. papillary layer of the dermis and in hypodermis, submucosa of the alimentary and respiratory tracts.

-Loose C.T. comprises all the main components of C.T. proper. The most numerous cells are fibroblasts and macrophages, but all the other types are present also. Collagen, elastic and

- Reticular C.T. fibers are appearing in this tissue. A major constituent of loose C.T. is the amorphous ground substance.

**Functions:** Its functions are the sum of the functions of its components (cells, fibers and matrix).

### 2. Dense connective tissue:

- It consists of dense C.T. fibers, fewer cells and little matrix.
- It is either; irregular or regular.

#### a- Dense irregular connective tissue:

- It is formed of irregular bundles of collagen fibers, few elastic fibers and fibroblasts in between them.
- It is present in most fascias, most sheathes (perichondrium, periosteum, dura mater, capsules and trabeculae of organs).

**Functions:** - It provides strength, flexibility and support for the organs.

- It provides sites for the attachment of muscles.

b- Dense regular connective tissue: either collagenous or elastic.

**Dense regular collagenous connective tissue:**

- It is present in cornea of the eye and tendon of muscles.
- It is white in color in fresh state due to the high content of collagen fibers.
- It is formed mainly of parallel bundles of collagen fibers which are separated from each other by areolar C.T. containing blood vessels, and lymphatic.
- The fibroblasts usually pass between and parallel to the fibers. Has a minimal matrix with poor blood supply.

**Dense regular elastic connective tissue:**

- It is an elastic type of C.T. which appears yellow in fresh condition.
- It is formed of condensed elastic fibers separated with areolar C.T. and fine collagenous fibers in between and few fibroblasts.
- It can be stained brown with orcein stain.

It is present in ligamenta flava (between the vertebrae), true vocal cords, ligamentum nuchae (in the back of the neck) and suspensory ligament of penis and large arteries.

**Functions:** It provides strength with ability to be stretched and return to the original form.

**(3) Adipose connective tissue:**

- It is similar to areolar C.T. in containing all its cells and fibers but very rich in fat cells.
- Fat cells form lobes and lobules.

**It is of two types:**

**a) The white (unilocular) adipose C.T.:**

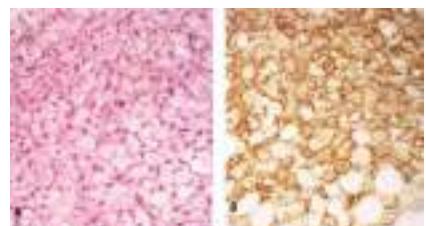
- It is present in: subcutaneous C.T., cheeks, omentum and mesenteries, axilla, in female mammary gland and gluteal region and around important organs (heart and kidneys).
- It is white or yellow in color due to the presence of carotenoids (normal color of the fat).
- It is formed of large adipocytes which contain one single fat globule, few mitochondria, and a small Golgi and small amount of smooth endoplasmic reticulum.

**Functions:** It acts as heat insulator and as fat storage area.

It gives the skin of the body its normal shape.

**b) The brown (multilocular) adipose C.T.:**

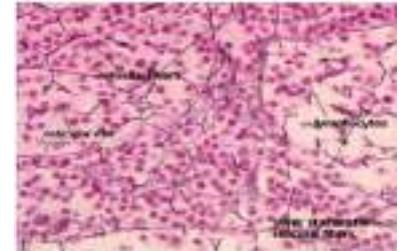
- It is present in mediastinum, between scapula and around the aorta of the fetus and young children.
- It is brown in color due to numerous blood capillaries.
- It has high mitochondrial cytochrome content
- The lysosomes contain brown pigment.





-It is formed of small adipocytes which contain multiple fat droplets, large number of mitochondria with numerous lysosomes with oval nucleus.

**Functions:** It acts as heat generators to warm the body when stimulated by adrenaline and nor-adrenaline. May transform into white type.



#### (4) Reticular connective tissue:

-It is present in the stroma of organs, glands and bone marrow.

-It is formed of a network of reticular fibers and reticular cells.

-The reticular cells are stellate shape with large pale nucleus

and many processes, the cells are continuous with each other by their process.

These cells resemble the U.M.C.; they can differentiate to macrophages, fibroblasts and other cells.

→ It can be stained brownish black with silver.

**Functions:** It provides support for organ architecture.

Made with love  
specially for BFOM 43



لا تنسونا من صالح دعائكم







## L18 Chromosomal structure and karyotyping

### Chromosomes:

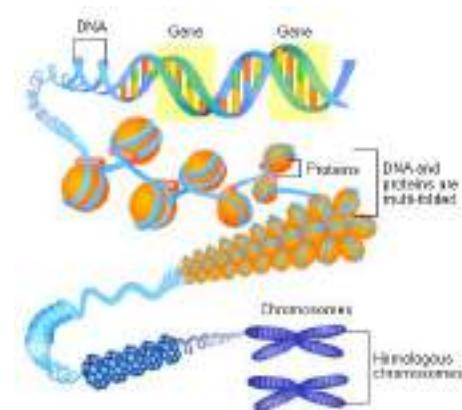
The nucleus is the organelle that houses chromosomes

Chromosomes consist of DNA, which contains heredity information and instructions for cell growth, development, and reproduction

- Chromosomes are present in the form of strings of double stranded DNA and **histones** (protein molecules) called chromatin.

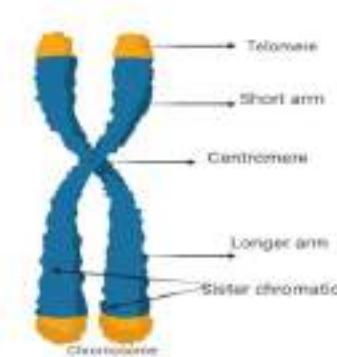
- The repeated units of chromatin granules called **nucleosomes**.

- When a cell is "resting" i.e. not dividing, the chromosomes are organized into long entangled structures called **chromatin**.

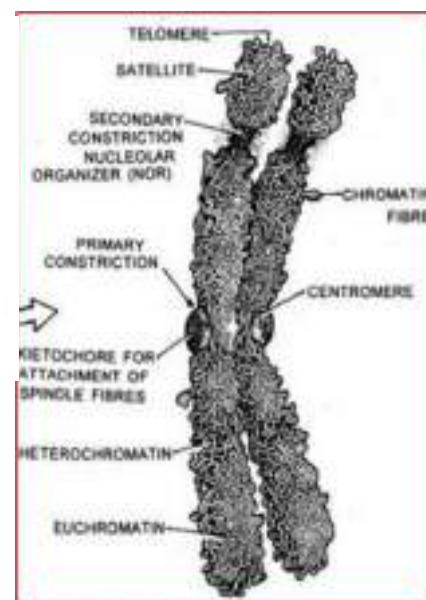


### Morphology:

- The chromosome appears as a cross-shaped structure due to the union of its 2 chromatids (S-chromosomes) at the central region known as the **centromere**.



- It has 4 arms radiating from the point of the centromere (long arm → q and short arm → p ).
- The stainability of the chromosome is not homogenous along the whole length of its chromatids.



### Classification:

#### A) According to the position of centromere:

The chromosome may be:

- Metacentric chromosomes:** Centromere lies near the middle of the chromosome such as chromosomes number **1, 3, 16, 19 and 20**, where p arm is equal to q arm.

- Submetacentric chromosome:** Centromere is present midway between the center of chromatids and their upper ends such as chromosomes number **2, 4 to 12, 17, 18 and X** chromosome, where p arm is shorter than q.

- Acrocentric chromosomes:** Centromere is present near one end thus the short arm p is very small such as chromosomes number **13, 14, 15, 21, 22 and Y** chromosome.

- Telocentric chromosomes:** Centromere is present at the terminal end (not in human).



### B) Denver classification:

The chromosome set can be classified into 7 groups

(A \_ G) in according to the chromosome length, the position of the centromere and the presence of specific landmarks.

- **Group A:**

-Chromosome 1,2 and 3.

-Large with approximately median centromeres.

-Chromosome 1 is the largest **metacentric** chromosome.

-Chromosome 2 is **submetacentric**.

- **Group B:**

Chromosome number **4-5**, they are large and **submetacentric**, chromosome number 4 is longer.

- **Group C:**

Chromosomes number **6-12** and **X** chromosome, they are medium sized and **submetacentric**. The chromosomes are arranged according to decreasing size pattern. Secondary constriction found in chromosome 9. Chromosome 12 has the smallest short arms of the group.

- **Group D:**

Chromosome **13, 14 and 15**.

Median-sized **acrocentric**. and have satellites.

- **Group E:**

-Chromosomes number **16 to 18**, they are smaller than Group D.

-chromosome 16 is **metacentric** and has secondary constriction and chromosomes **17 and 18** are **submetacentric**.

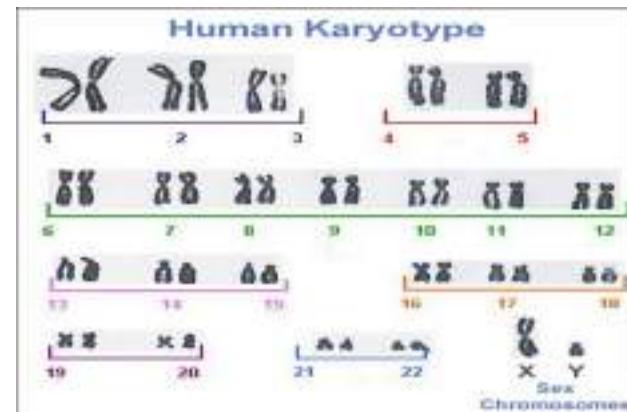
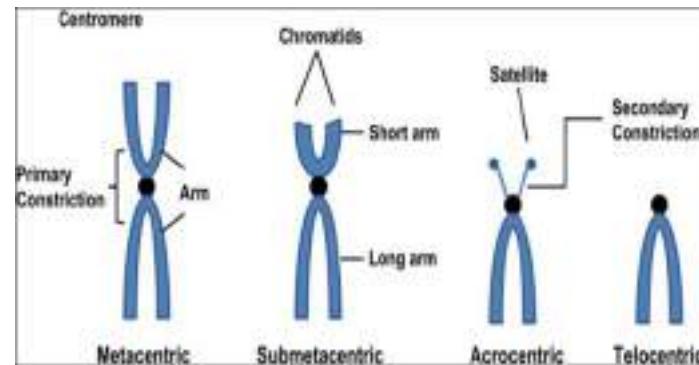
- **Group F:**

Chromosomes number **19 and 20**, they are short and **metacentric**.

- **Group G:**

-Chromosomes number **21, 22 and Y**, they are very short **acrocentric** chromosomes.

-Chromosomes 21, 22 are the smallest and contain satellites.





N.B:

\*Within these groups, chromosomes are arranged in descending order of length with their centromere on the same line.

\*The X chromosome is long, while the Y chromosome is short.

\*in female, one of the 2 XX chromosomes is inactive and remain highly condensed and stain darkly during interphase forming a Barr Body.

### X chromosome:

- It is one of the longest two or three chromosomes in the group C .

- In female, one X is stained slightly darker than the other.

### Y chromosome:

- Longer than 21 & 22.

- Long arms are less divergent.

- No secondary constrictions on the short, thus no satellites.

- Centric constriction is indistinct.

- Secondary constriction is seen in long arm.

- The terminal region of long arm are poorly defined.

- Usually found toward the periphery of the metaphase preparation.

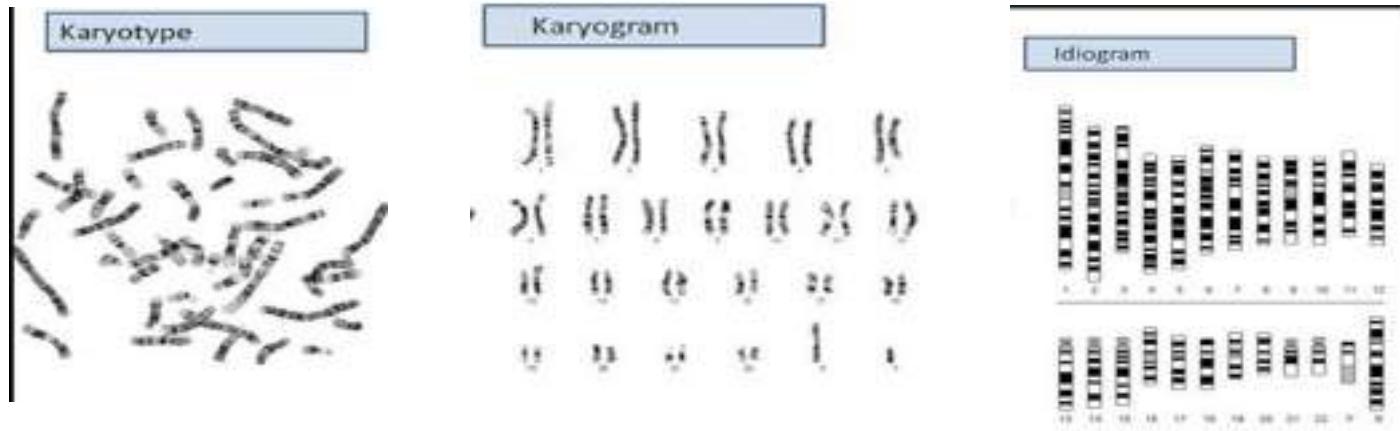
### Cytogenetics and karyotyping

**Cyto-genetics:** is a word for the study of chromosomes

**Karyotype:** is the number of chromosomes in a particular person

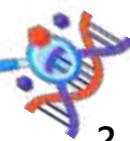
**Karyogram:** the array of chromosomes in a form suitable for analysis is ch.

**Ideogram:** is a schematic diagrammatic representation of the karyotype showing all the morphological features of chromosomes(chromosomes arranged in order of decreasing length, showing the location of genes as bands)

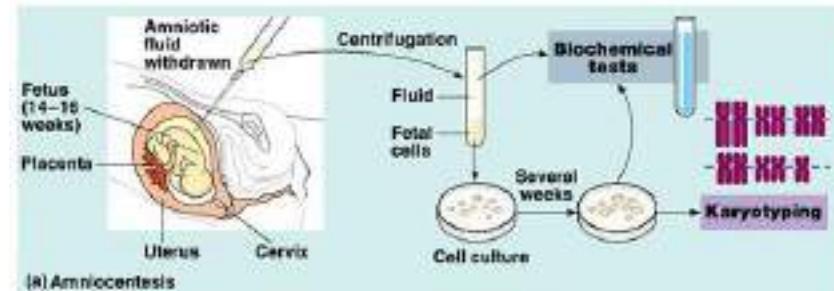


### Clinical importance of chromosomal study

1. Chromosomal studies and chromosomal mapping help in diagnosis of certain diseases and syndromes as Down's syndrome, mental retardation, abnormal sexual development as Turner and Klinefelter syndromes.



2. Diagnosis of repeated spontaneous abortion, and infertility.
3. Diagnosis of certain malignant diseases as chronic myeloid leukemia.
4. Karyotyping of fetal cells from amniotic fluid helps in prenatal diagnosis.
5. determination of the sex of the fetus.

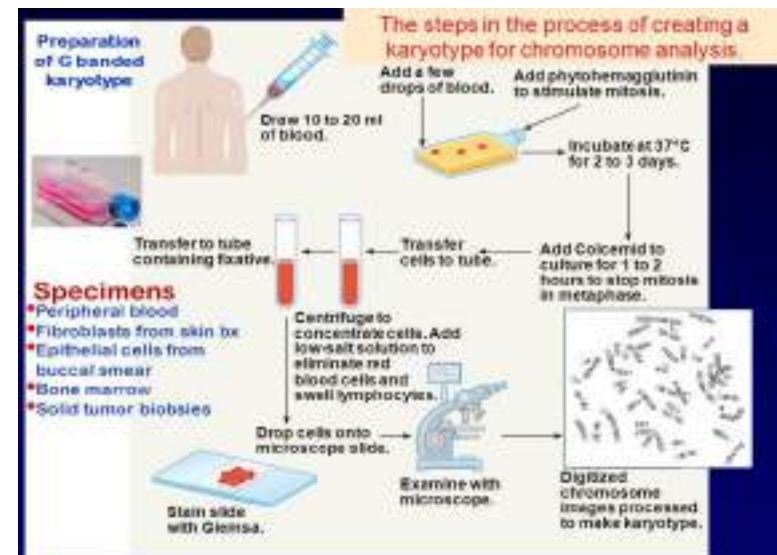


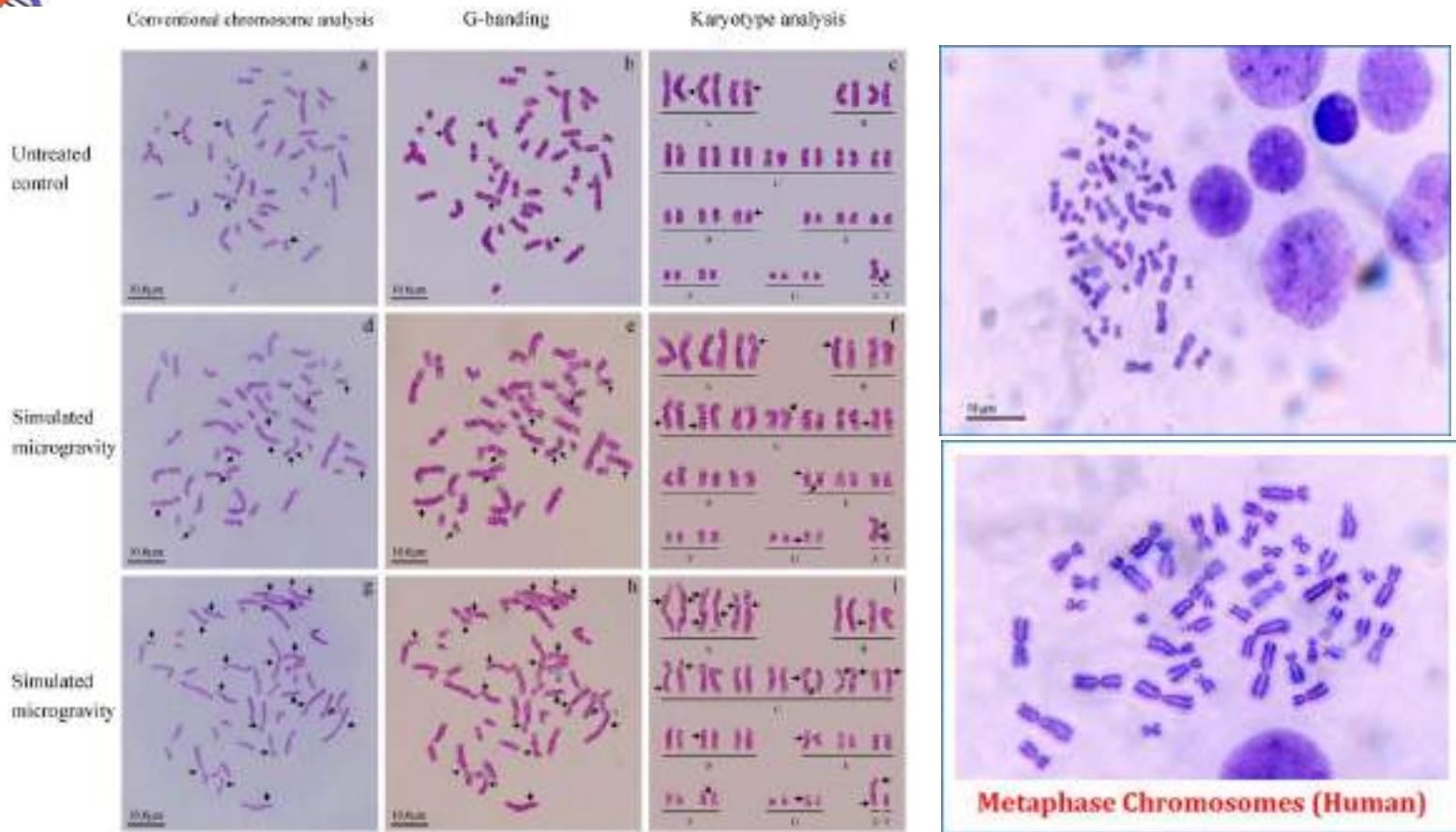
### Principal of chromosomal study:

- The morphology of a chromosome can best study at metaphase.
- The need of cells in metaphase requires tissue with a sufficient number of dividing cell (blood- bone marrow)
- The division of the cells is stimulated by addition of **phytohaemagglutinin** to the culture media.
- The basic steps in chromosome preparation of all tissues are the **disruption of the spindle apparatus** by **colchicine** (colcemid)
- The swelling of the cells obtained by **hypotonic solution**.
- The **spreading** of chromosomes on slides.
- **Staining by Giemsa** for G banding.

### Samples: are obtained from:

1. Peripheral blood leucocytes: provide the shortest and most convenient method for routine cytogenetic analysis. This takes 3 days.
2. Amniotic fluid.
3. Chorionic villus.
4. Fibroblasts.
5. Solid tumors.
6. Tissue effusion.
7. Lymph nodes and spleen.
8. Bone marrow (as from leukemic patients), it has high mitotic rate.





### Metaphase spread of chromosomes (karyotyping)

#### Identification of chromosomes:

##### 1-Morphological approach:

- Arms long or short

- Centromeric position

- Morphological features

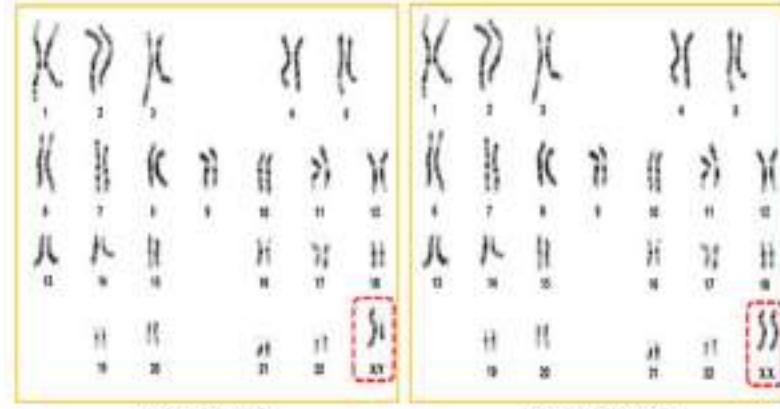
##### 2-Autoradiography:

Permits the localization of radioactive substances in tissue by means of the effect of **emitted radiation** on photographic emulsion.

##### 3-Chromosomal banding:

It is a part of chromosome that is clearly distinguishable from its adjacent segments by appearing darker or lighter as a result of new staining.

HUMAN KARYOTYPE (NORMAL)



Male (44XY)

Female (44XX)





### Types of banding:

a) Quinacrine-bands (Q-bands)

b) Giemsa-bands (G-bands)

\*The most frequently used type of banding is G banding.

\*This name is derived from the Giemsa stain.

c) Reverse-bands (R-bands) (reverse of G)

d) Constitutive heterochromatin bands (C-bands) (centromeric)

e) T bands (telomeric)

f) High resolution banding.

•When they are stained, the mitotic chromosomes have a banded structure that identifies each chromosome of a karyotype.

•Each band contains millions of DNA nucleotide pairs.

•metaphase chromosomes exhibit light and dark bands under appropriate staining conditions.

•The short arm, p, and the long arm, q, are divided into regions then bands which are then subdivided into sub-bands moving outwards from the centromere, band 1 being the nearest to the centromere.

Centromeres and telomeres are not

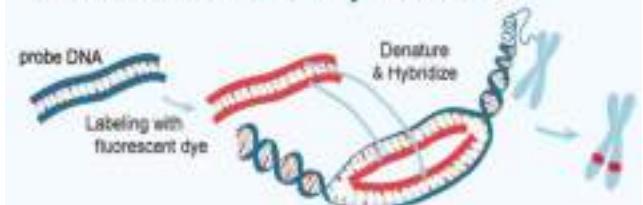
•numbered



### 4-Fluorescence In Situ Hybridization (FISH):

Used to visualize karyotypes using different combinations of DNA probes that bind to specific DNA sequences for each chromosome to produce spectral or sky karyotypes.

#### Fluorescence In Situ Hybridization



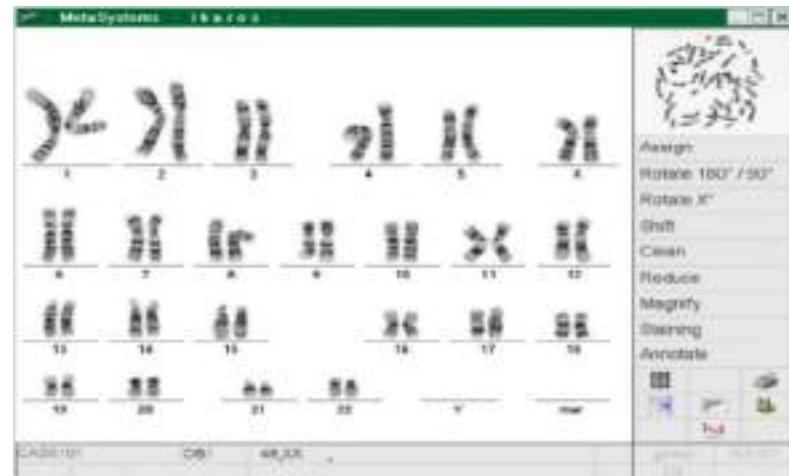
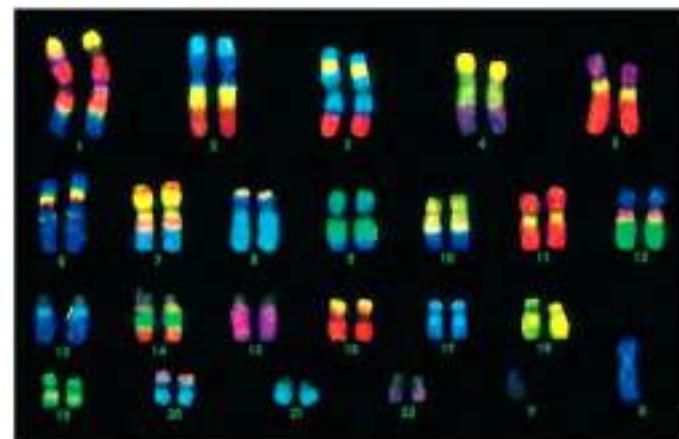


### How does FISH work?

-FISH involves the preparation of short sequences of single-stranded DNA, called probes, which are complementary to the DNA sequences needed to paint and examine.

-These probes which are labeled with fluorescent tags bind, to the complementary DNA and can be detected by fluorescent microscope.

-Unlike most other techniques used to study chromosomes, which require that the cells be actively dividing, FISH can be performed on non dividing cells, making it a highly versatile procedure.





## L19 : Numerical chromosomal abnormalities

### Number of chromosomes

Somatic cells	Gametes
(present in the whole tissues of the body) contain 46 chromosomes 22 pairs of identical chromosomes (autosomes) and one pair of sex chromosomes (XX or XY)	(sperms or ova) 22 autosomes plus X chromosome in female and plus, either X or Y chromosome in male

Male

Female

[twinkl.com](http://twinkl.com)

### Chromosomal Aberrations (Abnormalities)

It means variation in chromosomal number, structure or both.

- **Numerical aberrations:** there is abnormalities in the number of chromosomes.
- **Structural aberrations:** there is abnormalities in the structure of chromosomes

#### Causes of chromosomal aberrations:

1. Exposure to radiation.
2. Drugs as cytotoxic drugs e.g., endoxan.
3. Infection with German measles .
4. Pregnancy in old age.
5. Presence of chromosomal imbalance in the parents or in their families (family tendency).
6. Autoimmune diseases and hypothyroidism.

### Chromosomal aberrations

#### 1. Numerical aberrations

- Aneuploidy
- Polyploidy    1- triploidy              2- Tetraploidy              3- pentaploidy

#### 2. Structural aberrations

- |                    |                  |
|--------------------|------------------|
| 1- Deletion        | 6- Isochromosome |
| 2- ring chromosome | 7- Duplication   |
| 3- inversion.      | 8- Dicentric ch. |
| 4- Translocation   | 9- Fragile ch.   |
| 5- Insertion       |                  |



## Aneuploidy

Trisomy	Monosomy
<p><b>A- trisomy of autosome:</b>            -Down syndrome (trisomy 21),            -Edward syndrome(trisomy18)            -Patau syndrome (trisomy13).  <b>B-trisomy of sex chromosome</b>            -Klinefelter syndrome (47, XXY)            -super female (47, XXX)            -super male (47, XYY).</p>	<p><b>A- monosomy of autosome</b>  <b>B- Monosomy of sex chromosome:</b> Turner syndrome; 45, XO</p>

### Numerical Anomalies

#### 1- Aneuploidy

**Def:** It means variation in chromosome number range from addition or loss of one or more chromosomes.

**1- Monosomy:** means the loss of single chromosome as in

##### **A- Monosomy of autosome:**

- ≡ Autosomal monosomy is rarely observed in spontaneously aborted fetuses or in live births.
- ≡ All complete autosomal monosomies- lethal
- ≡ Can survive in mosaic forms.

##### **B- Monosomy of sex chromosome:** Turner syndrome; 45, XO

- In order to survive and develop embryo needs at least one X chromosomes

#### 2- Trisomy:

means possessing three copies of a particular chromosome instead of the normal two copies (disomy).

There is gain of one extra chromosome.

Most autosomal tri-somies are also lethal except some notable exceptions

##### **A-Trisomy of autosomes: as in :**

Down syndrome (trisomy 21) .  
 Edward syndrome (trisomy 18)  
 Patau syndrome (trisomy 13)

##### **B-Trisomy of sex chromosomes: as in**

Klinefelter syndrome (47, XXY)  
 super female (47, XXX)  
 super male (47, XYY).



## Trisomy of autosome



Fig. Karyogram of male trisomy 21 (Down syndrome; 47, XY, +21).

## Trisomy of autosome

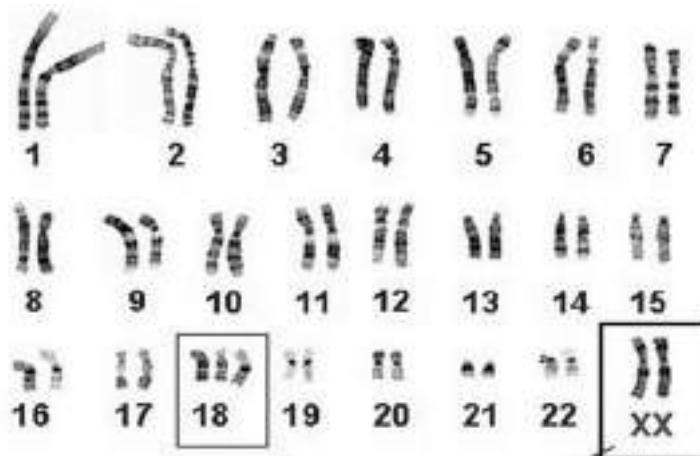


Fig. Karyogram of female trisomy 18 (Edward syndrome; 47, XX, +18)

## Trisomy of autosome

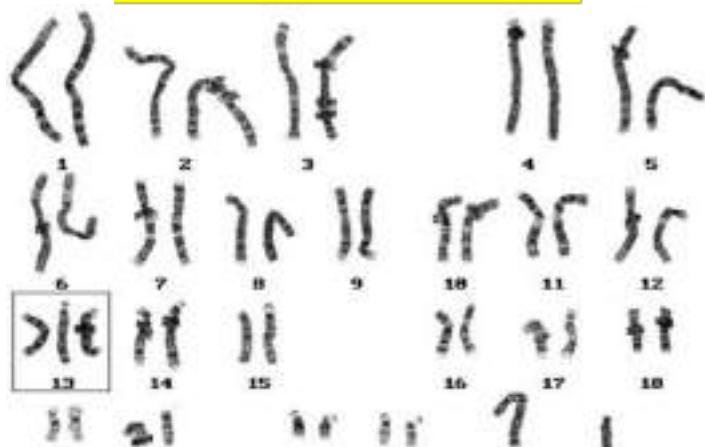


Fig. Karyogram of male trisomy 13 (Patau syndrome; 47, XY, +13).

## Trisomy of sex chromosome



Fig. Karyogram of trisomy sex chromosome (Klinefelter syndrome; 47, XXY)

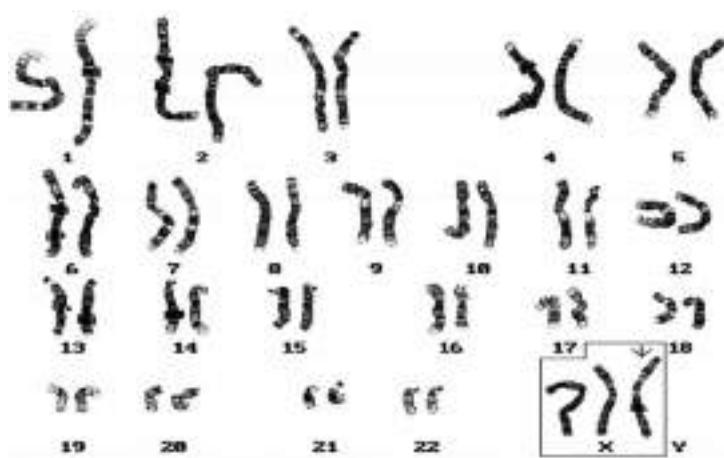
## Monosomy of sex-chromosomes



Fig. Karyogram of monosomy (Turner syndrome; 45, XO).

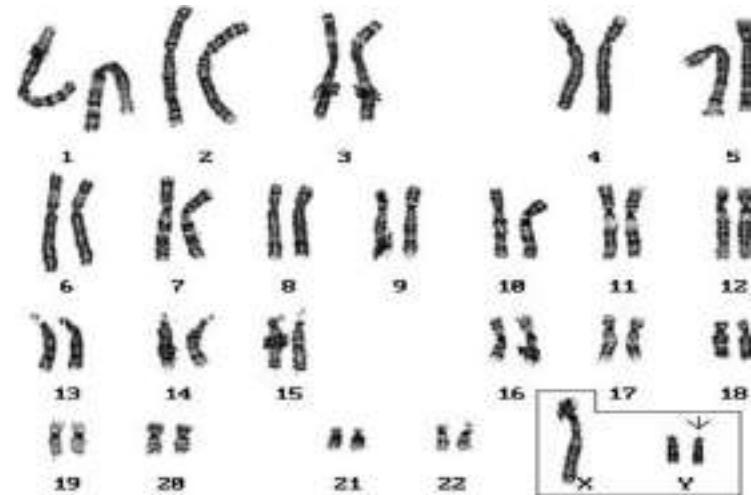


### **Trisomy of sex chromosome**



**Fig. Karyogram of trisomy sex chromosome (super female; 47, XXX)**

## **Trisomy of sex chromosome**



**Fig. Karyogram of trisomy sex chromosome (super male; 47, XYY)**

# CAUSES OF ANEUPLOIDY

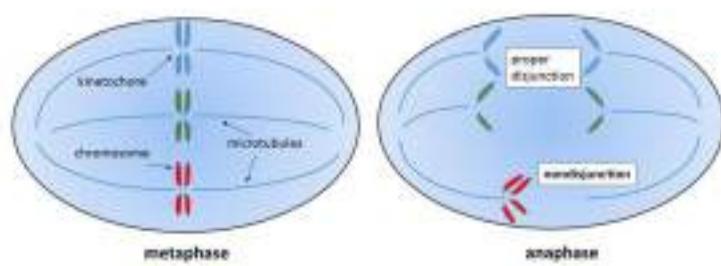
## A- Nondisjunction:

An accident of meiosis or mitosis in which a pair of homologous chromosomes or a pair of sister chromatids fail to separate at anaphase.

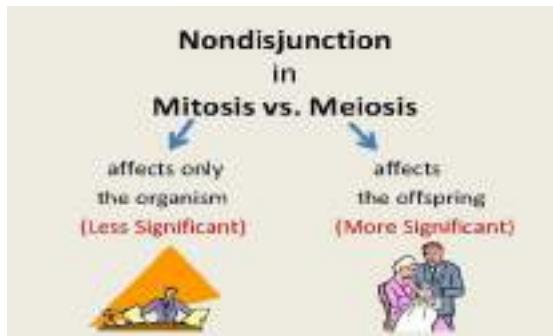
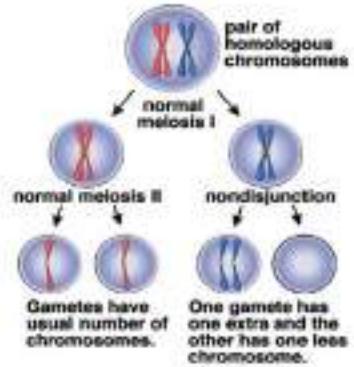
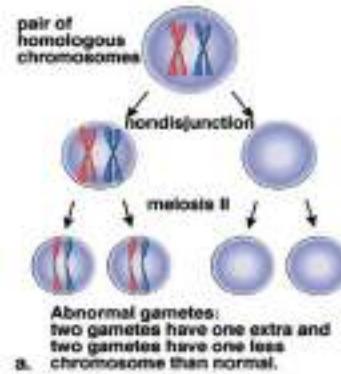
- Gaining a single chromosome, in addition to its pair (s) will result in daughter cell (s) having a defect that is referred to as trisomy.
  - The deletion of a chromosome in a daughter cell is referred to as monosomy.

## Nondisjunction in mitosis

It causes mosaicism



## **Nondisjunction of chromosomes during meiosis**



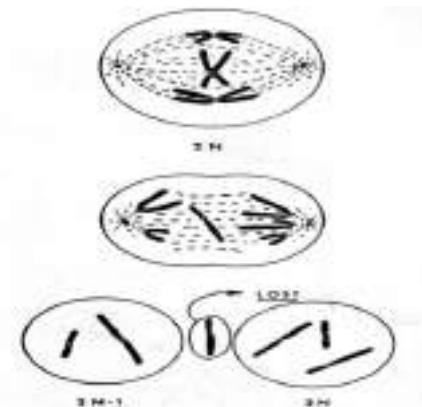


**NB:** Nondisjunction in mitosis does not affect offspring because it does not occur during the production of gamete (sex) cells!

### B- Anaphase lag:

chromosomal loss via micronucleus formation Caused by delayed movement of one chromosome or chromatid at anaphase. Resulting in daughter cell deficient of that chromosome or chromatid.

**Mosaicism :** Means that an individual with two cell lines derived from the same zygote. This is due to nondisjunction or anaphase lag.



## 2- POLYPLOIDY

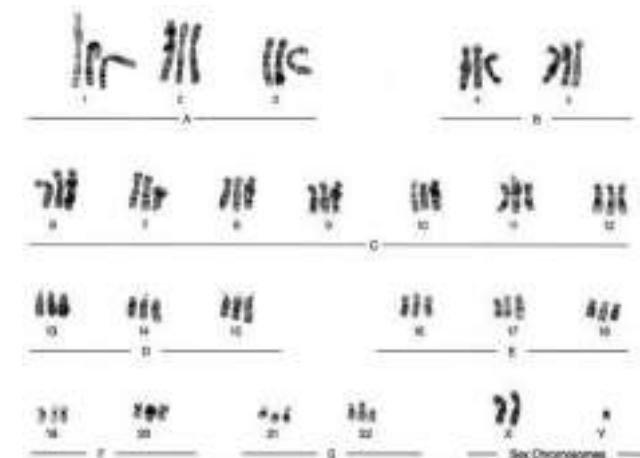
**Def:** It is a defect of a genome level; affecting the total haploid set (N)

**Triploidy:** is a term applied when the cell contains 3 chromosomes of each member

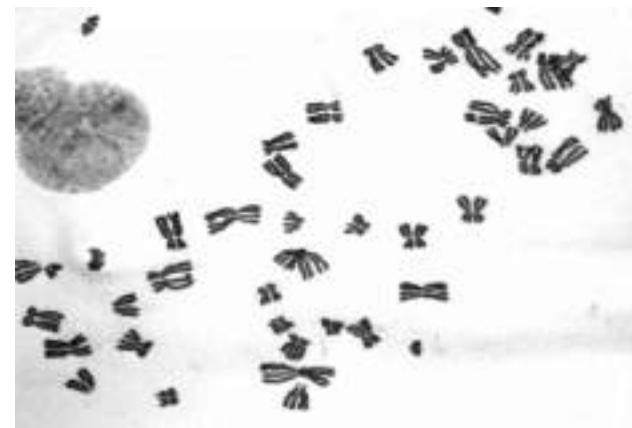
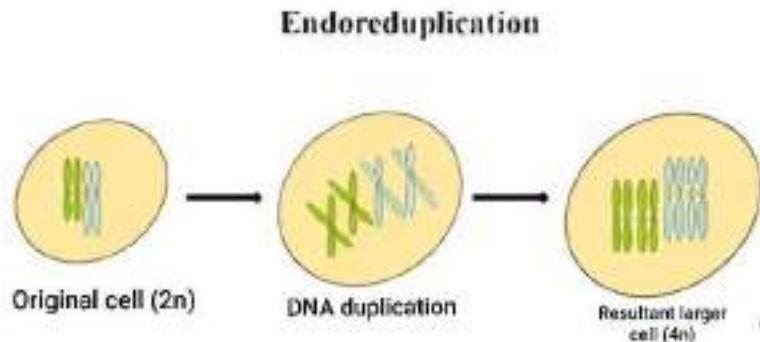
Similarly, tetraploidy, pentaploidy, polyploidy.

**NB:** Endoreduplication : is a special case of tetraploidy.

- There are two sequential DNA replications In S phase. Cell enters division containing 92 d chromosomes.
- Each chromosome pair appears to have another homologous pair in close apposition to it.



**Fig. Karyogram of triploidy; 69, XXY.**



**Fig: endoreduplication result of two sequential DNA replications.**



### Causes of chromosomal abnormality:

- **Spindle apparatus defects:** There is paralysis of the spindle apparatus results in failure of cytokinesis.
- **Abnormal separation of polar bodies:** failure of the second polar body to be extruded from the fertilized ovum with subsequent fusion with the male and female pronuclei lead to the formation of triploid zygote.
- **Abnormalities during oogenesis or spermatogenesis,** resulting in an abnormal oocyte or spermatozoon with a double chromosome complement (46, XX) instead of a haploid complement (23, X) .
- **Di-spermy** or fertilization of a normal egg by two normal sperm.
- **Drugs** affecting microtubule system as colchicine and vinblastine.
- **Virus infection** as rubella virus of German measles.



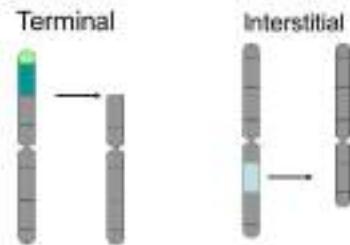
## L20 : Structural chromosomal abnormalities

It results from Chromosome breakage with or without subsequent union.

### 1- Deletion

- ✓ It is a loss of any part of a Chromosome (missing information).
- ✓ If the breakage is single, it is called terminal.
- ✓ If there are 2 breaks, it is called interstitial.
- ✓ If the deleted part lacks a centromere (acrocentric) it will be lost in the next division.

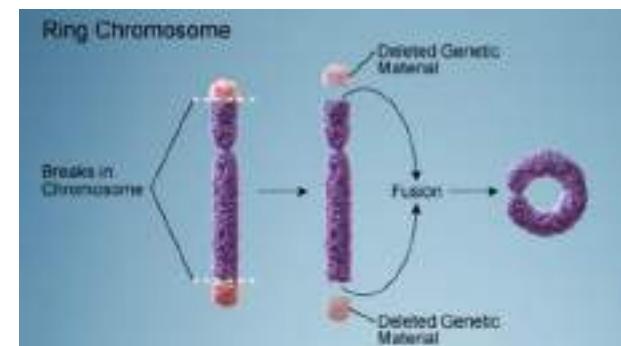
Two types of deletion



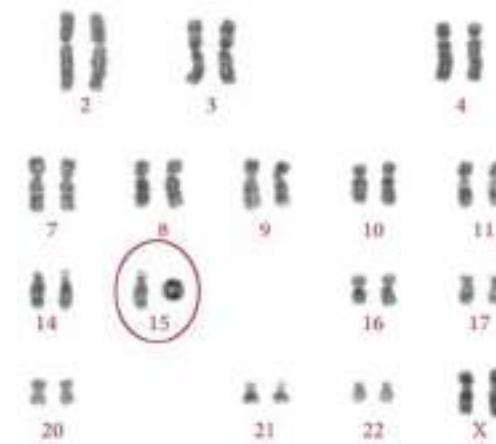
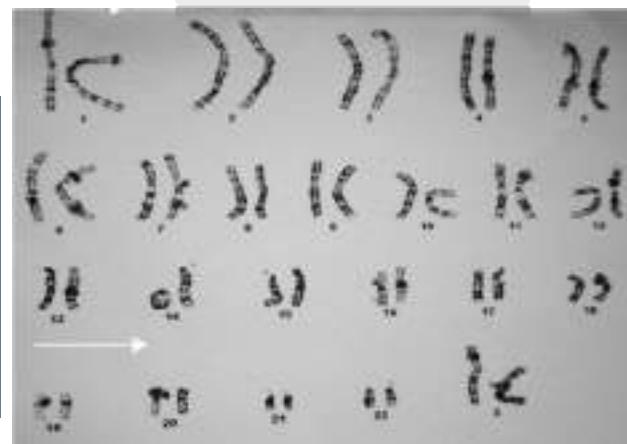
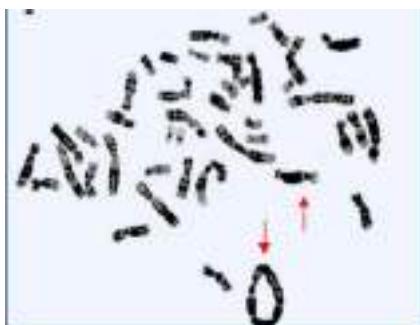
Wolf syndrome: it is a partial loss of short arm of chromosome 4	Cri Du Chat syndrome :It is partial loss of short arm of chromosome 5
	<p>Cri-Du-Chat syndrome or Cat-Cry syndrome</p>

### 2- Ring chromosome:

It is a special type of deletion that occurs when there are 2 breaks at the 2 distal ends of the same chromosome and the broken ends unite to form a ring.



Ring chromosome, 14





### 3- Inversion

It results from 2 breaks occurring in a chromosome and the healing of the fragments in such a way that a portion of the gene sequence of the chromosome has become rearranged in a reverse order or with deletion of the break part.

#### Types:

1. Paracentric inversion
2. Pericentric inversion

### 4- Translocation:

It is the transfer of chromosomal material between chromosomes.

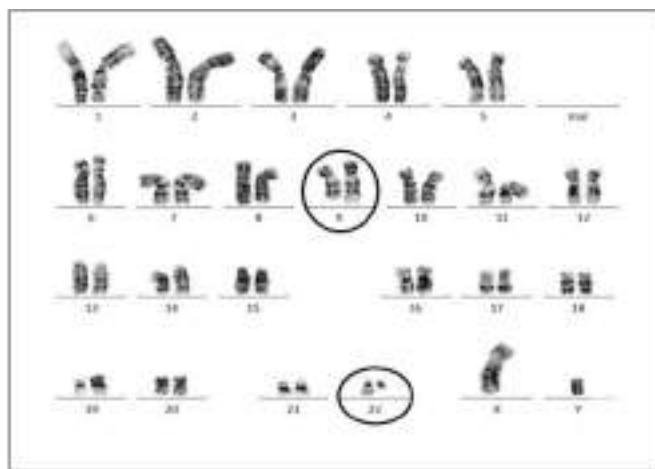
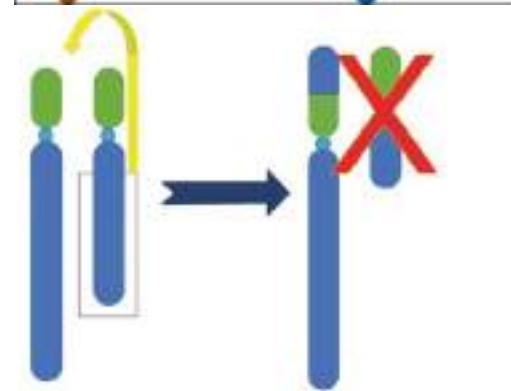
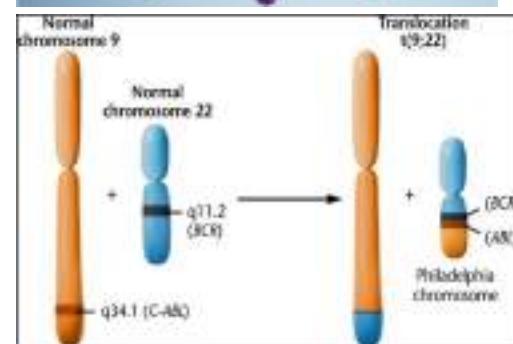
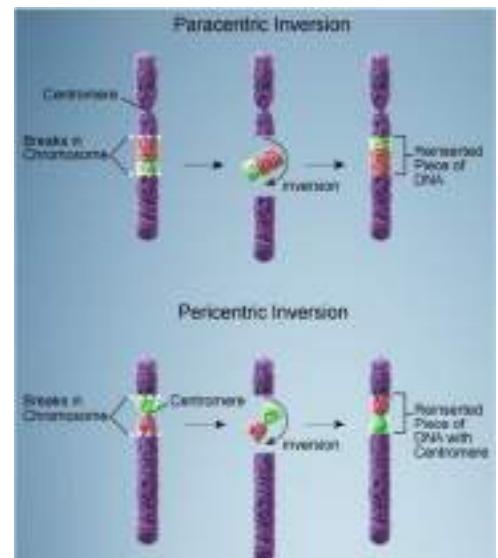
The process requires breakage of both chromosomes.

#### a) Reciprocal translocation

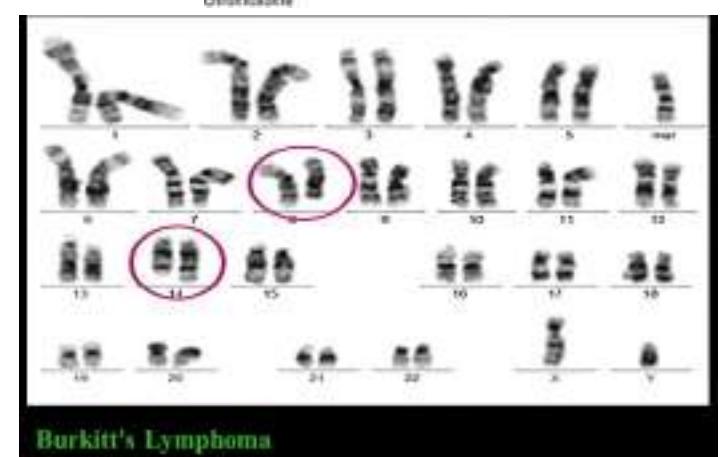
in which the chromosomal material distal to breaks in chromosomes is exchanged as in philadelphia chromosome (ch 9 and 22)

#### b) Robertsonian translocation :

- It arises from breaks at or near the centromere in 2 acrocentric non-homologous chromosomes with cross-fusion of the products
- translocation of two acrocentric chromosomes.
- Robertsonian translocation is when someone has 45 chromosomes instead of the usual 46. This happens when two chromosomes get stuck together, forming one long chromosome.
- Chromosomes 14 and 21 are the most frequently involved.



Philadelphia chromosome → reciprocal translocation; 9, 22

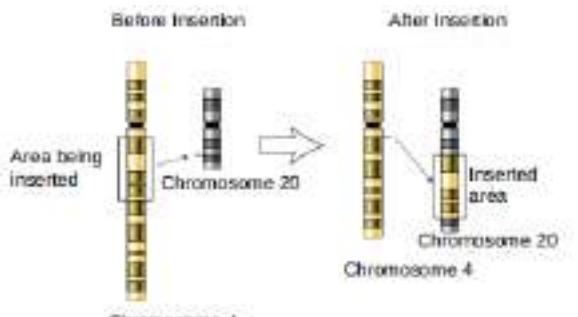


Burkitt's Lymphoma



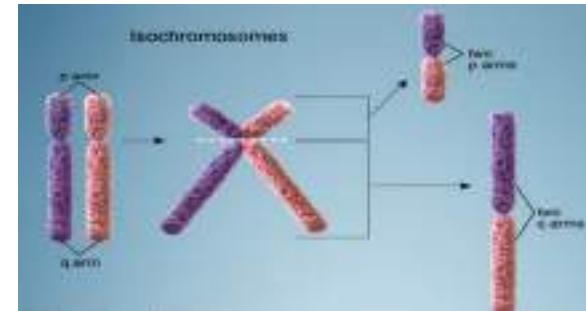
## 5- Insertion

Insertion occurs when a segment of one chromosome is inserted into another chromosome. This happens if there are two breaks in one chromosome and a single break in the other.



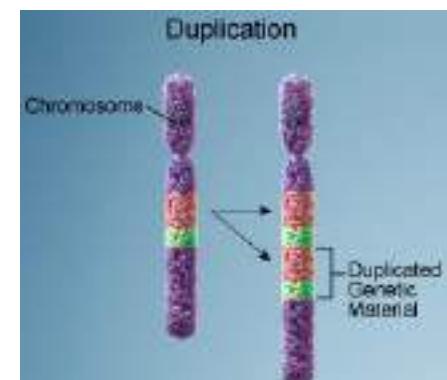
## 6- Isochromosome

- It is an abnormal chromosome which has deletion of one arm with duplication of the other (duplication deficiency)
- arms of the chromosome are mirror images of each other. Isochromosome arises when a normal chromosome divides transversely instead of longitudinally



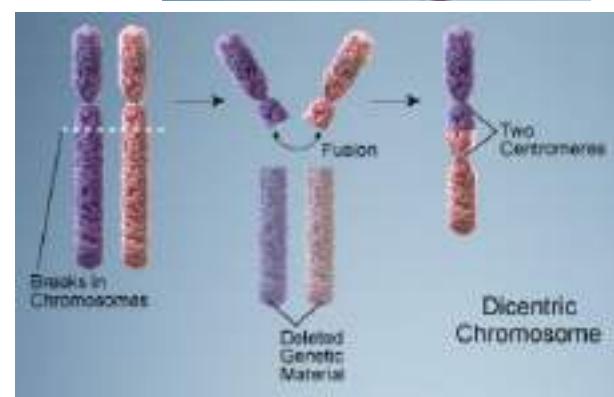
## 7- Duplication :

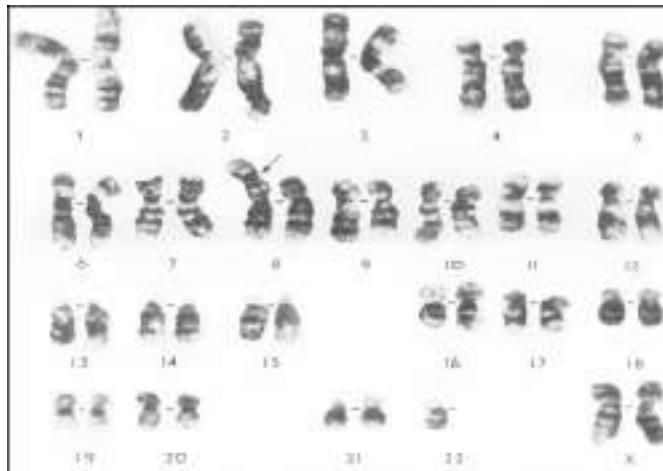
- It is the presence of two copies of a segment of a chromosome .
- It leads to the presence of double dose of genes .
- Duplication is more common and less harmful than deletion.



## 8- Di-centric chromosome

- Dicentric chromosome contains two centromeres.
- It is unstable because it is torn apart during mitosis and its parts are divided between the two daughter cells.
- Breakage of two non-homologous chromosomes can produce "sticky ends" that recombine end-to-end.



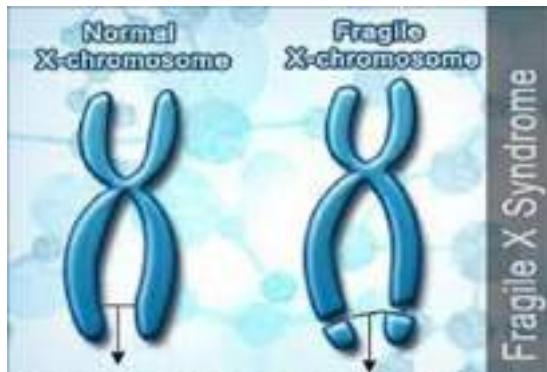


Dicentric chromosome , 8

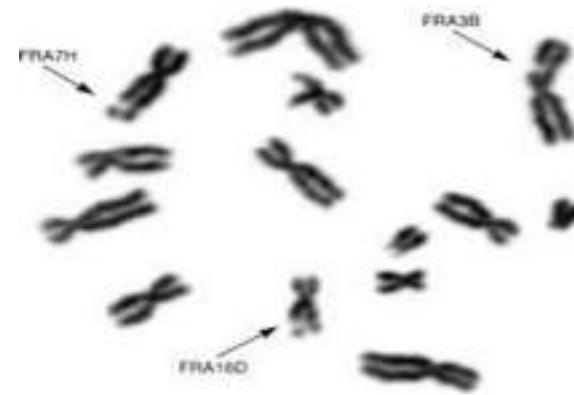
## 9- Fragile chromosome

The name comes from an unusual narrow place on the X chromosome that can be seen in a microscope; it is called a fragile site.

Fragile chromosome is susceptible to chromosome breakage. After Down syndrome, the second most frequent genetic cause of mental retardation is fragile X chromosome.



Fragile X Syndrome



### Causes of structural anomalies:

- Ionizing radiation:** it depends on dose, type of radiation and the period of exposure
- Chemicals:** as cytotoxic drugs, some antibiotics (tetracycline)



## Histo CBL 1 : Immotile Cilia Syndrome (Kartagener syndrome)

### Case Scenario

Nada a female baby was born after the second full-term pregnancy.

The baby was born by normal vaginal delivery with a birth weight of 300 g. Few hours after birth, she developed signs of respiratory distress, for which she was transferred to the neonatal department of children's hospital.

With detailed family history, it was revealed that the first child (a 7-year-old girl) had a history of **recurrent sinusitis** with **recurrent respiratory infections**.

On admission, the physical examination revealed moderate respiratory distress. Chest X-ray showed bronchopulmonary pathology and dextrocardia.

The ultrasound confirmed the diagnosis of **total situs inversus**.

Laboratory findings showed normal white cell-count.

Genetic study, as well as electron microscopy of the biopsy of the



Situs inversus



Sinusitis

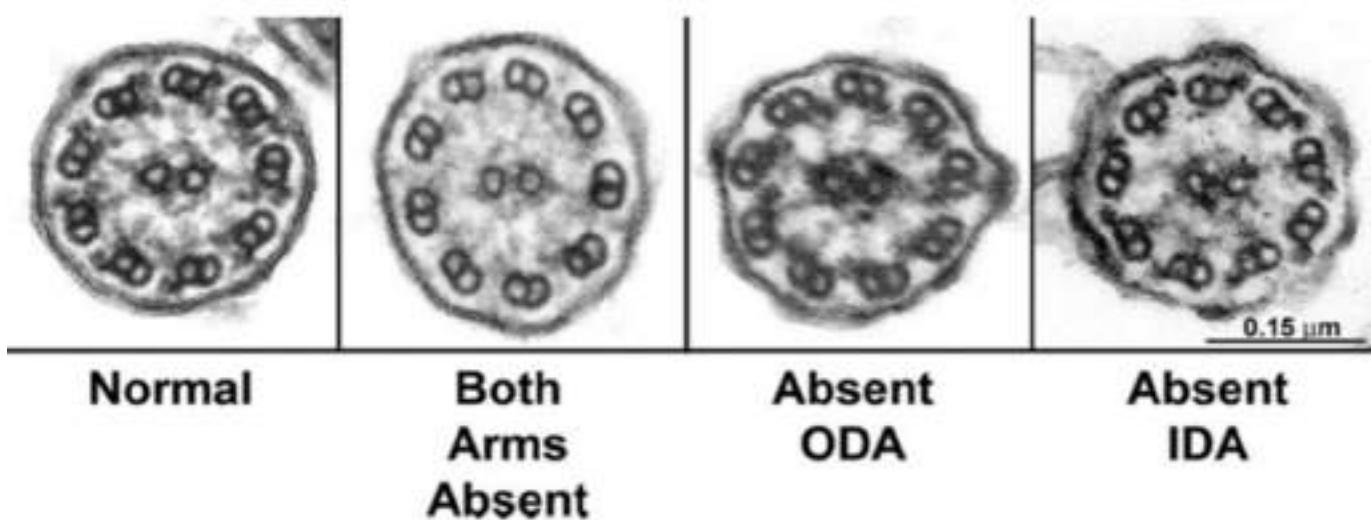


Bronchiolectasias

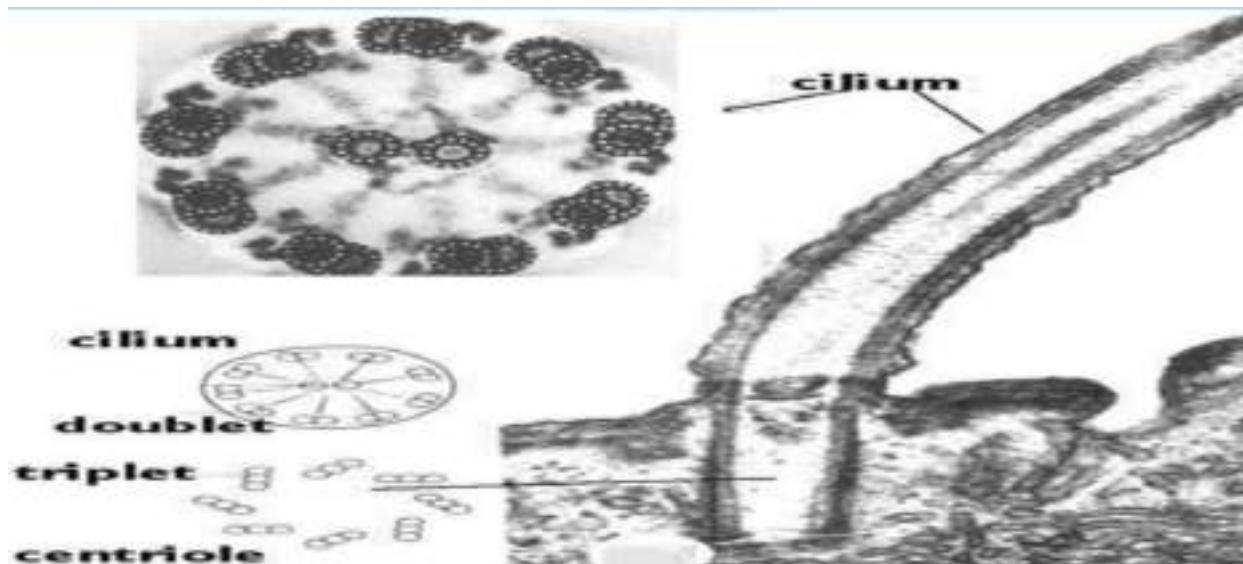
What is your diagnosis

Kartagener Syndrome





### Cilia by TEM



Mucociliary clearance

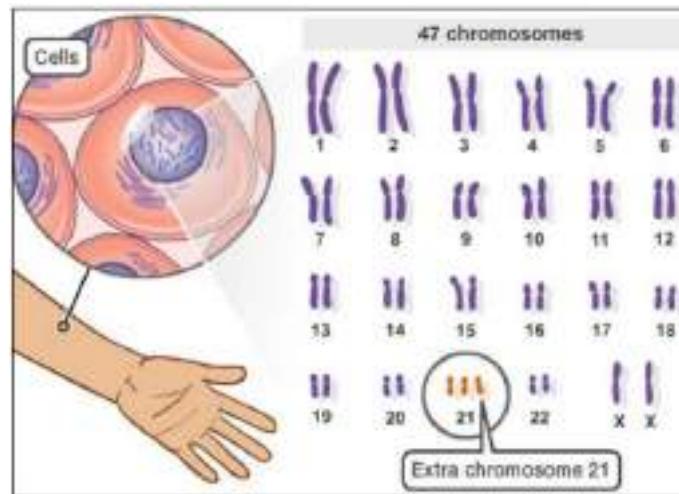
Diagnosing PCD in the UK



## Histo CBL 2 : Down syndrome

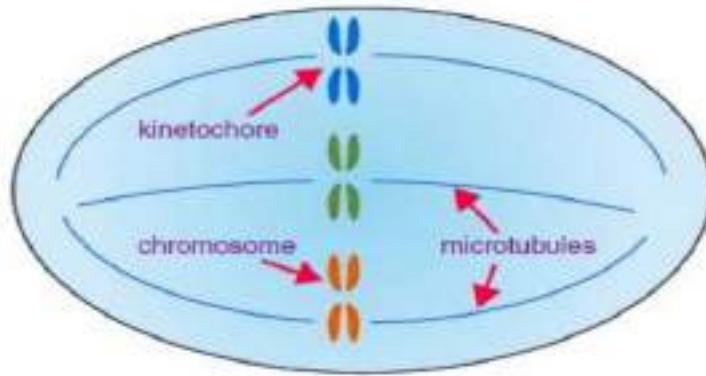
### What is Down syndrome?

- Down syndrome is a genetic condition where people are born with an extra chromosome.
- Most people have 23 pairs of chromosomes within each cell in their body, for a total of 46.
- A person diagnosed with Down syndrome has an extra copy of chromosome 21, which means their cells contain 47 total chromosomes instead of 46.
- This changes the way their brain and body develop

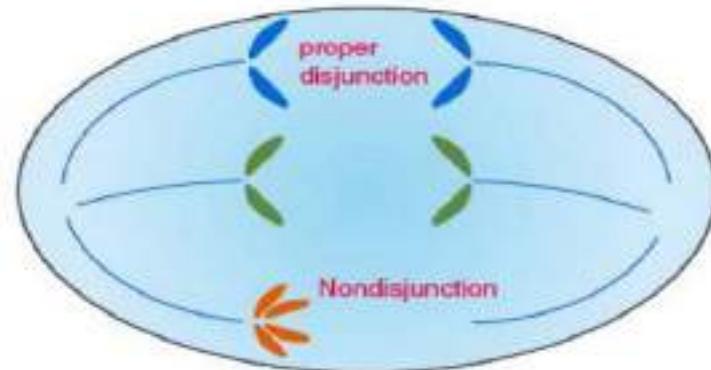


### The main cause:

- The main cause of trisomy is **Nondisjunction** of chromosome 21 during meiosis at the time of gamete formation.
- The abnormal cell with trisomy of chromosome 21 is fertilised giving rise to trisomy in all the cells of the foetus



Metaphase



Anaphase



### Risk Factors Of Down Syndrome

- Genetic factors

Children can inherit the genetic of Down syndrome from both their parents.

- Mother's increased age A woman who is above 35 years of age have a higher chance of having a baby with Down syndrome. This is because older eggs have an increased risk of improper chromosome division

### Physical signs of Down syndrome:

Physical signs of Down syndrome are usually present at birth and become more apparent as your baby grows.

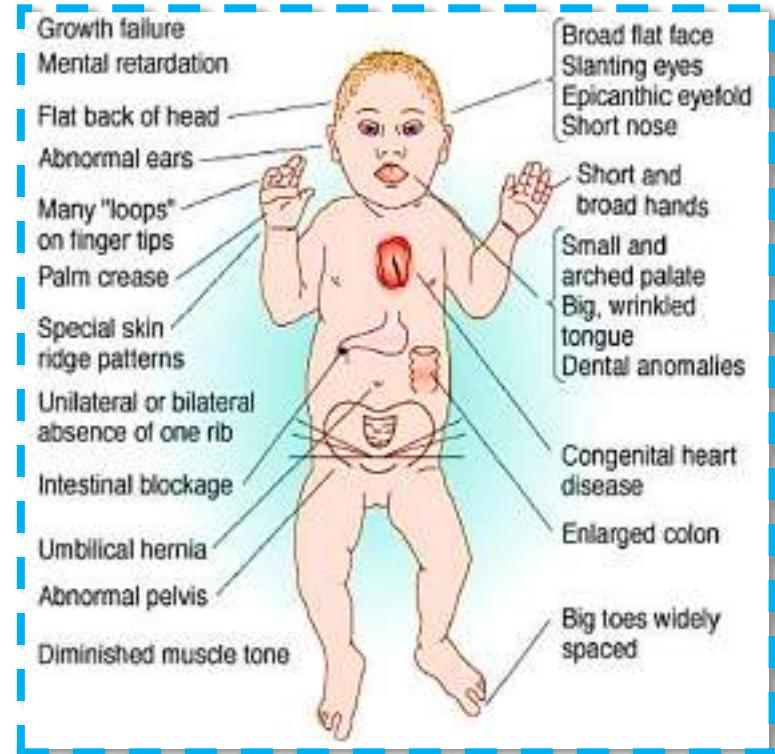
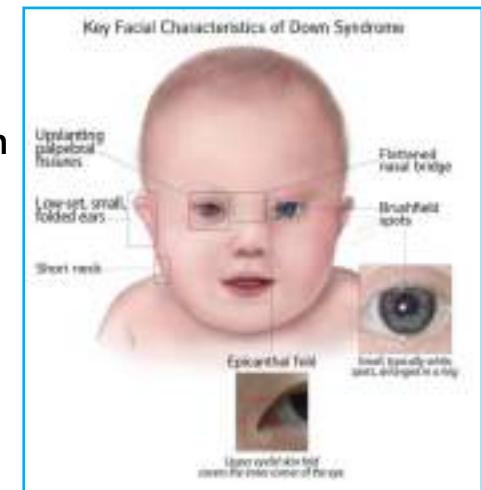
They can include:

1. A flat nose bridge.
2. Slanted eyes that point upward.
3. A short neck. •Small ears, hands and feet.
4. Weak muscle tone at birth.
5. Small pinky finger that points inward towards the thumb.
6. One crease in the palm of their hand (palmar crease).
7. Shorter-than-average height

As your child grows,

additional symptoms can arise because of the way that their body developed in the uterus, including:

1. Ear infections or hearing loss.
2. Vision problems or eye diseases.
3. Dental problems.
4. Being more prone to infections or illnesses.
5. Obstructive sleep apnea.
6. Congenital heart disease





### Cognitive symptoms of Down syndrome

- Your child with Down syndrome may have cognitive development challenges as a result of their extra chromosome.
- This can cause intellectual or developmental disabilities.
- Your child's ability to meet developmental milestones, or things that your child can do at a certain age, may differ from other children, including how they:
  - Walk and move (gross and fine motor skills).
  - Speak (language development skills).
  - Learn (cognitive skills).
  - Play (social and emotional skills).
- As a result, it may take your child longer to do the following things:
  - Toilet training.
  - Speaking their first words.
  - Taking their first steps.
  - Eating food independently

### Behavioral symptoms of Down syndrome

- Behavioral symptoms result of your child not being able to communicate their needs to you or their caregivers effectively.
- Behavioral symptoms of Down syndrome could include:
  - Stubbornness and tantrums.
  - Difficulty paying attention.
  - Obsessive or compulsive behaviors





### Complications

These complications can include:

1. **Heart defects;** About half the children with Down syndrome are born with some type of congenital heart defect.
2. **Gastrointestinal (GI) defects:** GI abnormalities occur in some children with Down syndrome and may include abnormalities of the intestines, esophagus, trachea and anus.
3. **Immune disorders;** Because of abnormalities in their immune systems, people with Down syndrome are at increased risk of developing autoimmune disorders, some forms of cancer.
4. **Sleepapnea:** Because of soft tissue and skeletal changes that lead to the obstruction of their airways.
5. **Obesity.**
6. **Spinal problems:** Some people with Down syndrome may have a misalignment of the top two vertebrae in the neck (atlantoaxial instability).
7. **Leukemia:**  
Young children with Down syndrome have an increased risk of leukemia.
8. **Dementia:** signs and symptoms may begin around age 50.
9. **Other problems:** dental problems, seizures, ear infections, and hearing and vision problems

### How is Down syndrome diagnosed before birth?

- A healthcare provider can suspect Down syndrome during pregnancy with prenatal screening tests.
- **Prenatal screening tests**
  - These tests assess your risk of having a child with Down syndrome rather than giving you a confirmation of a diagnosis.
  - Screening tests could be a blood test of the birthing parent's blood to look for indicators of Down syndrome.
  - Another screening test is an ultrasound.
  - During this imaging test, your provider will look for signs of Down syndrome, like extra fluid behind your baby's neck.
  - It's possible that a screening test could be normal and not show signs of Down syndrome when the condition is present



### Diagnostic tests during pregnancy

Diagnostic tests, on the other hand, will provide accurate information in detecting Down syndrome.

These tests include the following:

#### 1. Amniocentesis

- A small amount of amniotic fluid is obtained for examination with the help of a needle inserted into the abdomen.

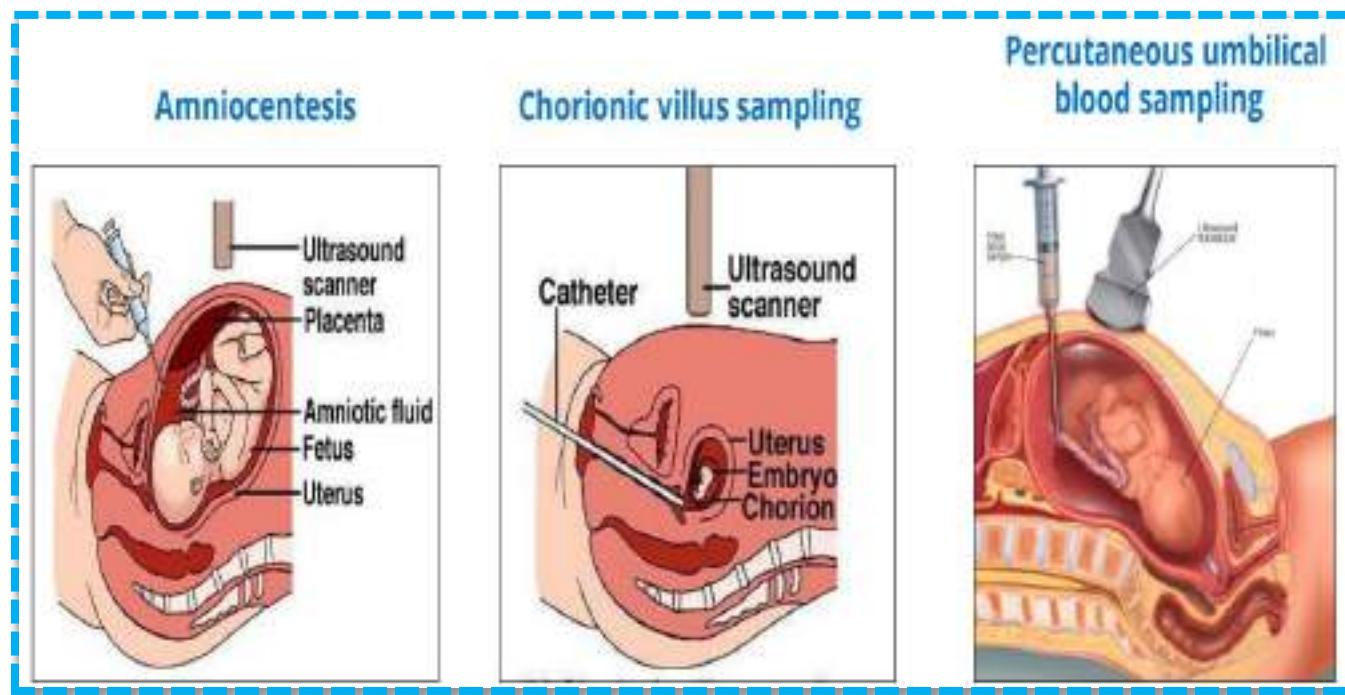
#### 2. Chorionic villus sampling

- A small sample of the placenta is analyzed which is obtained from the cervix or abdomen.

#### 3. Percutaneous umbilical blood sampling –

- A tiny sample of blood is taken from the umbilical cord for analysis.

These diagnostic tests are done inside the uterus which can increase the risk of miscarriage, foetal injury or preterm labour





### How is Down syndrome diagnosed after birth?

- After your baby is born, providers look for the physical signs of Down syndrome during a physical exam.
- To confirm the diagnosis, your baby's provider may perform a blood test called a karyotype test.
- In this test, your baby's provider will remove a small blood sample to study under a microscope.
- They'll look for an extra 21st chromosome to diagnose the condition.

### Who is on my child's care team?

- ✓ If your child has Down syndrome, they'll likely see a variety of specialists to make sure they're healthy. Their care team may include:
  - Primary care providers to monitor growth, development and medical concerns and provide vaccinations.
  - Medical specialists, depending on the needs of the person (for example, cardiologist, endocrinologist, geneticist and hearing and eye specialists).
  - Speech therapists to help them communicate.
  - Physical therapists to help strengthen their muscles and improve motor skills.
  - Occupational therapists to help refine their motor skills and make daily tasks easier.
  - Behavioral therapists to help manage emotional challenges that can come with Down syndrome.
  - Wearing glasses for vision problems or assisted hearing devices for hearing loss.

### Is there a cure for Down syndrome?

No.

- Down syndrome is a lifelong condition, and there isn't a cure.
- Symptoms of the condition are manageable, and treatment is available for any associated conditions that may arise

