

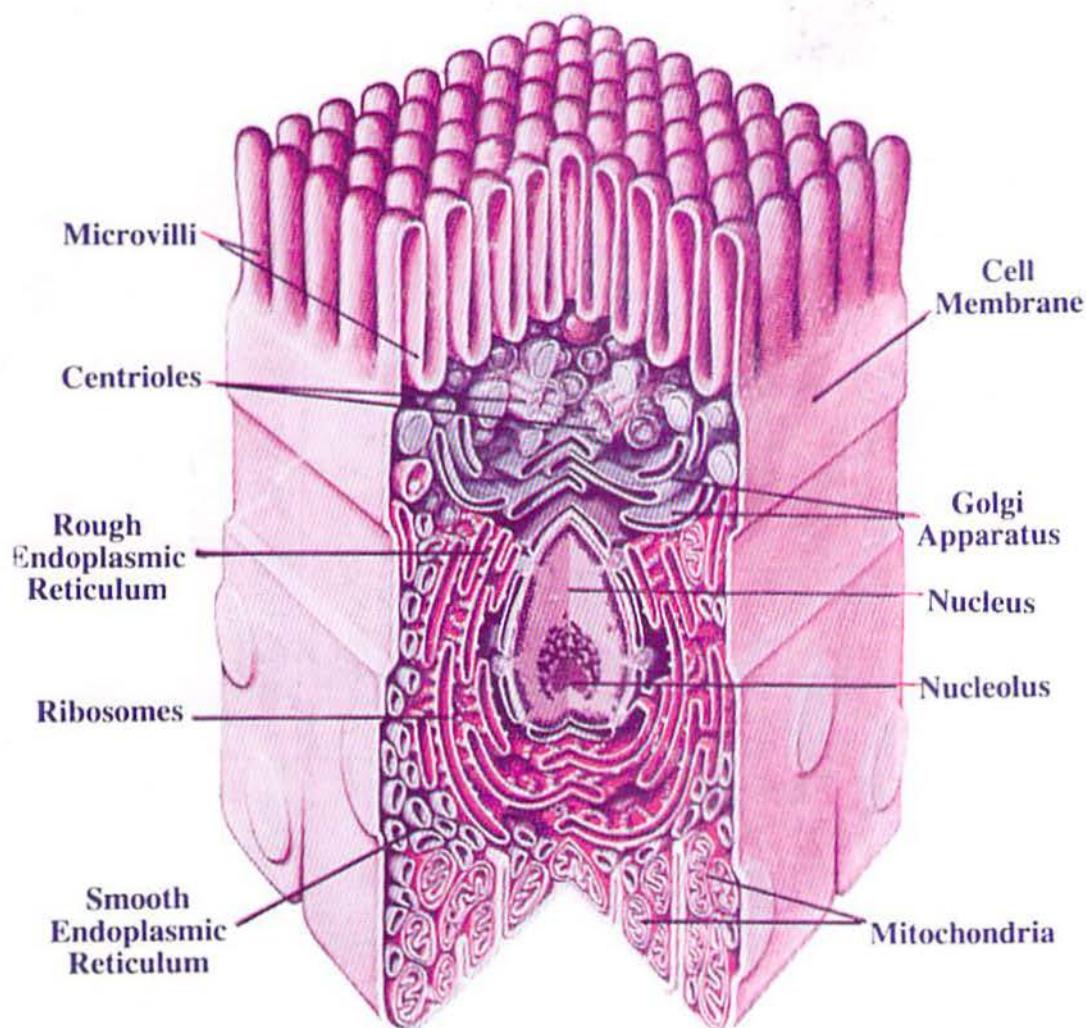
HISTOLOGY

Part 1
For Medical Students

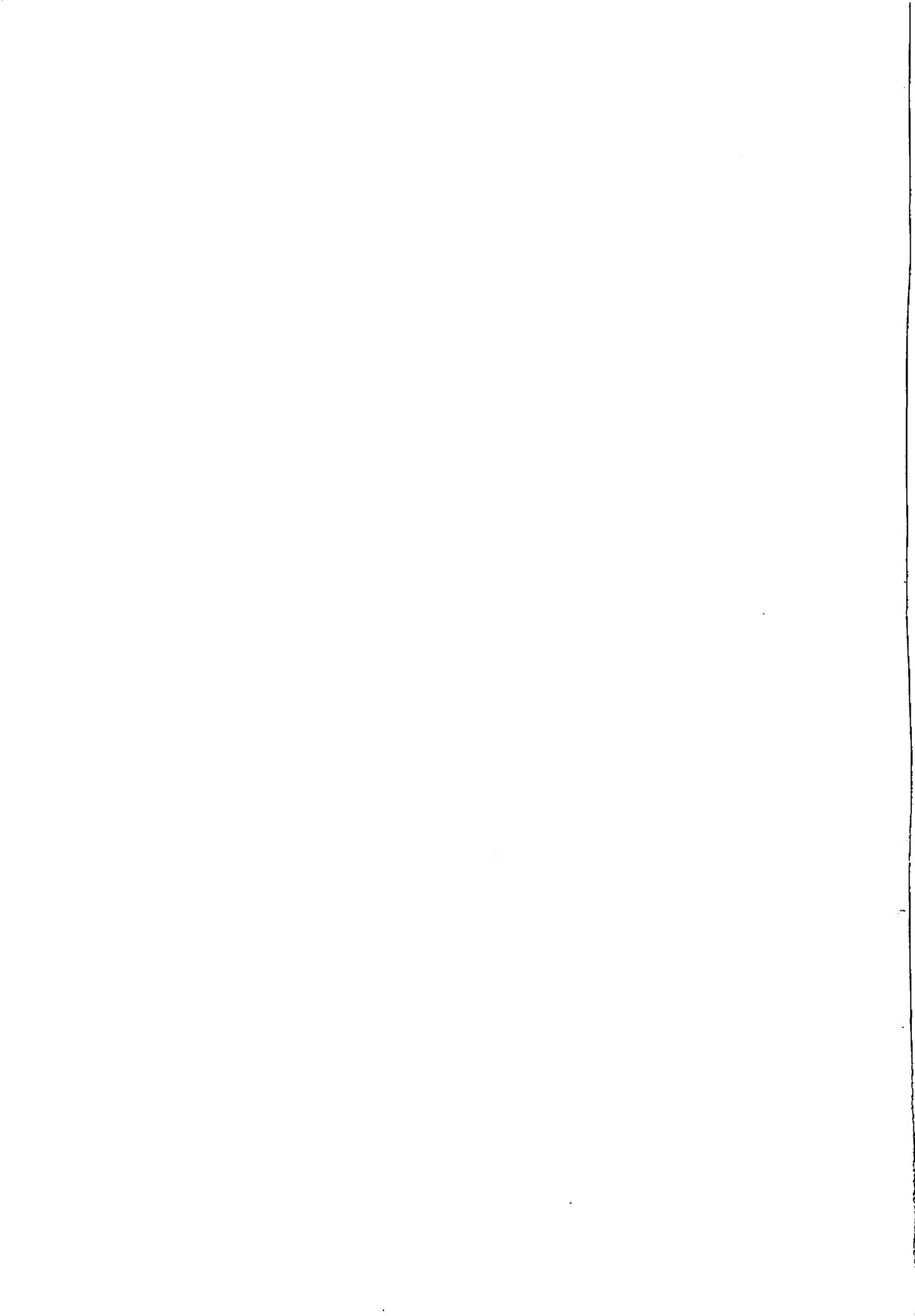
New Edition With Coloured Plates
And Electron Micrographs

By Professor

Zakaria Abd - ELHamid



One Cell



HISTOLOGY

For Medical Students

Part 1

By

Professor

Zakaria Abd - AL Hamid

M. B., B. Ch., D. M. Sc., M. D

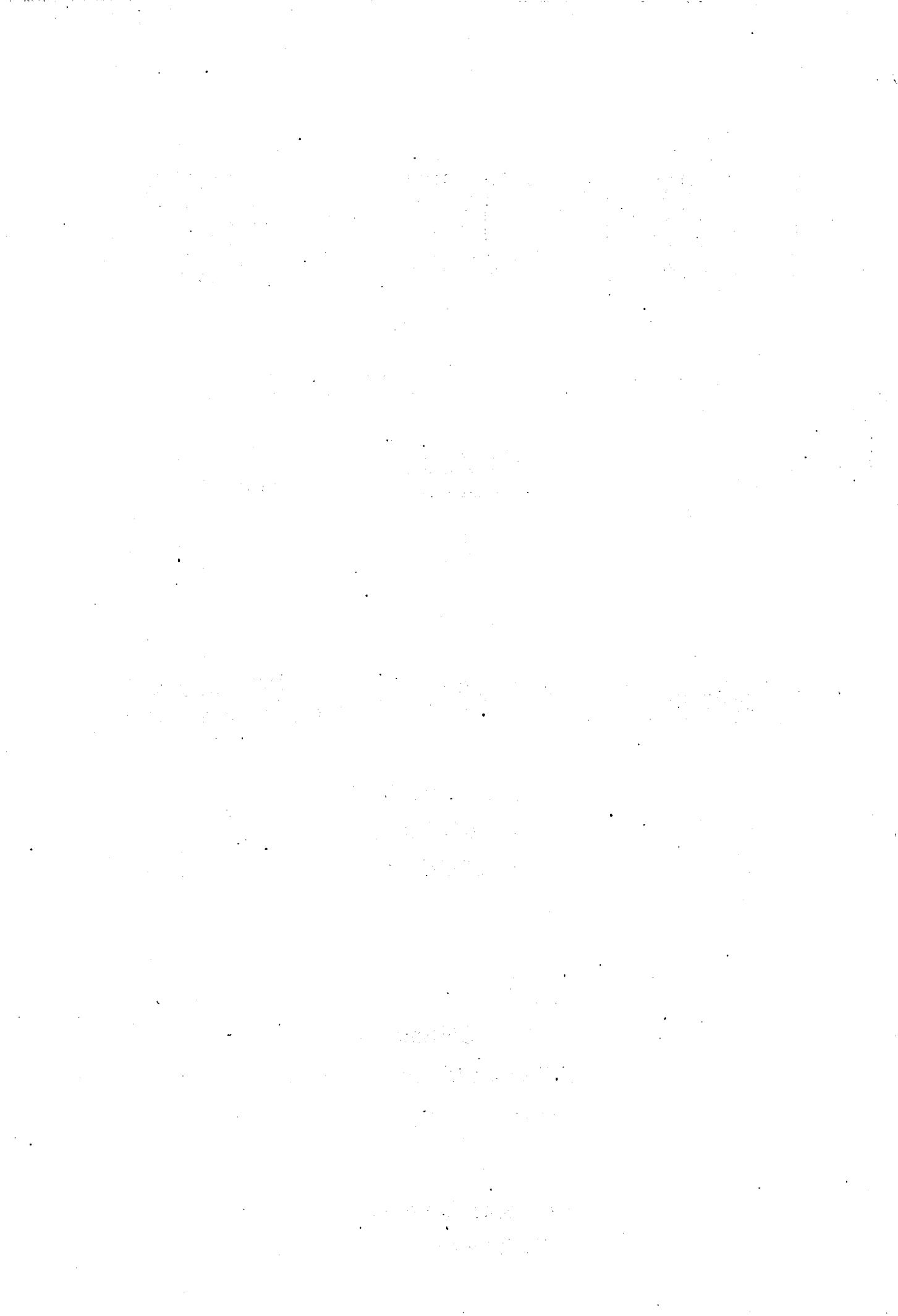
Professor of Histology

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New Edition
With Coloured Plates and
Electron Micrographs

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To The Author



Preface

* * This Text-Book of Histology is the outcome of fifty years of experience in teaching medical students and is written primarily for them. It is sufficiently detailed to satisfy the requirements of the undergraduates as well as the postgraduates.

The new edition of this book was prepared with the same objectives as those of the original work. The most apparent changes in this book were the inclusion of a number of electron micrographs and their accompanying text. Emphasis was laid upon the inter-relationship between structure and function, not only at the level of resolution obtained with the optical microscope but also at the ultra-structural level.

Another obvious change in this new edition was the inclusion of the chapter of genetics, and genomic studies. Genetics today, is penetrating into all fields of medicine. Its rapidly expanding methodology is enabling research workers to find answers to many questions. Our attention, therefore, becomes more focused on normal and abnormal cell divisions and on chromosomal as well as on genomic studies.

In addition to the considerable changes and additions to the text, a conscious effort has been made to increase both the quality and number of illustrations. The new coloured illustrations are original and are of the kind that seem to be the most helpful guide to students when actually examining their slides.

In presenting this book, I would like to express my appreciation for the help and encouragement that I have received from my wife.

Dr. Zakaria Abd - AL Hamid

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Introduction

Histology: involves the study of the microscopic structure of the cells, tissues and organs.

The Cells: are bound together to form different **tissues**.

The Tissues: are combined together to form different **organs**.

Several Organs: having correlated functions are grouped to form **Systems**.

In the study of histology, it is important for the student to understand the various types of microscopes and the different methods used in preparation of tissues, and the different methods used for staining cells, tissues and organs.

Microscopy

Several types of microscopes are used to study the detailed structures of the organs.

The Resolving Power of a microscope is a measure of the capacity of the microscope to separate clearly two points close together.

The resolving power of the **light microscope** is about **0.2 micrometer**.

The resolving power of the **Electron Microscope** is **0.2 nanometer**.

The most important units of measurements used in Histology are:

One centimeter (cm) = 10 millimeters (mm).

One millimeter (mm) = **1000 micrometers** = 1000 microns (u).

One micrometer (one micron) = **1000 nanometer (nm)**.

One nanometer (nm) = **10 Angstrom = 10 A°**.

Types of Microscopes

1. The Light Microscope (L/M)

In this microscope, we use **the day light or electric light** as a source of illumination.

The light is focused on the lens of the condenser by a mirror.

The Optical System of The Light Microscope Consists of:

a) The Eye Pieces which are near the eye.

They are of different magnifying powers: 5, 10 or 15

This means that the eye piece magnifies the object either 5 times, 10 times, or 15 times respectively.

- b) The Objective lenses are near the object to be examined.

Types of Objective Lenses:

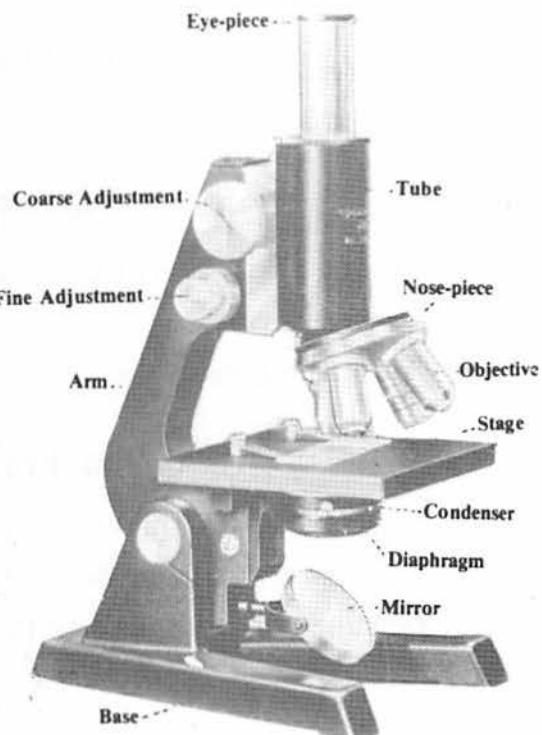
1. Low Power Objective (10).
2. High Power Objective (45).
3. Oil Immersion Objective (100). This lens when used, should be immersed in a drop of cedar oil. This oil should be put on the coverslide overlying the object to be examined.

How can we calculate the magnification of a histological section?

We multiply the power of the used eyepiece (10 for example) by the power of the used objective lens (45 for example).

So, the magnification of this examined histological section will be:

$$10 \times 45 = 450 \text{ times.}$$



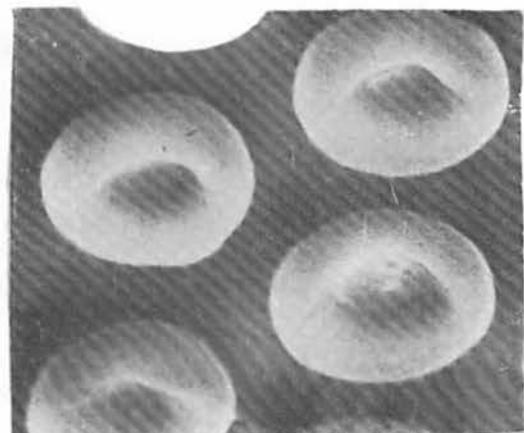
The Light Microscope

2. The Transmission Electron microscope (E/M)

- In this microscope, a beam of electrons is used as a source of illumination.
- The magnified image is received on a fluorescence screen or on a photographic plate.
- The E/M gives a very high magnification. It magnifies objects up to 100,000 times.

3. The scanning Electron Microscope

It is a special type of electron microscope by which we obtain a 3 dimensional image for the examined parts as red blood corpuscles and cilia of certain cells.



Red Blood Corpuscles Under Scanning E/M

4. The Atomic Force Microscope

It magnifies the examined fresh tissues up to 500.000 times.

5. The Ultraviolet Microscope

- In this microscope, the source of light is a beam of ultraviolet rays. The image is received on a fluorescence screen.
- The magnifying power of this microscope is up to 4000 times.

6. The Fluorescence Microscope

The source of light in this microscope is the ultraviolet rays which are harmful to the eye, so a filter should be inserted in its eyepiece. The fluorescent substances in the examined tissues will shine by giving off visible light. It is used to study the chemical components of the tissues.

7. The phase - Contrast Microscope

It is used to examine fresh tissues or living cells growing on a culture media.

The Basic Techniques Used For Preparation Of Tissues For Histological Studies

1. Microtechniques.
2. Tissue culture.
3. Spreading of blood films, bone marrow and tissue smears.

1. Microtechniques

These are the different types of techniques used to prepare sections from organs.

1. **The paraffin technique**, (is the most commonly-used method).
2. **The celloidin technique**, (is the most perfect used method).
3. **The freezing technique**, (is the most rapid used method).

N.B. The Microtechniques are used to prepare tissues for microscopic examination for learning purposes and to differentiate between normal and cancer tissues before, during and after operations.

A - The Paraffin Technique

In this method, soft and hard paraffin are used.

The following steps are followed in paraffin techniques:

1. Obtaining the tissue from the body:-

A very small fresh piece of tissue is cut out from the examined organs immediately after death or from patient before doing operation.

2. Fixation of tissues prevent tissue autolysis, The obtained tissue is put in a chemical fluid called fixative as formalin and the process is called fixation.

Functions and characteristics of a good fixative

- It hardens the tissue by coagulating its protein.
 - It prevents putrifaction and stops the autolytic changes by killing the bacteria.
 - It preserves the tissue in a condition similar to that existing during life.
 - It facilitates the process of cutting, staining and microscopic examination.
- 3. Washing:** The fixed tissues are washed in running tap water to remove the fixative.
- 4. Dehydration:** it is the process of gradual extraction and removal of water from the fixed tissue. It is done **through the following steps:** Putting the fixed tissue in 50% alcohol, then in 70% alcohol, finally in 100% alcohol (absolute alcohol).
- 5. Clearing:** By this process, the tissue becomes translucent. The tissues are treated with clearing agents as xylol or benzol to remove alcohol.
- 6. Impregnation:** The fixed tissue is put in melted **soft paraffin**.
- 7. Embedding In Hard Paraffin:** The tissue is then embedded in **hard paraffin** to form a block ready for sectioning.
- 8. Sectioning Or Cutting Of The Paraffin Block By The Microtome.**
- 9. Mounting:** The obtained thin paraffin sections are then put on clean glass slides smeared with glycerine. The sections are now ready to be stained.

Advantages Of The Paraffin Technique

- Paraffin technique takes a **short time** for its preparation.
- It gives serial sections which are important for research.
- It gives **very thin** sections, easy to be **stained** and to be **examined**.
- Paraffin sections are **very easy to be stained** with different stains.

Disadvantages of Paraffin Technique

- The used fixative dissolve the fat content of the cells during preparation.
- The used fixatives and heat may change the normal structure of tissues.
- It is not used in demonstrating the enzyme activities in tissues.

B - The Celloidin Technique

In this technique we use **celloidin substance** instead of paraffin.

- It is used to prepare large sections from the eye ball and brain stem.
- In celloidin technique, fixation, and washing steps are similar to those used in paraffin technique.
- **Dehydration And Clearing** are done in absolute alcohol and ether for 2 days.
- **Impregnation and embedding** are done first in thin celloidin (7.5%) and then in thick celloidin (15%).
- **Celloidin blocks** are preserved in 70% alcohol.
- **Sectioning of a celloidin block** is done by a special microtome.
- The obtained thick celloidin sections are stained in watch glasses.

Advantages Of Celloidin Technique

- It gives **perfect and clear** sections to demonstrate tissue details.
- The use of no heat **preserves the normal structure** of the tissues.
- It is used to prepare sections from large organs as eye and brain.

Disadvantages Of Celloidin Technique

- Celloidin technique **takes about one month** for its preparation.
- **No serial sections** can be obtained because the sections are thick and separated.
- The celloidin sections are **very difficult** to be cut and to be stained.

C- The Freezing Technique

- In this method, the fresh or fixed tissues are frozen, hardened and are cut with a freezing microtome in the **cryostat apparatus** within few minutes.

Advantages Of Freezing Technique

- It is a **quick method** used during operations for rapid diagnosis of tumours.
- It is used **in histochemistry** to demonstrate enzyme activities in cells.

Disadvantages Of Freezing Technique

- It gives **non-serial** separated and fragmented sections.
- It gives **thick sections** very difficult to be cut and to be stained.

2 - Tissue culture

This is a special technique by which living cells of the body (e. g. blood cells or tissue cells) are isolated and allowed to live, to divide and to grow outside the body. This is done by incubating living cells and tissues in special media.

Medical Uses Of Tissue Culture:-

1. Used in studying chromosomal patterns of individuals (**karyotyping**).
2. Used in diagnosis of certain tumours and in the different **researches of cancer**.
3. Used in cultivation of bacteria, and viruses, in order to prepare different vaccines.

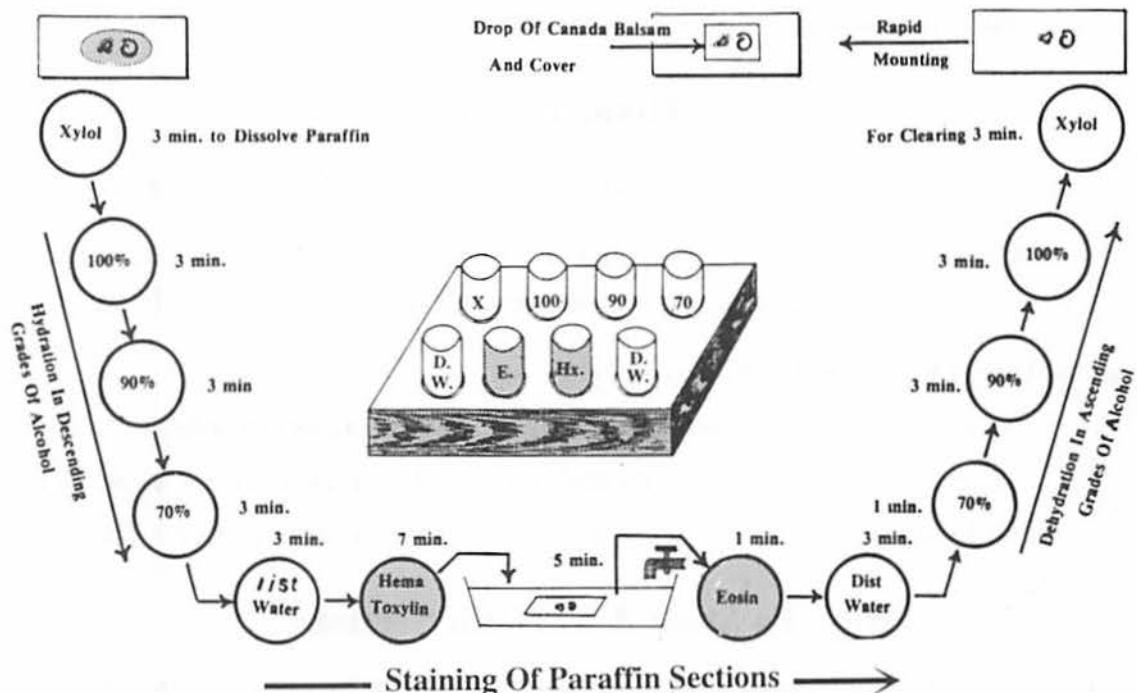
How To Stain A Paraffin Section?

- Paraffin technique is the most commonly used method in histological preparations.
- The prepared paraffin sections are usually stained with the most commonly used stains which are the **Hematoxylin and Eosin (HX & E)** stains.

These Are The Steps To Be Followed In Staining Of a Paraffin Section With Hematoxylin and Eosin (HX & E).

1. Identify the face of the slide upon which the paraffin section is present by scratching the paraffin and then label the slide face which contain paraffin.
2. **Dissolve the paraffin** by putting the slide in **xylol** solution for 3 minutes.
3. **Replace Xylol** by putting the slide in absolute alcohol for 3 minutes.
4. **Bring The Section Down To Water** by putting the section in descending grades of alcohol (in 100% alcohol, then in 90%, then in 70% alcohol and finally in distilled water) 3 minutes in each step. This process is called **hydration of the section**.
5. **Stain The Section In Hematoxylin For 7 Minutes.** This basic stain will stain the nuclei and the basophilic structures of the cytoplasm with a **blue colour**.

6. Put The Slide In Tap Water for 5 minutes in order to blue the section.
7. Put The Slide In Eosin For One Minute. This is an acidic stain, it stains the acidophilic structures of the cytoplasm with **red colour**.
8. Wash In Distilled water For 3 Minutes.
9. Dehydrate the slide in ascending grades of alcohol. Put it for one minute in 70% alcohol, then for 3 minutes in 90% and for another 3 minutes in 100% alcohol.



10. Put the slide in xylol in order to clear it from alcohol and to allow it to be miscible with Canada balsam. Leave the slide in xylol until you put a drop of **Canada balsam** on a clean **cover slip**.
11. **Mounting the section in Canada balsam** by removing quickly the slide from xylol with its face downwards and put it on the cover slip.
12. Examine the stained section and identify the structures present in it.

Precautions To Be Taken During Staining Of A Paraffin Section:

1. Make sure that the slide containing the section is facing you.
2. Xylol and water should never be mixed (if mixed they will form a milky solution).
3. Never allow the section to become dry in between two successive steps.

Types Of Stains

1. **Acidic stain:** as Eosin stain, Orange G. and Acid Fuscin. They stain the alkaline structures of the cytoplasm (as proteins) with **a red colour**.

2. **Basic Stain:** as **Hematoxylin**, **Toluidine blue** and **Methylene blue**. They stain the acidic structures of cytoplasm and the nucleus with a blue colour. **The cytoplasm** is usually alkaline in reaction in non-secretory cells, so it takes the acidic stain as **Eosin**. Thus it is **acidophilic in staining**, (it likes the acidic stains). **The nucleus is rich in nucleic acids**, thus it is constantly acidic in reaction, so the nucleus takes the basic stains as **Hematoxylin**. It is **basophilic in staining** (it likes the basic stains).
3. **Neutral stain:** as **Leishman stain** which is usually used to stain blood cells. It acts as a fixative for the blood film. It stains both the nuclei and cytoplasm of the white blood cells. It is commonly used to stain blood films.
4. **Vital stain as neutral red or trypan blue stains:** by these vital stains, we can stain living cells inside the living body as the staining of reticulo-endothelial phagocytic cells by injecting the dye into living animals.
5. **Supravital staining** is the staining of living cells **outside the body**, like the staining of the reticulocytes (immature red blood cells) with **brilliant cresyl blue**.
6. **Metachromatic staining** as the staining of mast cells with **toluidine blue stain**. This stain reacts with the mucopolysaccharides which are present in the granules of mast cells. This reaction will give rise to appearance of a **new violet colour** not related to the original **blue colour** of the stain.
N. B. The Orthochromatic stains react with the contents of the cells but they give **the same colour** of the stain.
7. **Physical stain:** as **Sudan III** which stain fat cells with orange colour.
8. **Trichrome Stains:** Each trichrome stain involves three types of stains as:
- Hematoxylin Van Gieson Stain:** It stains collagen fibres with **red**, muscles with **yellow**, nuclei with **blue** and epithelium with **yellow** colours.
 - Mallory Stain:** It stains collagenous and reticular fibres with **blue**, smooth muscles with **yellow**, and elastic fibres with **red** colours.
 - Azan Stain:** It stains muscles **red**, reticular fibres with **blue**, and the nuclei **red**.
 - Masson's Trichrome Stain:** It stains collagenous and reticular fibres with **green** colour, nucleus with **blue black** and cytoplasm with **red** colour.
9. **Silver Methods** to stain collagenous and reticular fibres with dark brown.
- **Iron:** It can be demonstrated in tissues by **potassium ferrocyanide**.
 - **Bilirubin:** It shows a blue reaction with ferric chloride.

- **Melanin:** It shows a blue reaction with potassium ferrocyanide.
- **Mucopolysacharides:** They give a red colour with P. A. S. Stain.
- **Hyaluronic acid:** shows a blue colour with Alcian blue stain.
- **Reticular Fibres:** are demonstrated by silver methods.
- **Elastic Fibres stain brown with Orcein:** and stain black with Verhoeff.
- **Collagenous Fibres:** give green colour with Masson's stain.
- **Lipid:** Fat can be stained orange with Sudan III, or black with Sudan black.
- **Neurones:** can be stained brown with silver stain.
- **DNA = Deoxyribonucleic Acid:** can be stained red with Feulgen reaction.
- **RNA = Ribonucleic Acid:** can be stained blue with basic dyes.
- **Methyle-Green Pyronin Stain:** gives a blue colour with DNA and a red colour with RNA.
- **Alkaline Phosphatase Enzymes:** can be demonstrated by Gomori's method.
- **Acid Phosphatase Enzymes:** can be stained by Azo-dye method.
- **Succinic Dehydrogenase Enzyme:** can be identified by Tetrazolium method.

Immunocytochemistry

- **Immunocytochemistry:** Tissues containing antigens are incubated in solutions containing labelled antibodies to these antigens. Combination of antigens and antibodies gives a coloured reaction on the examined tissue. This method is used to localize hormonal receptors on different cells and used also as tissue markers to detect cancer cells.

FISH Technique

- **Fluorescent In Situ Hybridization (FISH) Technique:** It is used to localize the sites of the genes on chromosomes. The previously prepared labelled radioactive DNA probes are used as antibodies to be hybridized with specific regions on chromosomes which are previously exposed to high pH in order to locate the positions of the different genes. The chromosomal region that binds to the radioactive probe during hybridization step are visualized by auto radiography. Localization of the sites of normal and diseased genes on the different chromosomes, are called Genomic Studies.

The Cell

Definition: The Cell is the structural and functional unit of the body organs.

The Cells are bound together to form tissues, the tissues, are combined to form **organs**. Several organs having interrelated functions constitute the different **systems of the body** as: digestive system, urinary system, etc.

Functions of Cells: The cells in the body perform **many functions** as: secretion, excretion, respiration, absorption, conduction, contraction, sensation and regulation of the other body functions.

Size of cells: The different body cells vary in size. Some cells are very small as certain cells of the cerebellum, while others are very large as the muscle cells. The majority of body cells are medium-sized.

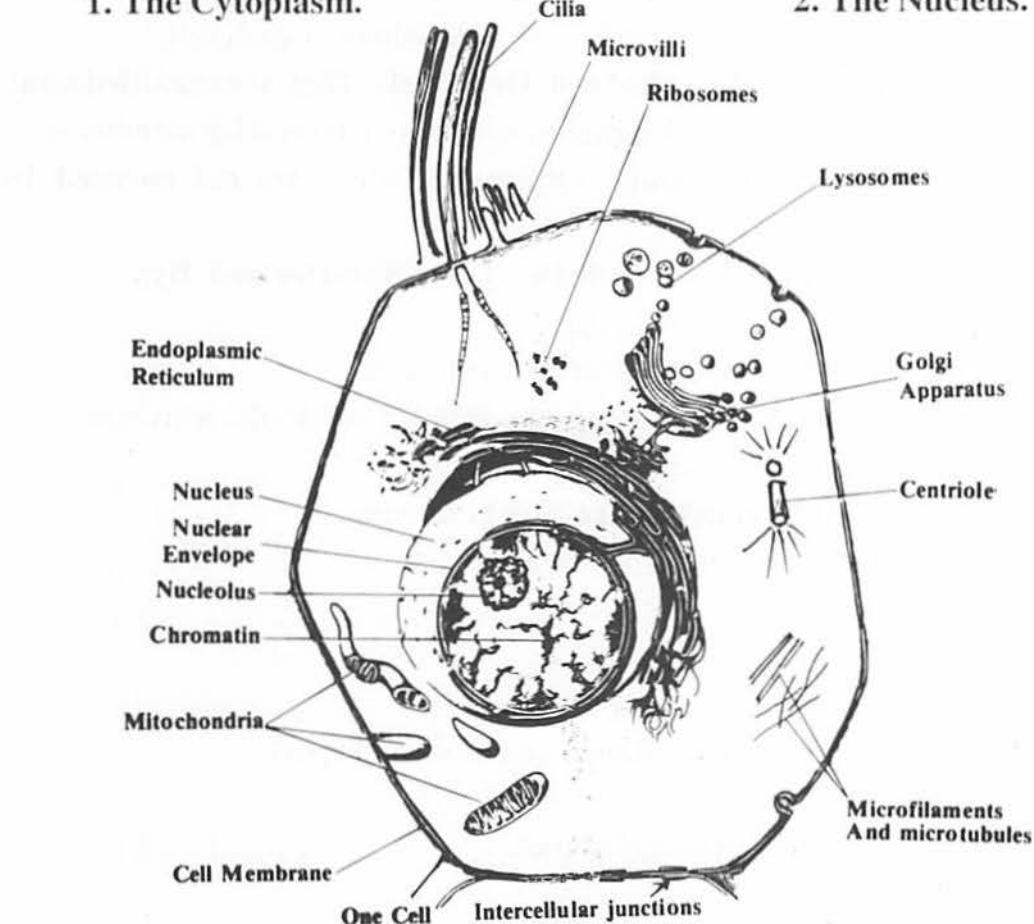
Shape of cells: The different body cells vary in shape. Some cells are rounded others are oval, flat, cubical or columnar in shape.

Eu-karyotic cells contain nuclei, Pro-karyotic cells contain no nuclei.

Structure of cells: Each cell is composed of the following two main parts:

1. The Cytoplasm.

2. The Nucleus.



A Diagram Of Cell Components

The Cytoplasm

The cytoplasm is formed of the following four main components:

1. **Cytoplasmic Matrix or Cell sap:** It is a colloidal gel-like solution of proteins, lipids, carbohydrates, minerals, enzymes, small molecules and ions.
2. **Cytoplasmic Organelles (Cell Organoids): They Are of Two Types:**
 - a) **Membranous Cytoplasmic Organelles:** They are small permanent organs which are enclosed in membranes. They perform important functions in each cell.
 - b) **Non-membranous Cytoplasmic Organelles.** They are special cell components which are not enclosed in membranes.
3. **Cytoplasmic Cytoskeleton:** They form a supportive network within the cytoplasm, these are: Microtubules, Microfilaments and Intermediate filaments.
4. **Cytoplasmic Inclusions (Cell Inclusions):** They are temporary components of certain cells. They are usually an accumulation of stored food as: glycogen and fat or an accumulation of pigments as: carbon and melanin.

Cell Organelles

The term Organelle means small Organ, each Organelle performs certain functions which are essential for the life and metabolism of each cell.

The Cell Organelles are also called cell Organoids. They are classified into:

1. **Membranous Cytoplasmic Organelles** which are covered by membranes.
2. **Non-Membranous Cytoplasmic Organelles** which are not covered by membranes.

The Membranous Cytoplasmic Organelles Are Characterized By:

- They are present in all nucleated cells.
- They are permanent components of the cytoplasm.
- They contain enzymes that participate in cellular metabolic activities.
- They are enclosed in membranes.

The Membranous Cell Organelles Are The Following:

1. The Cell Membrane or plasma membrane.
2. The Mitochondria.
3. The Golgi Apparatus.
4. The Lysosomes.
5. The Endoplasmic Reticulum (Rough and Smooth Types).
6. Peroxisomes.
7. Endosomes = Newly-formed lysosomes.
8. Coated Secretory Vesicles.

The Non-Membranous Cytoplasmic Organelles. They are not covered by membranes as: Ribosomes, centrioles, microtubules, microfilaments, cilia and flagella.

The Membranous Cell Organelles

1. The Cell Membrane

Definition: It is the outermost covering of the cytoplasm. It is also named **Plasmalemma or Plasma membrane.**

Functions: They have multiple functions to different body cells.

Thickness: Its thickness ranges from 8 to 10 nanometer (8 to 10 nm).

With The Light Microscope (L/M): It cannot be demonstrated because it is very thin.



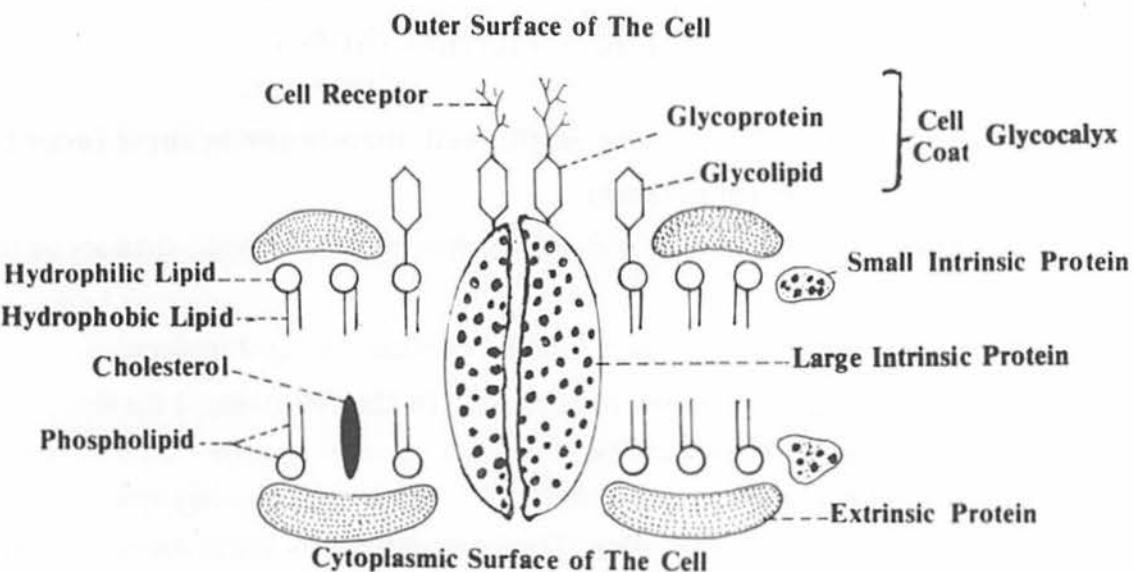
E/M Of 2 Adjacent Cell membranes

With The Electron Microscope (E/M); it appears as if it is formed of three layers, therefore it is called **tri-lamellar membrane.** Its outer and inner layers appear as dark lines, while its middle layer appears as a light area.

Staining: The coat of cell membrane is stained **red** with **PAS stain.**

Molecular Structure of The Cell Membrane: It is formed of **lipids, proteins and carbohydrates molecules covered by cell receptors.**

The Lipid, Protein and Carbohydrate Molecules Are Present In the Following Arrangement In the Cell Membrane:



A Diagram Of The Molecular Structure Of The Cell Membrane

1. The Lipid Molecules (30%)

- They form 2 layers (Bilayer) arranged in 2 rows inside the cell membrane.
- The Lipid Content is formed of: **Phospholipid** and **Cholesterol Molecules**.

1. Each phospholipid molecule is formed of two parts:

a) The Hydrophilic charged part of the phospholipid molecule.

- It forms the heads of the phospholipid molecules.
- It is called **hydrophilic** because it has a great affinity for aqueous solutions (it likes water).
- It is composed of charged lipid and is called **Polar Region**.
- It is present near the outer and inner surfaces of the cell membrane.

b) The Hydrophobic non - charged part of the phospholipid molecule.

- It is formed of the 2 tails of the phospholipid molecule.
- It is called **hydrophobic** because it has no affinity for aqueous solutions (it dislikes water).
- It is formed of non-charged lipid and is called **Non Polar Region**.
- The hydrophobic ends of the lipid molecule are directed inwards, they face each other in the central part of the cell membrane.

2. The Cholesterol Molecules: They are mainly present in the inner cytoplasmic aspect of the cell membrane.

Functions: The Lipids facilitate entrance of fat-soluble materials into the cell.

2. The Protein Molecules (60%)

The protein molecules are present in the cell membrane in these forms:

a) Extrinsic or peripheral protein:

- It is formed of protein molecules which are present on both surfaces of the cell membrane.
- It forms a non-continuous layer floating outside the lipid molecules.

b) Intrinsic or Integral protein: It is present in the following 2 forms:

- 1. Small intrinsic protein molecules** which are present as small collections of protein distributed among the lipid molecules. They contain enzymes.
- 2. Large intrinsic protein molecules:** They are present as large masses of protein. They are called **trans membrane protein**. They contain channels through which ions and water-soluble molecules can pass.

3. The Carbohydrate Molecules (10%)

- They are present only on the outer surface of the cell membrane.
- They are either linked to the protein molecules forming **Glycoproteins** or linked to the lipid molecules forming **Glycolipids**.
- The glycoproteins and the glycolipids form **The Cell Coat** on the outer surface.

The Cell Coat = Glycocalyx

The Cell Coat is a layer of glycoproteins and glycolipids which are present on the external surface of the cell membrane. It is called also **Glycocalyx**. It may be very thick or very thin according to the type and function of each cell.

The Cell Coat can be stained with **PAS stain**. It is very rich in **Cell Receptors**.

The Cell Receptors: They are present on the outer surface of the cell membrane. They receive chemical messages from the body cells. They control the entrance of hormones, drugs, viruses and bacteria into the cell.

N.B. The outer aspect of the cell membrane is covered by the cell coat and cell receptors while its inner aspect is rich in cholesterol.

Functions of the Cell Membrane

The Main Function of The Cell Membrane Is To Control the Exchange of materials Between The Cell And Its Surroundings; This occurs By:

1. Passive Diffusion of Small Molecules:

The cell membrane can allow dissolved gases, potassium ions and oxygen to pass into the cell. It also allows carbon dioxide and other metabolic wastes to leave the cell.

2. Active Transport of Materials:

Large molecules of sugars, amino acids and fatty acids in order to pass through the cell membrane, they should be combined with some **catalysts**. This combination requires energy and enzymes which are provided by the mitochondria.

3. Selective Transport of Materials: (Receptor Mediated Endocytosis)

The presence of **cell receptors** on the outer surface of cell membrane allow it to select which materials to enter the cell and which substances to be shut out.

The presence of these different receptors explains how drugs, hormones, bacteria and viruses act only on their target cells and not on other cells.

4. Transport of Solid Materials By Phagocytosis:

The cell membrane can engulf or allow solid materials to enter into the cytoplasm by the process of **phagocytosis**. These solid particles after their entrance into the cytoplasm are called **phagosomes**.

5. Transport of Fluid Materials By Pinocytosis:

By this process, the cell membrane can engulf droplets of fluid by a process similar to that of phagocytosis. The engulfed fluid becomes surrounded by a membrane to be changed into a **pinocytic vesicle**.

6. Expulsion of the Secretory Elements and the Residual Bodies Of the Cells By the Process of Exocytosis:

The cell membrane can release the secreted hormones and enzymes of the cells from the cytoplasm to outside of the cell and also it can get rid of the residual bodies of the cells by the **Process of Exocytosis**.

7. Sodium-Potassium Pump Function:

The cell membrane is continuously pumping sodium ions (+ve) to outside of the cell, it

also can pick up potassium ions (-ve) to the **Phagocytosis Pinocytosis And Exocytosis** inside of the cell.

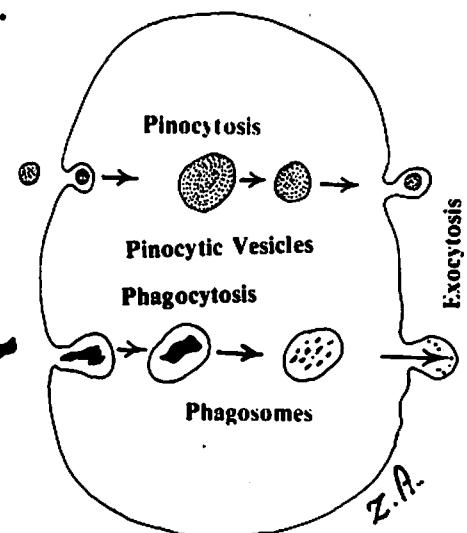
8. Conduction of Nerve Impulses: In nerve and muscle cells, the cell membranes facilitate conduction of nerve impulses from one cell to another.

Functions Of Cell Coat or Glycocalyx

The cell coat which is formed of glycoprotein and glycolipid and is present on the external surface of the cell membrane has the following functions:

9. Adhesion Of Cells: The cell coats help in adhesion of adjacent cells.

10. Recognition Of Cell Types: The cell coats enable cells to recognize cells of their own special kind. This is of importance during surgical transplantation of kidney, heart and skin grafts.



11. **Recognition of chemical messages and nerve signals by the cell receptors:**
The cell membrane receptors can receive chemical messages and neurotransmitted signals from other cells.
12. **Formation of Cell Immunity or Antigenicity:** the cell coat plays an important role in the development of cell immunity against infection. It reacts with the administered vaccines forming a protecting layer of **antibodies** on the cell surface, these prevent the entrance of living harmful bacteria and viruses into the cell.
13. **Formation of cell Allergy:** the cell coat reacts with some materials producing cell allergy which protect the body against certain harmful agents.
14. **Formation of Basal Laminae and Basement Membranes:** the cell coat and the surrounding collagen participate in the formation of basal Laminae and **basement membranes** of cells.

Cell Membrane Modifications

15. **The Cell Membrane** may be modified to form the following structures.
 - a) **Micro - Villi:** These are projections from the cell membranes. They increase the absorptive surface areas of the cells. **They are present in the cells of:** intestine, liver and kidney. They are formed of **microfilaments**.
 - b) **Cilia:** These are projections from the cell membranes. They can push fluids or particles in one direction. They are present in cells of trachea and Fallopian tube. They are formed of **microtubules**.
 - c) **Flagellae:** These are extensions of the cell membrane of certain cells. They form the tails of sperms which help in sperm movements.
 - d) **Presence of Basal and Lateral Infolding of Certain Cell Membranes.**
 - e) Presence of different types of **Cell Membrane Junctions** between certain cells which help in their functions and their adhesions.

Adhesions Of The Cells

Adhesions of the cells are controlled by the following:

1. The binding action of the **cell coats** of the two adjacent cell membranes.
2. Presence of **calcium ions** in the intercellular space.

3. Presence of **microfilaments** in the inter-cellular space.
4. Presence of the following different types of cellular junction.

Types Of Cellular Junctions

1. The Tight or Occluding Junction:

In this type, the two cell membranes of the two adjacent cells fuse with each other completely at certain points.

2. The Gap or Nexus junction:

In this type, the two adjacent cells are communicated with each other by narrow channels. Through these channels; ions, small molecules and nerve impulses pass from one cell to another.

3. The Adhering Type Of Junction:

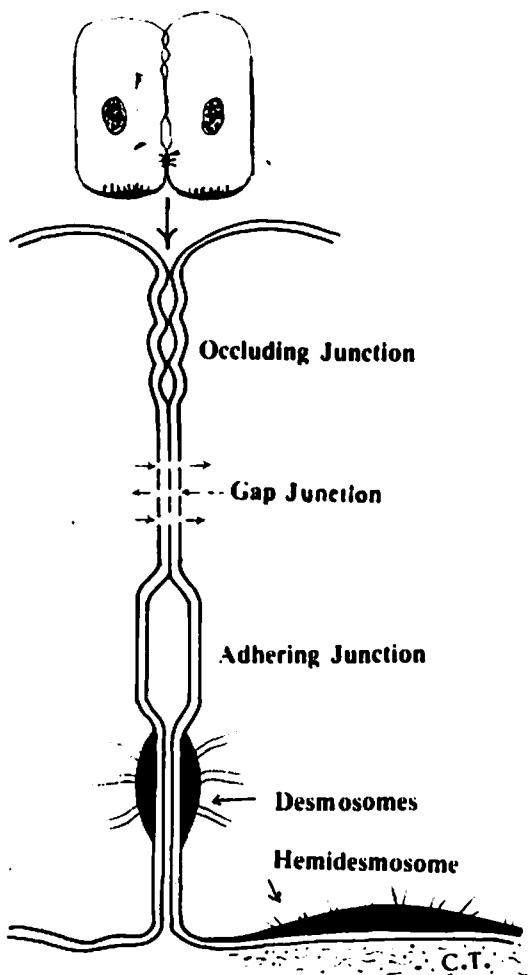
In this type, the two cell membranes are separated by a wide inter-cellular space about 20 nanometer wide. It is filled with actin filaments.

4. The Desmosomal Type Of Junction:

It is present between epithelial cells of skin. Some parts of the two cell membranes of the two adjacent cells are thickened, **cytoplasmic microfilaments** are embedded like hair pins in these thickened parts of the cell membranes.

5. The Hemidesmosomal Type Of Junction:

This junction takes the form of half a desmosome. It is present in the basal epithelial cells of the epidermis of skin.



Types Of Cellular Junctions

2. Mitochondria

Definition: They are **membranous cell organelles** present in all nucleated cells.

They contain enzymes. They are concerned with the **production of energy**.

Site: Mitochondria vary in location in the cytoplasm from one cell to another.

Structure: They are formed of; protein, lipid, DNA, RNA, Zinc, Calcium, Magnesium and Oxidative enzymes

Shape: The mitochondria word means,

Mitos = thread + chondros = granules

- **With The Light Microscope (L/M):** They appear as rods, granules or filaments.
- They may swell and change their shape.

The mitochondrial matrix is rich in:

Enzymes of Krebs cycle and of fatty acids oxidative enzymes.

- They are very sensitive to temperature and pH.

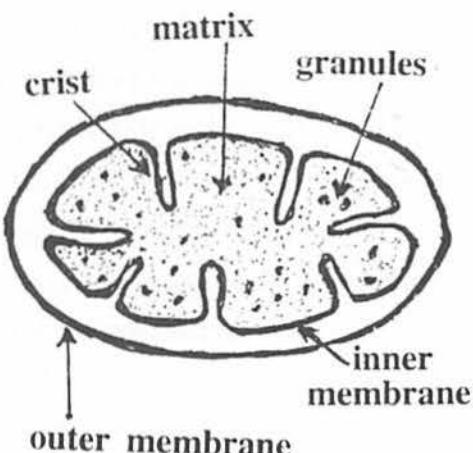
With the Electron Microscope (E/M):

Each mitochondrion appears as a vesicle surrounded by two membranes: **The outer membrane** is smooth, while **the inner membrane** is rough because it projects into the cavity of the mitochondrion forming shelves called **cristae**.

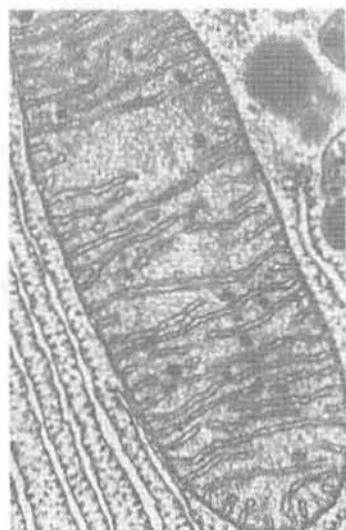
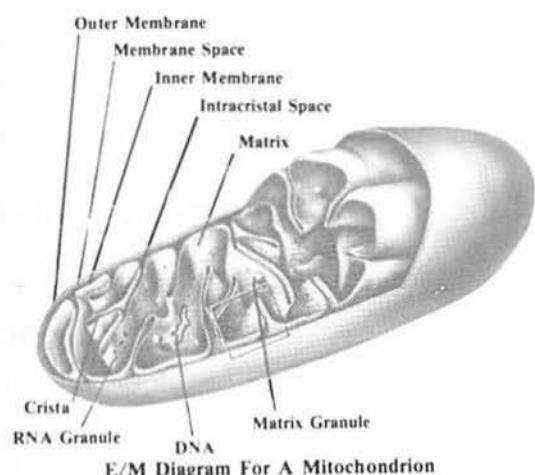
Number of Mitochondria: It varies from one cell to another. About 1000 Mitochondria are present in one liver cell, but no mitochondria are present in red blood corpuscles.

Staining of Mitochondria: They stain black with **iron hematoxylin** and green with **Janus green** stains.

- **Mitochondria can divide** in order to increase their number.
- **They contain DNA** which carries some genetic characters.
- Their life span is about 10 days.



One Mitochondrion



E/M Of One Mitochondrion

Functions of Mitochondria

- They are responsible for **cell respiration**.
- They are considered as the **power house of the cell**.
- They **supply energy** to all cellular activities.
- They contain the enzymes of the **oxidation and phosphorylation processes**.
- **The electron transport system** of the mitochondria can produce and store energy through **formation of ATP from ADP**.
- Mitochondria regulate the metabolism of **calcium and magnesium ions**.
- **N. B:** Mutations of Mitochondrial DNA cause **muscular dystrophy diseases**.

3. Endoplasmic Reticulum

Definition: They are membranous cell organelles formed of communicating wide and narrow tubules. They synthesize protein, carbohydrate, lipid and regulate mineral metabolism.

There are Two Types of Endoplasmic Reticulum; Rough and Smooth:

a) Granular or Rough Endoplasmic Reticulum

Definition: It is formed of communicating flat tubules (cisternae) with rough surfaces.

Its surface is **covered by ribosomes**. It synthesizes protein.

Position: It extends between nuclear membrane and cytoplasm.

It is present in great amounts in **protein forming cells** as: Fibroblast, Osteoblast, plasma cells and pancreatic cells.

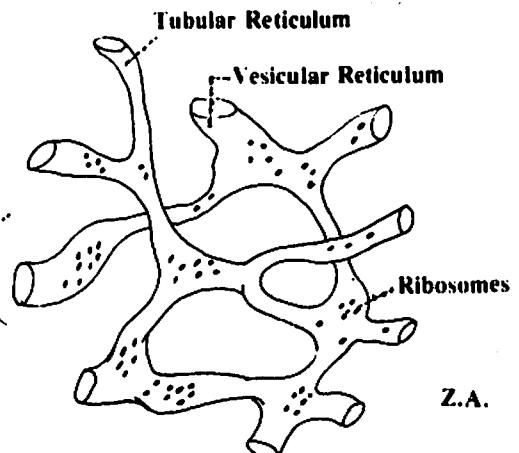
Under (E/M): They are formed of communicating flat tubules (cisternae) covered by **ribosomes and Ribophorin receptors**.

Staining: They stain blue with hematoxylin.

They are basophilic due to presence of Ribosomes.

Functions of Rough Endoplasmic Reticulum:

1. The rough endoplasmic reticulum and the attached ribosomes form protein.



Rough Endoplasmic Reticulum

- They store the formed protein.
- They package the formed protein. The packaged proteins travel through the cytoplasm as transfer vesicles to fuse with Golgi apparatus.
- They form the protein needed for the formation of lysosomal enzymes.

b. Non-Granular Smooth Endoplasmic Reticulum

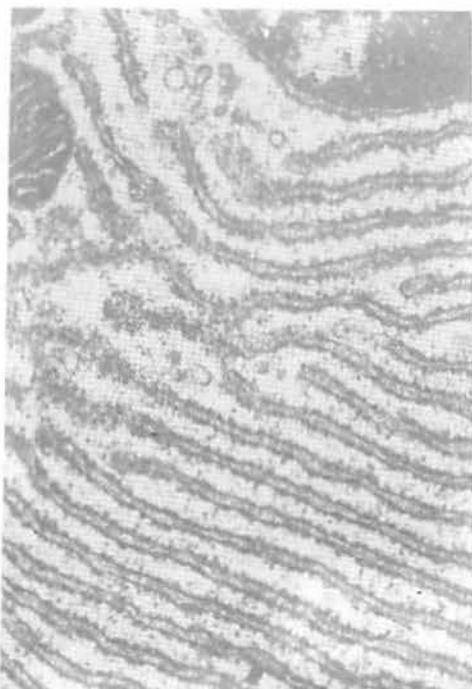
Definition: They are membranous cell organelles, formed of anastomosing narrow tubules with smooth walls. They are responsible for **lipid, carbohydrate and mineral metabolism**.

Position: It extends between the nuclear membrane and cytoplasm.

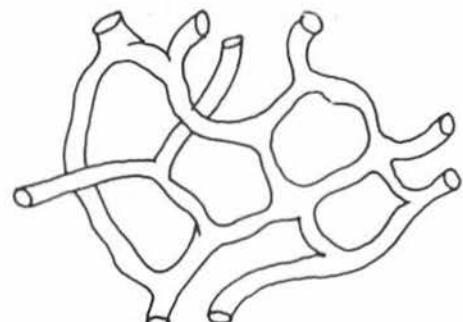
- It is present in great amounts in the cells which **synthesize lipid and carbohydrate as:** liver and endocrine cells.
- **By The Light Microscope:** It cannot be demonstrated with hematoxylin stain.
- **By The Electron Microscope,** it appears as fine anastomosing tubules with smooth walls. There are **no ribosomes on their outer surfaces.**

Functions Of Smooth Endoplasmic Reticulum:

1. Synthesis of Lipid.
2. Synthesis of Glycogen.
3. Regulation of mineral metabolism.
4. Regulation of HCl formation.
5. Regulation of muscular contraction through the release of calcium ions.
6. They play a role in detoxification of excess drugs and hormones.



Rough Endoplasmic Reticulum E/M



Smooth Endoplasmic Reticulum



E/M Of Smooth Endoplasmic Reticulum

4- Golgi Apparatus

Definition: Golgi apparatus is a membranous cell organelle. It is responsible for accumulating, concentrating, packaging, storing and adding specific materials to the secretory products of the cell.

Position: In nerve and liver cells, it surrounds the nucleus. In secretory cells, it is present between the nucleus and the free border of the cell.

Stain: It stains brown with silver stain.

It is not stained with Hx and E, its position is indicated by a non-stained area called **Negative Golgi Image**.

Shape: With light microscope, it appears as a network.

Golgi Apparatus with The Electron Microscope Appears In The Following Three Forms:

1. Flat Vesicles or Golgi Saccules:

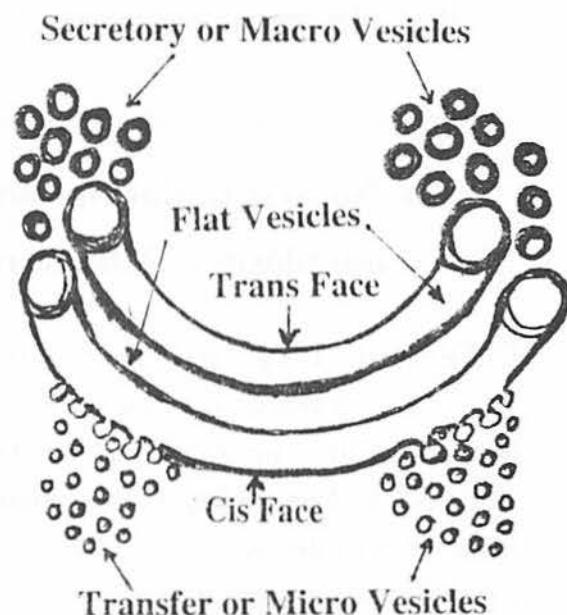
- They are formed of small flat sacs.
- The sacs are arranged above each other forming stacks.
- Each stack has a concave mature surface called **Trans Face** and a convex immature surface, called **Cis Face**.
- In these flat vesicles Golgi apparatus can do glycosylation and sulphation of protein.

2. Transfer or Micro Vesicles:

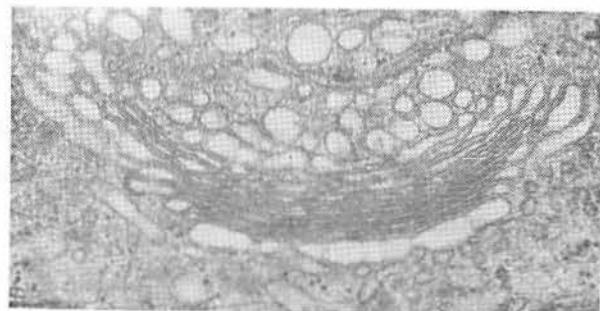
- They are small rounded sacs (vesicles) filled with protein.
- These transfer vesicles originate from the rough endoplasmic reticulum.
- They fuse with the flat vesicles of Golgi apparatus where their contents are transformed into Secretory Vesicles.

3. Secretory or Macro Vesicles

- In Golgi apparatus the entered proteins are collected, concentrated and enveloped by membranes to be transformed into the following Vesicles:-
 - a) **Excretory Vesicles** containing the excreted enzymes (zymogen granules) and the excreted hormones.



E/M Diagram For Golgi Apparatus



E/M Picture Of Golgi Apparatus

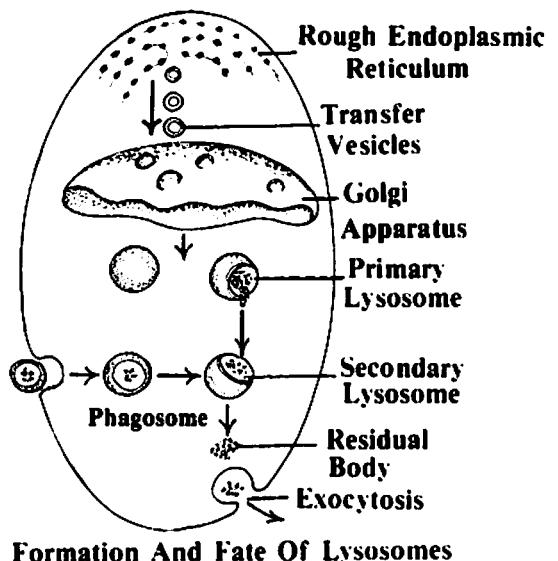
- b) Excreted protein vesicles which migrate from Golgi area to the cell membrane. They help in the process of **renewal of cell membranes**.
- c) **Lysosomal Vesicles:** They carry inside them the lysosomal enzymes. These Lysosomal vesicles remain in the cytoplasm as **primary Lysosomes**.

Function of Golgi Apparatus

1. Golgi apparatus is responsible for collecting concentrating and packaging the secretory products of the cells.
2. It adds sulfates (Sulphation) to certain secretory products of the cells.
3. It adds carbohydrates (Glycosylation) to some secretory products of the cell.
4. Golgi apparatus plays an important role in **Keeping the cell membrane and the cell coat in a good condition**. It provides additional protein to the secreted products which close the perforated areas of the cell membrane after excretion.
5. Golgi apparatus and the endoplasmic reticulum share in **the formation of lysosomes** and the secreted hormones and enzymes.

5. Lysosomes

- **Definition:** Lysosomes are membranous cell organelles present in all kinds of cells. They contain **hydrolytic enzymes** for the intracytoplasmic **digestion** of nutritive substances, and removal of residual and foreign bodies.
- **Number:** Their number vary from one cell to another. They are more present in phagocytic (eating) cells.
- **Shape and Size:** They are spherical in shape, their diameters vary from 0.2 to 0.4 micron.
- **With the fluorescence microscope; Lysosomes Appear In These 2 Forms:**
 1. **Primary Lysosomes:** appear as **homogeneous** rounded vesicles, surrounded by single membranes.
 2. **Secondary Lysosomes:** appear as **heterogeneous** rounded bodies because they contain the digested elements.



Enzymatic Contents: They contain hydrolytic enzymes as: Proteases, nucleases, lipases, glycosidases and are rich also in acid phosphatase enzymes.

Origin Of Lysosomes: They are formed through the interaction between the rough endoplasmic reticulum and Golgi apparatus by a process called **Trans-Golgi Network Process or GERL Process.**

Steps of Formation of Lysosomes

1. The lysosomal enzymes are protein in nature, they are synthesized in the **Rough Endoplasmic Reticulum.**
2. These lysosomal enzymes migrate to Golgi apparatus as **transfer vesicles.**
3. In **Golgi apparatus**, the enzymes are phosphorylated in the **Trans Golgi Network** and then are concentrated and enveloped to be transformed into **lysosomes.**
4. The newly-formed lysosomes are budded off from Golgi apparatus to enter the cytoplasm and now are called **Primary Lysosomes.**

Fate of Primary Lysosomes

1. **Primary Lysosomes** may circulate in the cytoplasm and remain as such if they are not fused with any cytoplasmic foreign bodies or nutritive elements.
2. **Primary Lysosomes**, may fuse with foreign bodies or with nutritive materials or with old mitochondria to be changed into **secondary lysosomes.**

Types of Secondary Lysosomes

- a) **Hetero-Lysosomes;** formed by fusion of primary lysosomes with **exogenous** substances as bacteria.
- b) **Autophagic Lysosomes;** formed by fusion of primary lysosomes with the **endogenous** residual bodies of old organelles as old mitochondria.
- c) **Multi-vesicular Bodies;** formed by fusion of primary lysosomes with the engulfed liquid elements which are called **Pinocytic Vesicles.**

Fate of Residual Bodies of Lysosomes

- a) **Residual Bodies** may be excreted from the cell by **Exocytosis Process.**
- b) **Old Residual Bodies** may accumulate in cardiac muscles and in nerve cells to form **lipofuscin granules** or age pigments.

Functions of Lysosomes

1. Lysosomes during life are concerned with **intracytoplasmic digestion** of nutritive materials.
2. Lysosomes, play an important role in **defending** the body against invading organisms, they **can kill bacteria** and viruses.

3. They can digest old mitochondria before their disposal outside the cell.
4. They can hydrolyse the protein which is reabsorbed by the cells of the kidney tubules preventing escape of protein in urine.
5. They can loosen the stored inactive hormones in the endocrine cells in order to change these hormones into active forms as in thyroid gland.
6. They facilitate the process of penetration of sperm to ovum during fertilization as the heads of sperms are rich in lysosomes.
7. Lysosomes of the blood leucocytes destroy the phagocytosed bacteria and viruses.
8. Lysosomes are concerned with the post-mortem changes in the body after death. When cells approach death as in oxygen deficiency, lack of blood supply or in cell infection, the escaped lysosomal enzymes will destroy the whole cells after death. Lysosomes are sometimes called **Suicidal Bags**.

6. Peroxisomes or Microbodies

- They are small cell organelles surrounded by membranes. They contain peroxidase and catalase enzymes which remove H₂O₂ from the cells.
- The smooth endoplasmic reticulum and polysomes share in their formation.
- They remove toxic molecules from liver and kidney cells.
- Deficiency in their enzymes cause diseases of nervous and muscular systems.

7. Coated Secretory Vesicles

They are small vesicles covered by protein membranes called **clathrin**. They may contain **digestive enzymes** and are called **Zymogen Granules**. They may contain **condensed hormones**. They are formed through the interaction between Rough Endoplasmic Reticulum and Golgi apparatus.

8. Endosomes and the Coated Ingested Vesicles

Any circulating molecule (as hormones) in order to enter the cell it is now called **Ligand**. This hormone binds to its receptor on the cell membrane where it will be covered by a protein capsule called **clathrin** and it is now called **Ingested Coated Vesicle**. These vesicles fuse with the **early formed lysosomes called Endosomes**. The enzymes of endosomes allow the hormonal contents of the ingested coated vesicles to separate from its capsule and to diffuse in the cytoplasm.

B - The Non - Membranous Cell Organelles

1. The Ribosomes

Definition: They are rounded or oval cytoplasmic organelles formed of ribo-nucleoprotein (RNA + Protein), They synthesize proteins.

Site Of Their Formation: They are formed in the nucleolus, They pass through the nuclear pores to reach the cytoplasm.

Staining: They are basophilic in staining, they can be stained with basic stains.

Different Forms of Ribosomes In Different Cells

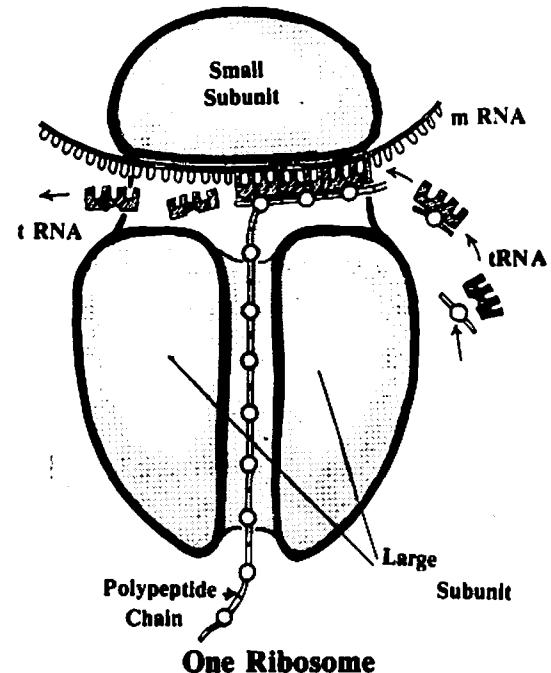
1. **Free Ribosomes:** They are scattered freely in the cytoplasm. Their number may increase in: growing cells, secretory cells, cancer cells and during cell division.
2. **Attached Ribosomes:** They are attached to the outer surface of the rough endoplasmic reticulum by ribophorins and are called **Ribosomal RNA**.
3. **Ribosomes** with the rough endoplasmic reticulum form isolated bodies in nerve cells and are called **Nissl's granules**.
4. **Polysomes:** Ribosomes may be attached to each other by messenger RNA to form rosettes or spiral structures called **Polysomes**.
5. **Microsomes:** Small fragments of ribosomes.

Ribosomal RNA are formed in the Nucleolus of the Nucleus.

E/M Picture: Each ribosome is composed of 2 subunits, one of which is twice the size of the other.

The large subunit of the ribosome is formed of 2 parts, between these two parts a **polypeptide chain is present**. The formed proteins are segregated from these polypeptide chain and then pushed into the rough endoplasmic reticulum.

Functions Of Ribosomes: Ribosomes with the organization of **transfer RNA** and **messenger RNA** form the different types of proteins. **Free ribosomes** form the cytoplasmic protein and **Attached ribosomes** form the secreted protein..



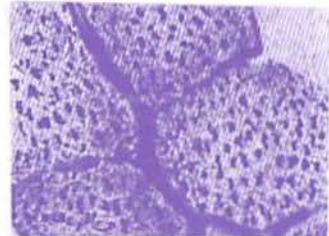
Diagrammatic Structure
Of One Ribosome



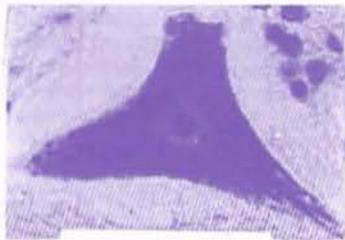
Golgi Apparatus
In Nerve Cells



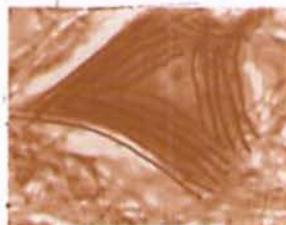
Golgi Apparatus In
Cells Of Epididymis



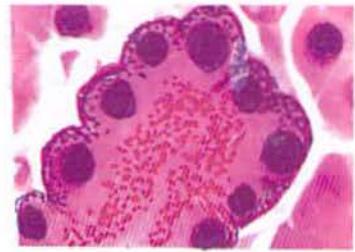
Mitochondria In Muscle
Cells (Iron Hx Stain)



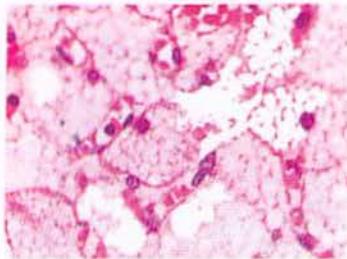
Nissl's Granules
In Nerve cell



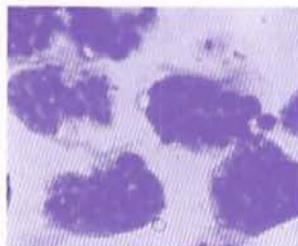
Neurofibril
In Nerve Cell



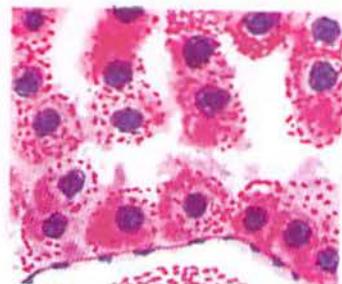
Pancreatic Acinus With
Peripheral Ribosomes And
Central Zymogen Granules



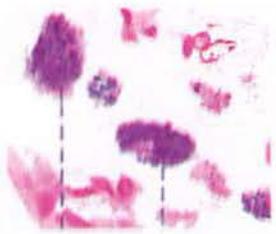
Unstained Fat Vacuoles
In Fat Cells



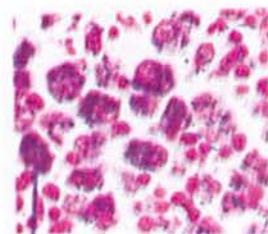
Fat Droplets Stained
Black With Osmic



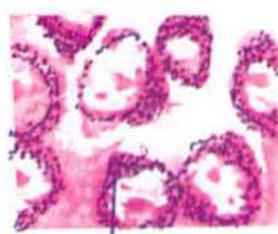
Glycogen Granules
In Liver Cells
(Best's Carmine Stain)



Exogenous Dust
Granules In
Macrophages



Endogenous Haemosiderin
Granules In Macrophages



Melanin Granules
In Skin Cells

Zakaria

2. Centrioles

Definition: They form the cytoskeleton of the cell. They are present near the nucleus in an area called **Centrosome**, which contains a pair of **centroiles**. The centrosome is formed of two centrioles.

Structure: The pair of centrioles are tubular structures, which are at right angles to one another. Each centriole is a hollow cylinder, closed at one end while the other end is opened.

Staining: They can be stained with iron hematoxylin.

N.B. Centrioles are **not present** in erythrocytes and mature nerve cells.

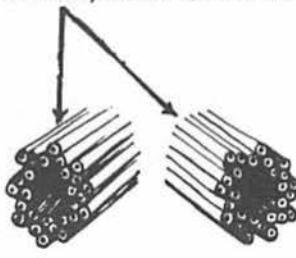
E/M Picture Of Centrioles:

Each centriole is a hollow cylinder, its wall is formed of 27 microtubules embedded in a protein matrix. The 27 microtubules are arranged in the wall of the cylinder in the form of 9 bundles. Each bundle is formed of three microtubules called **triplets**. The 9 bundles are arranged in a characteristic radiating pattern around an axial structure which appears as a cartwheel.

Functions Of Centrioles

1. They play an important role during **cell division**. At the beginning of cell division, the two cenrioles develop another two daughter centrioles. Each pair of centrioles migrate to both sides of the dividing cell. They are surrounded by an area of cytoplasm rich in protein called **Micro-Tubular Organizing Centre (MTOC)**. From this area, microtubules are formed to form the mitotic spindle across the cytoplasm of the dividing cell.
2. The centrioles contribute in the formation of **cilia and flagella** in certain cells.

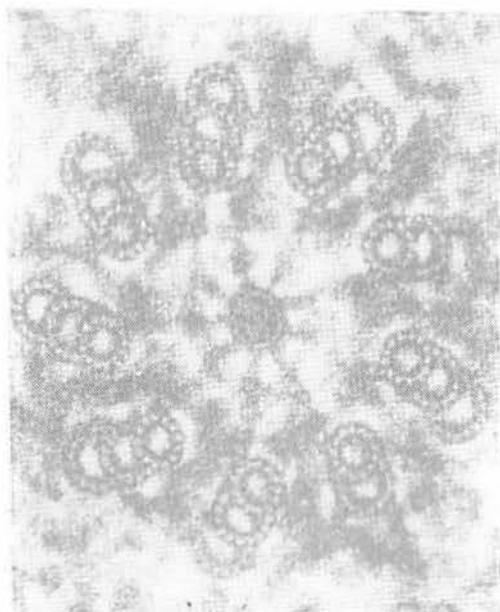
2 Centrioles, Each Of 27 Microtubules



Centrioles



E/M Picture of Two Centrioles



One Centriole (E/M)

3. Cilia

Definition: Cilia are formed of **microtubules** covered by the cell membrane. They extend from the free surface of certain cells. They help in the movement of fluids, mucus or other structures from one place to another.

Sites: Cilia are found on the surfaces of cells which line the respiratory and female genital tracts.

E/M Picture: Each cilium is formed of:

A Basal Body, A Shaft and A Rootlet:

1. The Basal Body Of The Cilium:

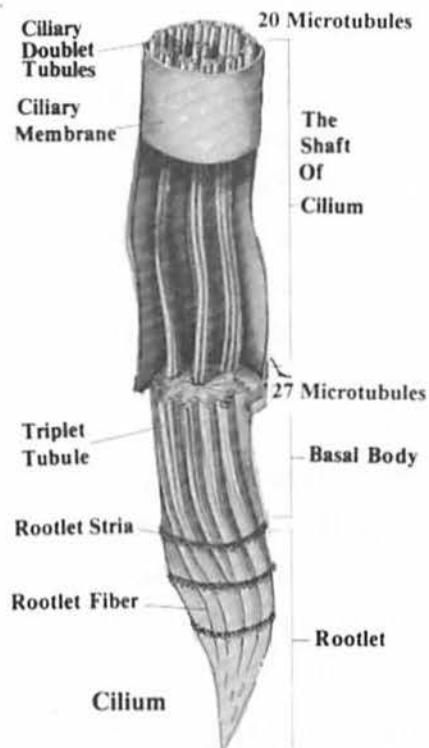
Each cilium is formed of a single centriole which migrates to the surface of the cell to form the basal body of the cilium. Thus, the basal body of the cilium is similar in its structure to the centriole. It is formed of **27 Microtubules** arranged in 9 bundles each bundle is formed of 3 microtubules (**Triplet Tubules**).

2. The Shaft Of The Cilium

(Axoneme): It is formed as a result of the growth of **20** microtubules of the basal body pushing the cell membrane outwards over themselves. The peripheral part of the shaft is formed of **18** peripheral microtubules arranged in **9** bundles,

each bundle is formed of **2** microtubules, called **Doublet**. The central part of the shaft of a cilium contains **two** more central tubules called **singlets**.

3. Rootlet Of The Cilium: It is formed of minute **Rootlet Fibres**, these fibres are microtubules which extend from the basal body of the cilium into the cytoplasm in order to fix the basal body of the cilium to the cytoplasm.



Diagrammatic Structure
Of One Cilium

Functions Of Cilia

1. They help in the movements of fluids or small bodies in one direction over the surface of the ciliated cells.
2. Each rod and cone in the retina of the eye is covered by a single modified cilium called **stereo cilium**, stereo cilia have an absorptive function.

Stereo Cilia: They are **non-true cilia**. They are **micro villi** formed of micro filaments (not microtubules). They are present in the **Eye, Ear and Epididymis**.

4 . The Flagella

The flagellum is similar in its structure to the cilium, but it is rather longer. In man the only cell with a single flagellum is the spermatozoon, it forms its tail and facilitates its movements.

II - Cytoskeleton Of The Cell

- It forms the skeleton of each cell and is responsible for its specific shape.
- It consists of **microtubules, microfilaments and intermediate filaments**.

1. The Microtubules

- They are present in all kinds of cells.
- They are cylindrical filamentous structures about 25 nm in diameter.
- They are formed of protein known as tubulin which is present in a soluble form.
- They appear as tiny circles in cross section.
- They are formed by the centrioles from the cytoplasmic protein.
- They are of variable lengths and are sufficiently elastic to bend without breaking.
- **Each Microtubule** is formed of 13 parallel **Protofilaments**.

Functions of Micortubules

- They form the **skeleton** of the cell.
- They facilitate transport of particles in the cytoplasm through the action of **Kinesin**.
- They are concerned in the **formation and movement** of cilia and flagella **through the action of their Axonemal Dynein**.
- They play an important role during cell division, they can push the two pairs of centrioles apart in order to complete the process of cell division.
N. B. For the treatment of cancer, they use vinblastin or colchicine, which prevent formation of microtubules by the centrioles in order to stop cell division.

2. The Microfilaments

- The cytoplasm of certain cells may contain **microfilaments, each is from 7 to 10 nm in diameter**.

Types Of Microfilaments

1. **Thin Actin Filaments** are formed of protein called **G and F Actin**. They are found in muscle cells, in microvilli and in the cytoplasm of all cells.
2. **Thick Myosin Filaments** formed of protein (myosin) and are found in muscles.
3. **Intermediate Filaments which are of the Following 7 Subtypes.**
 - a) **Keratin Filaments** present in cells of **skin**, hairs and nails.
 - b) **Desmin Filaments** present in smooth muscles.
 - c) **Vimentin Filaments** present in connective tissue fibroblast cells.
 - d) **Neuro-Filaments** present in nerve cells and in their processes.
 - e) **Glial Filaments** present in neuroglia cells.
 - f) **Tonofilaments** are present at the junctions of cell membranes.
 - g) **Terminal webs**; are present at the base of microvilli.

Microvilli

- They are finger like projections present on the surface of certain cells of the body as: cells of intestine, liver and kidney.
- They are formed of microfilaments covered with cell membranes.
- They increase the process of absorption and the surface area of the cell.

III - The Cell Inclusions

These are **temporary** components of the cytoplasm. They are non-living materials which are produced as a result of cell activities. They appear and disappear at different periods during the whole life of the cells.

These are examples of the cell inclusions:

1. Stored food elements as carbohydrate and fat.
2. Coloured pigments; formed by the body or enter the body from outside.
3. Crystals.

1. Stored Food

- a) **Carbohydrates:** They are stored as glycogen in liver and muscle cells.
Under Electron Microscope, glycogen appears in **these two forms**:
 1. **Alpha Glycogen Granules** which appear as single large granule.
 2. **Beta Glycogen Granules** which appear as multiple granules as in muscle cells. **Glycogen can be stained with Best's carmine or with PAS stains.**
- b) **Fat:** It is stored in fat cells of the adipose connective tissue. Fat can be stained red with **Sudan 3** or black with **Sudan black**.

2. Pigments

Pigments are often found in certain cells. They are classified into:

1. **Exogenous pigments:** They come to the cells from outside as:
 - a) **Carotene pigments:** which are present in carrots and tomatoes.
 - b) **Dust pigments:** Dust may enter the body through the respiratory system.
 - c) **Minerals:** Silver and lead may enter the body through the skin.
 - d) **Tattoo marks:** Some men draw on the skin of others certain tattoo marks.
2. **Endogenous Pigments:** These pigments are formed by the body cells as:
 - a) **Haemoglobin Pigment:** It is formed by the red blood corpuscles.
 - b) **Haemosiderin Pigments:** present in the macrophage phagocytic cells.
 - c) **Melanin Pigment:** It is formed by melanocyte cells of the skin.
 - d) **Lipofuscin or Lipochrome Pigments:** Present in nerve cells and heart muscles.
3. **Crystals:** These are cell inclusions as calcium carbonate.

The Nucleus

Definition: The Nucleus is called **Karyoplasm.** It is the largest organelle in the cell. It plays an important role in heredity, in cell division and in controlling all cellular functions. **Blood RBC and blood platelets have no nuclei.**

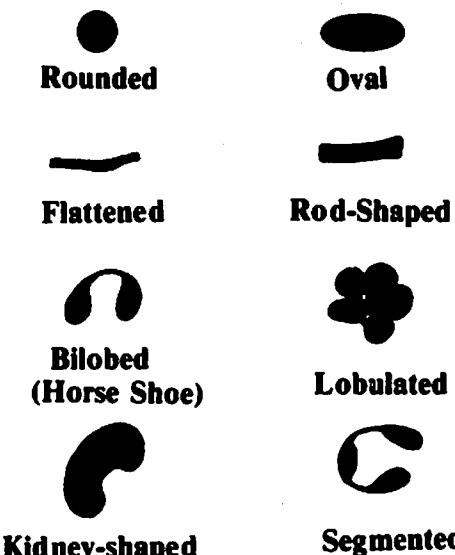
Number: Usually each cell contains one nucleus. Two nuclei may be present in some liver cells and some superficial cells of the transitional epithelium, while many nuclei are present in the osteoclast cells of bone and in skeletal muscle cells.

Size: The nucleus may be; small, medium-sized or large.

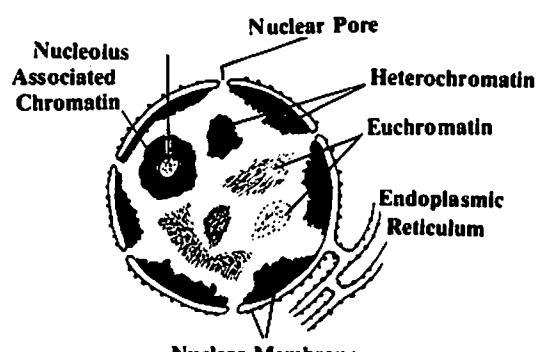
Shape: There are various shapes for the nuclei. They may be rounded, oval flattened, rod-shaped, bilobed (horse shoe), lobulated, kidney-shaped, or segmented.

Position: The nucleus may be central, eccentric, peripheral or basal in position.

Staining: The nucleus is a basophilic structure. It can be stained with basic stain as hematoxylin because it is rich in nucleic acids (DNA + RNA)



Various Shapes Of Nuclei



E/M Diagram Of A Nucleus

Structure Of Nucleus

The nucleus consists of the following FOUR Components:

1. Nuclear membrane or nuclear envelope.
2. Nuclear Sap (Karyolymph) or nuclear matrix.
3. Nucleolus.
4. Nuclear Chromatins are Of 2 Types Euchromatin and Heterochromatin.

1. Nuclear Envelope or Nuclear Membrane

- It is a dark basopilic membrane which surrounds the nucleus.
- With Light Microscope (L/M), it appears as single dark membrane.

With E/M: It is formed of the following 2 thin membranes:

- a) **Inner Fibrillar Membrane** rich in chromatin fibres on its inner aspect.
- b) **Outer Granular Membrane;** rich in ribosomes on its outer surface. It is continuous with the rough endoplasmic reticulum.

Nuclear Pores: The nuclear membrane contains many **nuclear pores**. At these pores the inner and outer nuclear membranes form a **nuclear membrane complex** which is formed of: peripheral spokes and a central plug. This plug acts as a **diaphragm** which regulates the passage of protein from cytoplasm to enter the nucleus and ribonucleoprotein to leave the nucleus to go to cytoplasm.

2 - The Nuclear sap or Nuclear Matrix (Karyolymph)

It is a protein solution present between the condensed chromatin and is formed Of: Nucleoproteins, enzymes, phosphorous, potassium and calcium.

According to the amount of nuclear sap in the nucleus we have the following two types of nuclei:

1. **The open face nucleus** in which there is a **large amount** of nuclear sap as the nucleus of **liver cell**.
2. **The condensed nucleus** which contains less amount of nuclear sap, but it has a very condensed chromatin network as in case of the nucleus of **lymphocyte**.

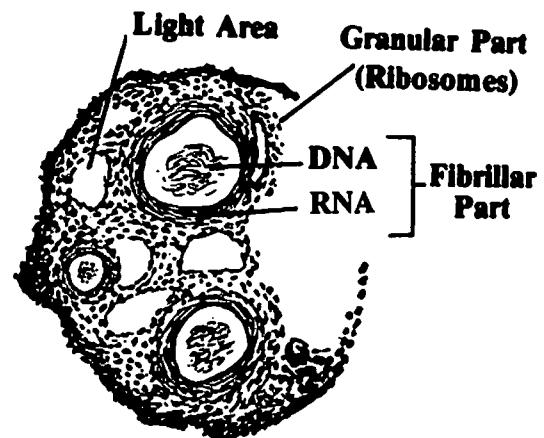
Functions Of Nuclear sap:

- (1) It has a role in Gene Transcription.
- (2) It is the site for chromosomal duplication and ribosomal movement.

3 - The Nucleolus

- The nucleolus is a basophilic mass formed of **many ribosomal RNA**. and **few inactive DNA**. It is surrounded by chromatin materials.
- The nucleolus disappears during cell division but it reappears in new daughter cells.

- The nucleolus may enlarge in size in protein-forming cells and in rapidly growing cancer cells.
- By light microscope (LM), it appears as a dark basophilic mass.
- By Electron Microscope (E/M), the nucleolus is formed of **light and dark areas**:
 - a) The **light areas** are very rich in nuclear sap and are called **Pars Amorpha**.
 - b) The **dark area** is called **Nuclear Organizer**, it is surrounded with **granular and fibrillar parts**:
- The **Granular Part or Pars Granulosa** is formed of granules of **mature ribosomal RNA**.
- The **Fibrillar Part or Pars Fibrosa** is formed of filaments of **newly formed ribosomal RNA** called **Nucleolonema**.



E/M Diagram Of A Nucleolus

Functions Of The Nucleolus:

- It forms the **Ribosomal RNA (Ribosomes)**

4 - The Chromatin Material

Definition: Chromatin materials are the basophilic particles and threads from which chromosomes are formed during cell division.

Structure: Chromatin Materials are formed mainly of nucleoprotein which is formed of **DNA bound to basic proteins called Histones**.

Staining: They are basophilic in staining due to presence of **DNA**.

With The light Microscope: The chromatin materials appear as darkly-stained basophilic granules or lightly-stained filaments.

With E/M: The darkly-stained chromatin is distributed within the nucleus as:

1. **Peripheral Chromatin:** which lies close to the inner side of the nuclear membrane.
2. **Chromatin Islands:** which are the condensed scattered masses between the nuclear membrane and the nucleolus.
3. **Nucleolus Associated Chromatin:** which are the condensed chromatin materials present around the nucleolus.

There Are Two Types Of Chromatin: Euchromatin and Heterochromatin.

1. **The Euchromatin or the Extended Chromatin is Charactarized By:**

- They are **not visible** by the light microscope because they are very thin threads.
- They represent the **extended (uncoiled)** parts of the chromosomal threads.
- They stain **very lightly** with the basic stains.
- They are the **most active chromatin**.
- They control **protein synthesis**.

2. The Heterochromatin or the Condensed Chromatin is Characterized By:

- They are **visible** by light microscope as coarse granules.
- They appear as **masses** of nucleoprotein called **nucleosomes**.
- They stain **dark** with the basic stains.
- The genes present in the condensed chromatin are **inactive**.
- They **do not** direct any protein synthesis.

Functions Of Chromatin:

1. It directs and guides protein synthesis inside the cell.
2. It stores the genetic informations of the individuals.
3. From the DNA of the chromatin material; the **Messenger** and the **Transfer Ribonucleic acids** are formed.

Nucleic Acids

They are the bases of life, they control the cellular functions. They are of **2 Types DNA and RNA**.

1. Deoxy-Ribonucleic Acid = DNA

- DNA molecules are long threads present in: the nuclear chromatin, in the chromosomes and in the mitochondria.
- DNA represent the hereditary substances or **genes**.
- Each DNA molecule consists of chains forming double helix.
- Each chain (helix) is formed of alternating phosphate and sugar (deoxyribose).
- The 2 chains of DNA molecule are linked transversely by means of **nitrogenous bases** which extend laterally from each sugar group.
- There are many millions of the nitrogenous bases in a single DNA molecule.
- The genetic instructions are coded on DNA molecules.
- There are **4 types of nitrogenous bases in DNA Molecule which are.**

1. Adenine (A).	_ Sugar _ P04 _	_ Sugar _ P04 _	_ Sugar _
2. Thymine (T).	A	G	A
3. Guanine (G).	II	III	II
4. Cytosine (C).	T	C	T

_ Sugar _ P04 _

The Chains Of a DNA Molecule

- DNA carries and stores the genetic informations of each cell.
- The individual piece of information coded on DNA is called a **gene codon**.
- DNA transfers the genetic informations by **The Following 2 Processes**.
 - a) **Replication of DNA** to form more DNA.
 - b) **Transcription of DNA** to form three types of RNA (Ribo Nucleic Acids).

2. Ribonucleic Acids = RNA

In general RNA is similar in its structure to DNA, but with the following differences:

1. **DNA** is present mainly in the nucleus, while **RNA** is present in the nucleus and cytoplasm. However, **DNA** is also present in the mitochondria of the cytoplasm.
2. With **Methyl-Green-Pyronin Stain**, **DNA** takes a **blue** colour, while **RNA** takes a **red** colour.
3. **Each RNA molecule** is formed of a single strand or helix. However, some of the regions of **RNA** may contain double helix.
4. **Each RNA strand** contains ribose sugar instead of the deoxyribose found in **DNA**.
5. **RNA molecule** contains the four different nitrogenous bases found in **DNA**, except that **Thymine** is replaced by another nitrogenous base called **Uracil (U)**. Accordingly, the 4 nitrogenous bases in RNA are cross linked with each other as follows:

$$\mathbf{A = U \text{ and } G \equiv C}$$

6. There are three types of RNA which are manufactured by the Deoxyribonucleic Acid (DNA).

These Are The Three Types Of RNA:

(1) Ribosomal RNA = r-RNA = Ribosomes

- They are formed in the nucleolus from loops of DNA.
- They move to the cytoplasm and are known as **Ribosomes**.
- In the cytoplasm, they may be attached to the rough endoplasmic reticulum or may be present free in the cytoplasm.
- **Functions:** They are the sites for protein synthesis. They are considered as factories for protein formation.

(2) Messenger RNA = m RNA

- The information codes for protein synthesis are present on the DNA molecules.
- From these DNA molecules **messenger RNA** are formed.
- The newly formed messenger RNA move to the cytoplasm carrying the messages and the informations which control the Processes of Protein Synthesis.

- They carry the **messages** from the DNA by means of **3 letter codes** called the **Codons or Genes** which can start and can stop protein synthesis.
- Each m-RNA can direct the synthesis of many identical proteins, it also contains signals which indicate where to begin and where to end protein formation.

3. Transfer RNA = tRNA

Transfer RNA are formed inside the nucleus from DNA.

- **Each Transfer RNA has 2 arms**, one is attached to amino acid and the other is called **anticodon**.
- There are different forms of **t RNA** which transfer specific amino acids to the factories of protein synthesis which are the **Ribosomes**.

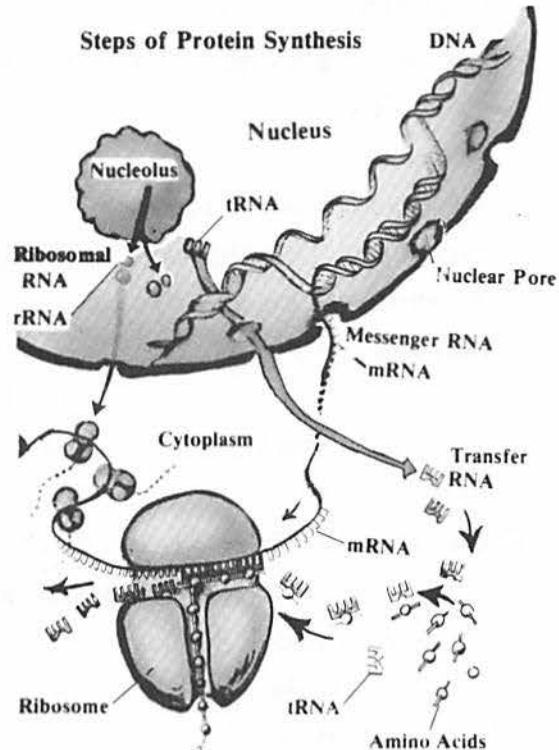
Steps Of Protein Synthesis In The Cell

These are the steps of protein synthesis in the cytoplasm:

1. The inherited genes on the DNA direct the cells to manufacture their specific types of proteins which share in formation of hormones, enzymes,... etc.
2. DNA molecules have the ability to form copies of DNA by **replication of DNA**.
3. DNA can also manufacture three kinds of RNA by the process of transcription of DNA, **These RNA are:**
 - a) Ribosomal RNA = protein factories.
 - b) Messenger RNA = code carriers.
 - c) Transfer RNA = Amino acid transporters.

Whenever the messenger RNA reach the factories of protein synthesis which are the **Ribosomal RNA or Ribosomes**,

these ribosomes read the secret messages which are present on the Messenger RNA. Then, the ribosomes call for the Transfer RNA. **These transfer RNA** can pick up the wanted amino acids from the cytoplasm. They transport these amino acids to the ribosomes. After the detachment of amino acids from the Transfer RNA, the transfer RNA goes back to the cytoplasmic pool to pick up new amino acids, and wait to be called again and so on. From these amino acids, the ribosomes manufacture the protein needed for the formation of hormones and enzymes.



Functions of the Nucleus

- The nucleus **controls** all the functions of the cell.
- It is a store house for **genetic informations**.
- The nucleus regulates the processes of **cell division**.
- It is an active centre for the **formation of the different types of RNA**.

The Life Cycle Of The Cell

The somatic cells start their life as daughter cells after mitotic cell division. They then perform their specific functions till they divide again.

The Cell Cycle is the changes which occur in the cell during its division (**mitosis**) and during its rest (**interphase**).

The cell cycle is divided into: Mitotic part and Interphase part:

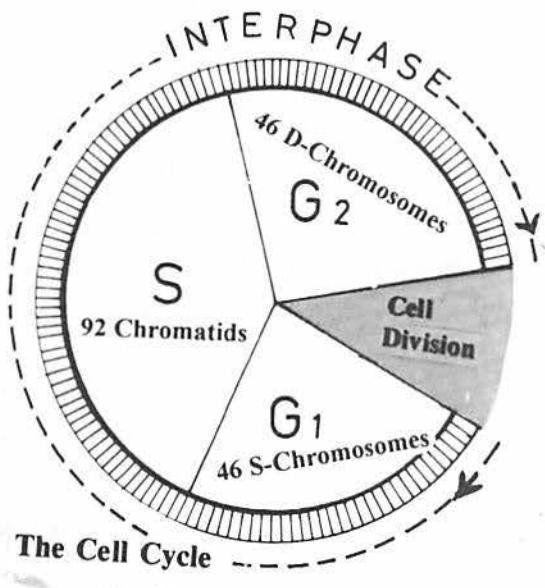
1. **The Mitotic Part Of The Cell Cycle** is the period of cell division in which each cell divides by mitosis to give two daughter cells.
2. **The Interphase Part Of The Cell Cycle** is the period of cell rest in which the cell is in a resting condition before starting another cell division. This interphase period is further subdivided into three stages: **G₁** - then **S-Stage** then **G₂-Stage**.

Stages Of the Interphase

a) G-1 Stage (Gap One Stage)

This is the period of time between the end of mitosis and the beginning of the next **S-Stage**.

In this **Gap One Stage**, the nucleus of each daughter cell has 46 chromatids which are called **S-chromosomes**. These chromosomes contain single amount of DNA. Some cells may leave this stage permanently to perform their specialized functions, these cells are then called **End Cells**.



b) S-Stage or Synthesis Stage:

This period follows the **G₁-Stage**. In this stage the actual amount of DNA is **duplicated** through the process of synthesis and replication of DNA molecules. So that we have **46 identical pairs of chromatids** in this stage (92 chromatids).

c) G - 2 - Stage (Gap two Stage)

This is a very short period of time which lies between the S-Stage and the beginning of the next mitosis. In this stage each pair of the identical chromatids become joined together at the centromere to form the chromosomes of the next cell division (next mitosis). The chromosomes of this **G - 2 - stage** are called **D-chromosomes**, They contain double the amount of DNA.

The 2 centrioles are also duplicated into 2 pairs in this G2-Stage. Thus, The Cell in G2-Stage contains 46 pairs of identical **D-chromosomes** and 4 centrioles.

Types Of Cells In Relation To Their Cell Renewal

There are three types of cells in the body which are classified according to their capacity for regeneration and renewal.

1. Non-Renewing Cells:

- These cells cannot divide. They are **not replaced** by new cells after their death. Example of these cells are: **The Nerve Cells** and **Heart Muscles**.

2. Continuously Renewing Cells:

- These cells are unable to divide; but when they die, they are replaced by daughter cells arising from mother cells called **Stem Cells** of the same family.

These Stem Mother Cells are of the following 2 types:

- Unipotential stem cells** which produce one type of cells as testicular cells which produce spermatozoa.
- Multipotential stem cells** which produce many cells as bone marrow cells which produce different types of blood cells.

3. Potentially - Renewable Cells:

These cells are normally not dividing, but at a time of need they can divide and renew their kinds of cells. as endocrine cells and liver cells.

Cell Death

There are 2 processes for cell death: **Necrosis and Apoptosis**:

- Necrosis:** is due to exposure of cells to injury, toxins or lack of oxygen.
- Apoptosis:** It is a **Programmed cell Death**, it is due to **normal termination** of the life span of the cells.

Nuclear Signs of cell Death: Nuclei become smaller. (**Pyknosis**) or fragmented (**karyorrhexis**) or complete disappearance of the nucleus(**karyolysis**).

Genetics

Genetics is the science of studying the inheritable differences and similarities. It includes many branches, but the most important ones for the medical students are:

1– The Cytogenetics.

2– The Medical genetics.

Cytogenetics

Cytogenetics is the study of heredity at the cellular level through cytological techniques and chromosomal studies.

A human being originates by the union of two gametes, the ovum and the spermatozoon. These cells contain all the characteristics that the new individual inherits originally from his or her parents.

Cell Divisions

Types Of Cell Divisions:

1. Amitosis: (direct cell division).

- It is a simple division of the nucleus and cytoplasm.
- It occurs in **lower animals** like amoeba and in certain cells of the placenta and embryo.
- It is a process of **asexual** reproduction of cells.

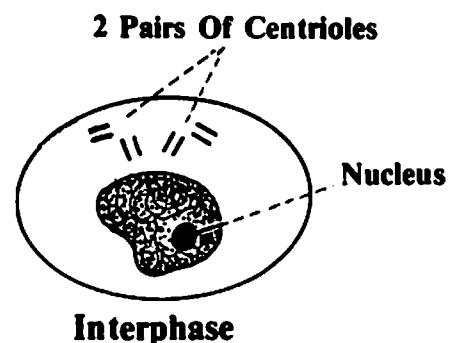
2. Meiosis: (reduction cell division).

- It occurs in the germ cells which are present in the testis and ovary during formation of gametes.
- It gives daughter cells, each one contains **half the number** of chromosomes (haploid number).
- It gives half the amount of genetic material in the daughter cells.

3. Mitosis: (indirect cell division).

- The term mitosis (mitos = thread, osis = process) is the process in which threads of chromosomes appear during the stages of mitosis.
- It occurs in the general cells of the body (somatic cells).
- It gives daughter cells, each cell contains a **full number** of chromosomes. (diploid number).

The daughter cells will have the same amount of genetic material as the mother cells



Mitosis (Indirect Cell Division)

When a cell begins to divide by mitosis certain changes occur in its cytoplasm and in its nucleus:

In the cytoplasm, a spindle-shaped structure is formed by the microtubules which originate from the cytoplasm. This spindle, plays an important role in bringing the chromosomes to the middle of the dividing cell and in the separation of its chromatids or chromosomes

In the nucleus, the chromatin materials change into 46 chromosomes. Each chromosome is formed of 2 chromatids which separate from each other during cell division. Each chromosome divides normally in a longitudinal manner into 2 chromatids. The half number of these chromatids move towards each pole of the dividing cell. In each new daughter cell and during its interphase, each chromatid (**S-chromosome**) changes into a **D-chromosome**, thus the **46 chromatids** form again the full number of chromosomes which are now called **D. chromosomes (46)**

Stages of Mitosis

Mitosis has four phases (prophase, metaphase, anaphase and telophase).

The whole process takes from 1 to 2 hours.

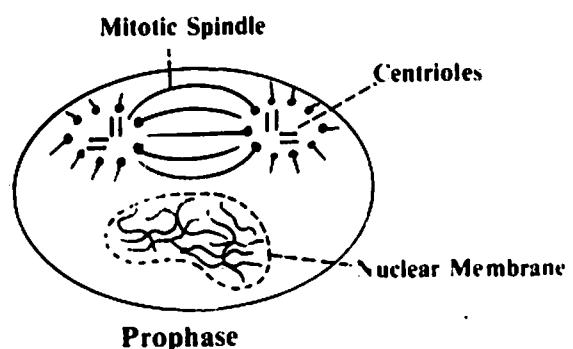
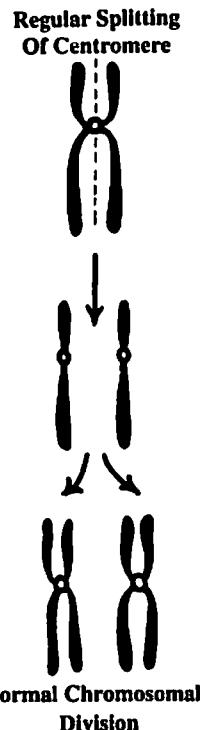
1. Prophase Stage: (Pro = before)

Before beginning the prophase stage, the cell is present in the G₂ stage of the interphase. It contains 4 centrioles and 46 D-chromosomes.

- Each pair of the centrioles move to one pole of the dividing cell.
- The centrioles form continuous type of microtubules to form the mitotic spindle.
- The nuclear envelope and nucleolus disappear.
- The chromosomes are now short and thick.

2. Metaphase Stage (Meta = Between)

- At this stage, the mitotic spindle is well formed and its microtubules are attached to the centrioles.
- The chromosomes are now arranged in the equatorial plane of the cell. They are short and thick.
- Each chromosome is formed of 2



chromatids which are connected with each other at a point called **Centromere**.

At this centromere there are two rounded protein bodies called **Kinetochores**. These Kinetochores form another type of microtubules called **chromosomal microtubules**.

- Therefore, The mitotic spindle is formed of:

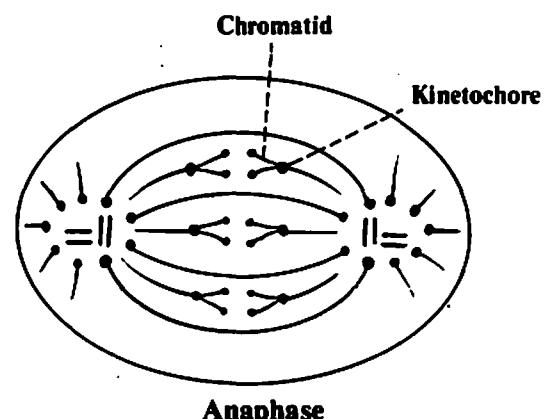
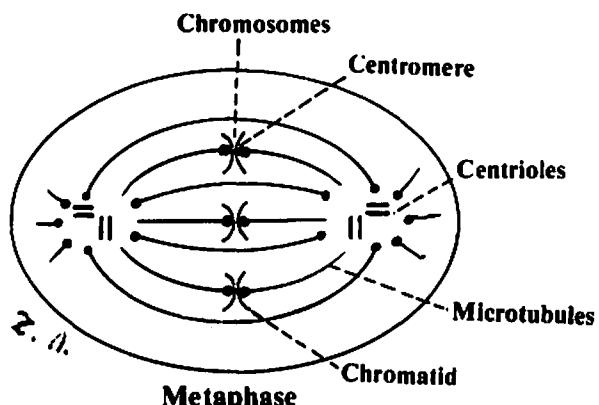
A. Cytoplasmic Microtubules which arise from the cytoplasm and are attached to the centrioles.

B. Chromosomal Microtubules which arise from the **kinetochores** of the chromosomes and are attached to the chromosomes.

3. Anaphase Stage (Ana = Apart)

- At this stage, the two chromatids split at the centromere by normal longitudinal division, therefore the dividing cell contains now 92 chromatids.

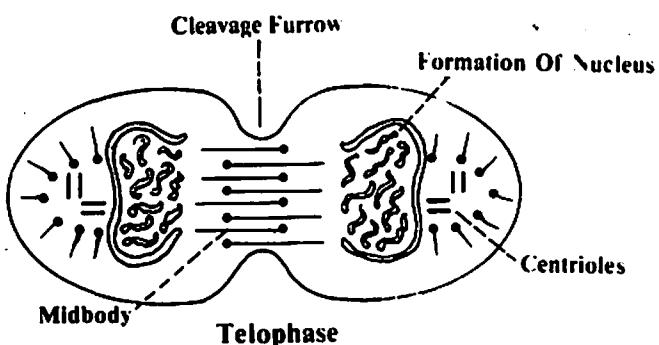
- Half of the chromatids move towards one pole of the dividing cell and the other half (46) move to the other pole. The separation and movements of chromatids are carried out by the elongation and interaction of both chromosomal and cytoplasmic microtubules.



4. Telophase Stage (Telo = End)

- In this stage a constriction begins to develop at the midpoint of the elongated cell, which is called **cleavage furrow**.

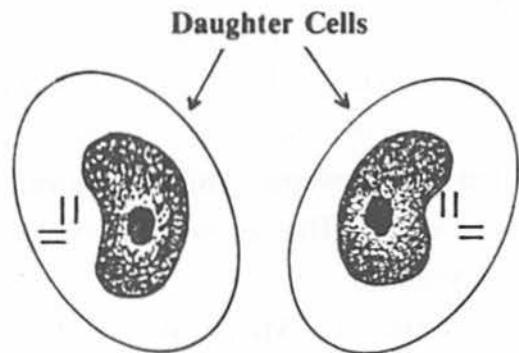
- **The 2 groups of chromatids** (each group is formed of 46 chromatids) move to the new daughter cells. These chromatids are then transformed into **chromatin threads** and then into **46 S-chromosomes**.



- The nucleoli, the nuclear sap and the nuclear membrane are now **reformed** to constitute the nuclei of the new daughter cells.

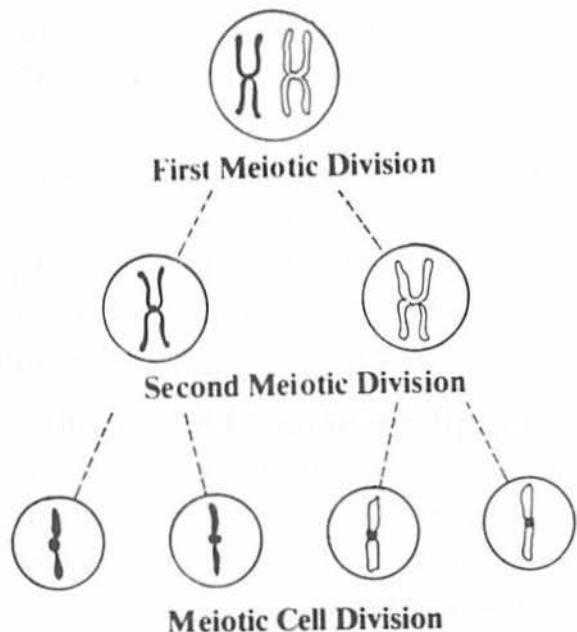
- The **cleavage furrow** which encircles the cell progress until it divides the mother cell into 2 daughter cells, each contains 46 single chromatids called **S-chromosomes**.

Now the daughter cells enter into the **G1-Stage** of the interphase.



Meiosis (Reduction Cell Division)

- This type of reduction division occurs only in the germinal cells of the **testes and ovaries**.
- Each mother cell gives rise to **four cells**; each of the new daughter cells has only the **haploid number** of chromosomes (23).
- **In males**, all the new 4 daughter cells, are **viable spermatozoa**.
- **In females**, only one of the new 4 daughter cells is a viable egg cell, and the other 3 fail to develop and are known as **polar bodies**.
- Meiosis consists of **two nuclear divisions** which follow each other without DNA replication (No S Stage - no duplication of DNA).
- The first meiotic division involves the separation of chromosomes leading to formation of 2 **haploid nuclei** (each nucleus contains 23 chromosomes). Each chromosome is formed of 2 chromatids.
- The second meiotic cell division: It occurs in the previously formed 2 haploid nuclei resulting from the first meiotic cell division. In this second meiotic division longitudinal separation of chromatids occurs in their 23 chromosomes giving rise to 2 nuclei, each nucleus **contains 23 chromatids**. These chromatids will be transformed **into 23 chromosomes**.



1 - First Meiotic Cell Division

It occurs through four phases: Prophase, Metaphase, Anaphase and Telophase:

1. **The Prophase:** It takes a long time, 22 days to form spermatozoa in males and from 12-45 years in females to form Oocytes.

The Prophase Stage includes the following 5 Steps:

- a) **Leptotene:** In this step the 46 chromosomes appear as thin threads.
- b) **Zygotene:** The 46 chromosomes become arranged in 23 pairs. Each pair is composed of 2 homologous chromosomes called **Bivalents**. One member of the bivalent is originally from the father and the other one is originally from the mother.
- c) **Pachytene:** in which the chromosomes become shorter and thicker.
- d) **Diplotene:** The bivalent chromosomes are arranged close to each other, therefore their arms cross each other forming **X-Shaped Chiasma**.
- e) **Diakinesis:** Appearance of **mitotic spindle** between the dividing cells.

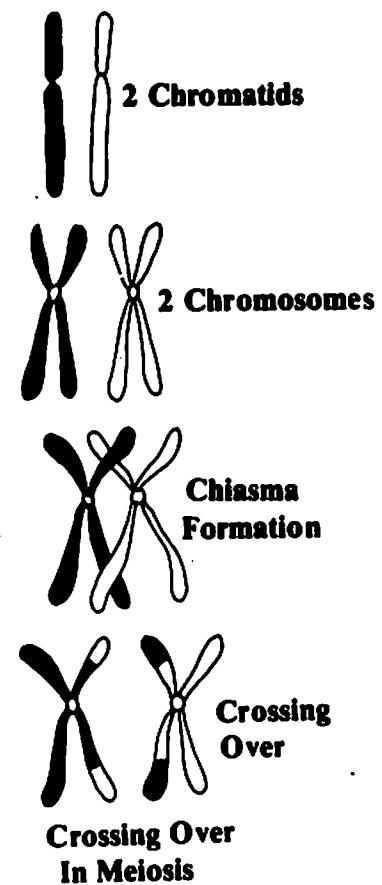
Crossing Over Of Chromosomes

The chromatids of the homologous chromosomes (one from the father and the other from the mother) may come to lie across each other forming a **chiasma** (**Chiasma = X-Shaped crossing**). Due to fragility of chromatids, they break at the site of crossing. The detached chromosomal parts will unite with the corresponding homologous chromosomes. Thus, the heredity characters from both father and mother will become represented in their offsprings.

2. **The Metaphase Stage of the First Meiotic Cell Division:** The mitotic spindle is well developed. The 23 pairs of homologous D-chromosomes become arranged in the equatorial plane.

3. **The Anaphase Stage:** Each pair of the homologous chromosomes separate from each other. Each group of the separated 23-chromosomes move towards the corresponding pole of the dividing cell.

4. **The Telophase Stage:** At each pole of the dividing cell, the 23 chromosomes become surrounded by a nuclear membrane to form the nucleus of the daughter cell.



N. B. The daughter cells resulting from the first meiotic cell division are now called “Secondary Oocytes” or “Secondary Spermatocytes”. Each contains a haploid number of D-chromosomes (23 D-chromosomes).

The first meiotic cell division is followed by a short period of time (interphase) in which the cell does not pass into the S-stage (No duplication of DNA). After this short period, the cell enters into the stages of the second meiotic cell division.

2 - Second Meiotic Cell Division

This process takes place in each cell of the two resulting daughter cells from the first meiotic cell division.

**The second, meiotic cell division comprises the ordinary 4 phases of mitosis:
These Are The Stages Of The Second Meiotic Cell division:**

- At prophase: The mitotic spindle is formed. The 23 chromosomes are attached to the spindle and each chromosome is formed of 2 chromatids.
- At Metaphase: The 23 chromosomes become arranged along the equatorial plane of the cell.
- At Anaphase: Each chromosome splits into 2 chromatids, half of these chromatids (23) move towards each pole of the dividing cell. Each chromatid will change into an S-chromosome in the new daughter cell.
- At Telophase: The 23 S-chromosomes become elongated and thinner and a nuclear membrane is formed around each nucleus forming 2 nuclei. Each nucleus contains half the original number of chromosomes = 23.

Differences Between Mitosis And Meiosis

Mitosis	Meiosis
<ol style="list-style-type: none">1. It is an indirect cell division.2. It occurs in Somatic cells of the body.3. It consists of one set of nuclear mitotic cell division.4. Chromosomes are arranged singly.5. No crossing of chromosomes.6. No exchange of genes.7. It gives 2 daughter cells, each with 46 chromosomes (full number).	<ol style="list-style-type: none">1. It is a reductional cell division.2. It occurs in testes and ovaries.3. It consists of 2 sets of division, First and Second Nuclear Divisions.4. Chromosomes are arranged in pairs.5. Crossing over occurs.6. Exchange of genes occurs.7. It gives 4 daughter cells, each with haploid number of chromosomes (23).

Abnormalities In Cell Division

1. Nondisjunction = (Non-Separation of Chromosomes) or Chromatids:

During normal cell division, each daughter cell receives an exact number of chromosomes or chromatids. If abnormal division occurs, as **nondisjunction** = (non-separation of chromosomes or chromatids), one daughter cell may receive both chromosomes and the other daughter cell will receive none of them.

For example if nondisjunction occurs at the **first meiotic division**, all four products or gametes will be abnormal, two gametes having an extra chromosome and two gametes being deficient of one chromosome.

If non-separation occurs at the **second meiotic division**, only two gametes are abnormal, the other two will have a normal number of chromosomes.

2. Misdivision Of Centromere (Formation Of Isochromosomes).

Normally the centromere divides **longitudinally** giving rise to two identical chromatids.

Sometimes, abnormal **transverse division** may occur. This misdivision of the centromere will give rise to **non similar chromatids**. These non identical chromatids change in the daughter cells into **isochromosomes**. One of these isochromosomes will have **two long chromatids** and the other isochromosome will have **two short chromatids**.

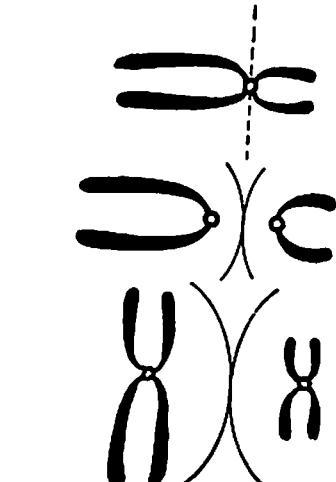
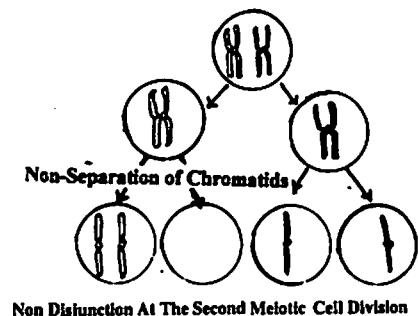
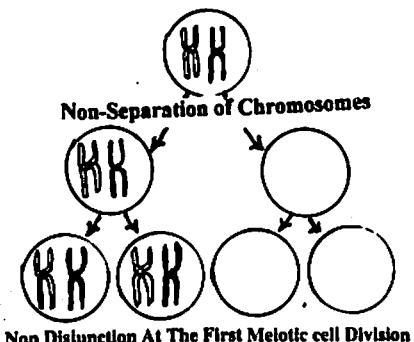
Human Chromosomes

- A human being is formed of billions of cells; These cells are of The Following Two Types:

- Somatic cells which are present in the whole tissues of the body.
- Gametes which are the sperms and ova.

- Each somatic cell nucleus contains 46 chromosomes which are as follows:

1. 22 Pairs of identical chromosomes known as **autosomes**.
2. One Pair of **sex chromosomes** which differ according to the sex:-
 - In female somatic cell, the sex chromosomes are called **XX chromosomes**.



Formation of Iso chromosomes

- In male somatic cells, the pair of sex chromosomes are different, one being a long X chromosome and the other is a small Y chromosome.
- Each gamete (ovum or sperm) contains 23 chromosomes.
In Females, the sex chromosomes in the mature ova are all alike X.
In Males, the sex chromosomes in sperms are unlike, so that we have 2 types of sperms some with X and other with Y chromosomes.

Karyotyping

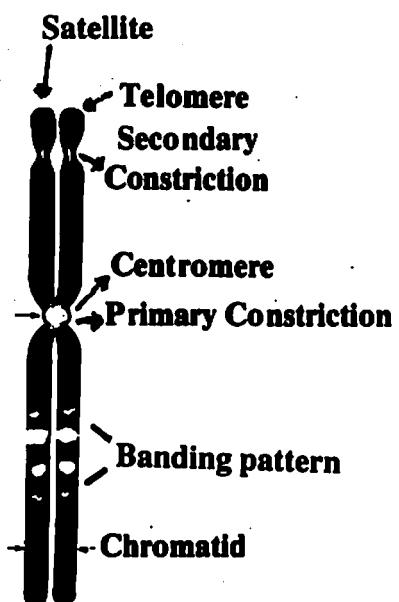
Karyotyping is the study of the number, type and arrangement of chromosomes in the individuals. **Karyotyping is done through the following steps:**

The blood lymphocytes are the most convenient cells for chromosomal studies.

1. From the venous blood of the examined person, a sample of blood is obtained. To prevent clotting of this blood, a heparin substance is added to this blood sample.
2. The blood is then centrifuged to separate lymphocytes from other cells.
3. The lymphocytes are then incubated in a suitable culture medium.
4. Phytohaemagglutinin is added to the culture medium to stimulate division.
5. The cultured lymphocytes are incubated for three days.
6. We stop cell division of lymphocytes at metaphase by the addition of colchicine.
7. The cultured cells are then treated with hypotonic solution.
8. Samples from the cultured cells are then spread on the slides by the drop method.
9. The chromosomes are then fixed, stained, examined and photographed.
10. The photographed chromosomes are cut, matched into pairs, and individually studied. Now this step is done through the use of Image Analyzer.

The Structure Of A Human Chromosome

- Each D-chromosome is formed of 2 identical chromatids connected together at the centromere.
- Each chromatid has a long arm called (q) arm and a short arm called (P) arm.
- Small portions called Satellites are attached to the short arms of these chromosomes: 13, 14, 15, 21 and 22. The Telomeres are the terminal ends of the chromatids.
- On the chromatids there is identical series of bands which form the banding pattern.
- According to the length of chromosomal arms and to the position of centromeres, the chromosomes are classified into the following 4 types:

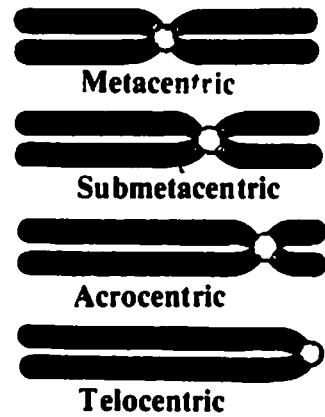


**A Diagrammatic Structure
Of One Chromosome**

Types of chromosomes

- There are Four types of chromosomes according to the position of the centromeres:

- 1. Metacentric Chromosome:** In which the centromere is median in position.
- 2. Submetacentric Chromosome:** In which the centromere is present midway between the centre of the chromatids and their upper ends.
- 3. Acrocentric chromosome:** In which the centromere is present more near to the terminal ends of the chromatids.
- 4. Telocentric Chromosome:** In which the centromere is at the terminal ends of the chromatids.



Types Of Chromosomes

- In karyotyping, the individual 22 pairs of human chromosomes are numbered serially from 1 to 22 and are grouped into 7 groups: A,B,C,D,E,F, and G.

Group A: includes the longest 3 pairs of chromosomes 1,2 and 3.

Group B: includes 2 pairs of chromosomes 4 and 5.

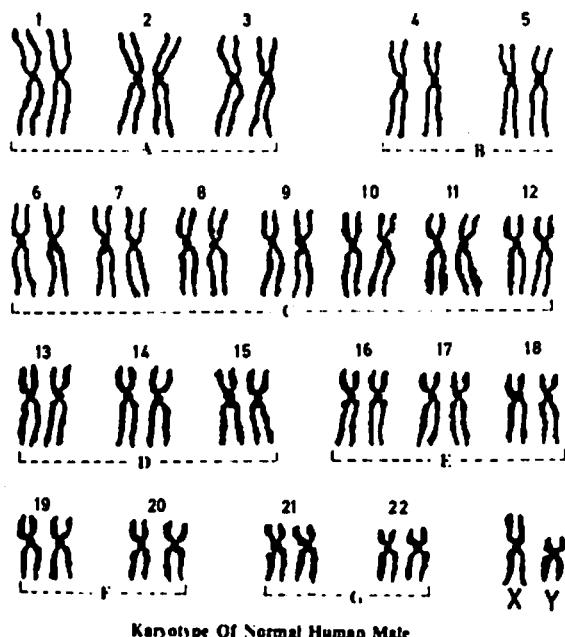
Group C: includes chromosomes 6,7,8,9,10,11 and 12.

Group D: includes chromosomes 13,14 and 15.

Group E: includes chromosomes 16,17 and 18.

Group F: includes chromosomes 19 and 20.

Group G: includes chromosomes 21 and 22.



Karyotype Of Normal Human Male

- The last pair of chromosomes are the **sex chromosomes** which may be: XX in females. or XY in males.
- The X chromosome is long, while the Y chromosome is short.

The Clinical Importance Of Chromosomal Studies

- 1. Chromosomal studies** help in diagnosis of certain diseases and syndromes as: Down syndrome (mongolism) and mental retardation.
- 2. Diagnosis of primary amenorrhoea, repeated abortions and infertility.**

3. Diagnosis of certain malignant diseases as chronic myeloid leukaemia.
4. Karyotyping of foetal cells helps in prenatal diagnosis of certain diseases and in determination of the sex of the foetus (either male or female).

Chromosomal Aberration (Abnormalities)

Causes Of Chromosomal Aberrations

1. Infection with German measles; its virus causes fragmentation of chromosomes.
2. Radiation; causes some chromosomal damage.
3. Auto-immune diseases may cause chromosomal abnormalities.
4. Pregnancy in old women may give children with congenital syndromes.
5. Presence of chromosomal imbalance in the parents or in their families.

Types Of Chromosomal Abnormalities

1. Numerical Abnormalities; in which there is an abnormal number of chromosomes, less or more than 46 chromosomes.
2. Structural Abnormalities; in which there are abnormalities in the structure of chromosomes.

(A) Aberrations In Chromosomal Number

- Normally the number of chromosomes in each sperm or ovum is 23 = haploid.
- The normal number of chromosomes in a zygote is 46 = diploid number.

Diploidy or Euploidy: It means presence of normal chromosomal number 46.

Polypliody: Presence of multiple basic numbers as; 92, or 138

Aneuploidy: Presence of fixed abnormal number as; 45 or 47.

Mosaic Person shows different chromosomal numbers in his different cells.

Trisomy

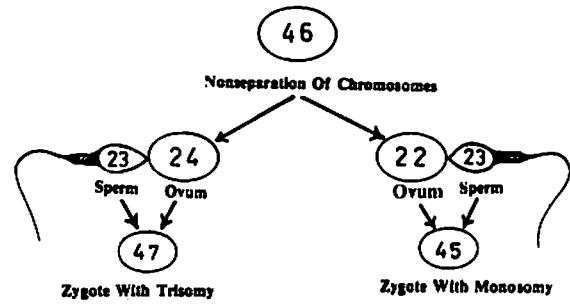
- The chromosomes are present in pairs. Sometimes, an extra chromosome may be present, this will result in the presence of three similar chromosomes instead of two. This will lead to the presence of 47 chromosomes instead of 46. The commonest is trisomy 21 (Down syndrome or Mongolism).

Down Syndrome = Mongolism

Mongolism = Down syndrome = Trisomy 21

- The cells of these children contain 47 chromosomes instead of 46. The extra chromosome is similar to the pair of chromosomes number 21, so this disease is called **Trisomy 21 or G-trisomy syndrome**.

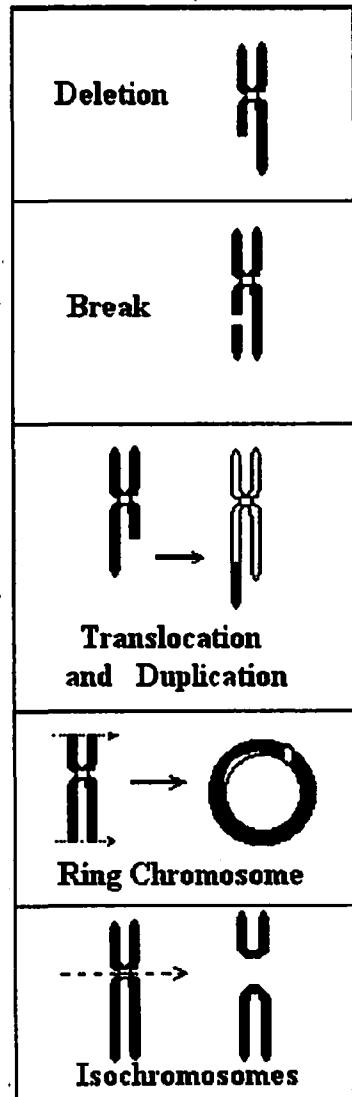
The Mongol Infant is mentally retarded with mongolian face, small oral cavity, with a protruded tongue and with short broad neck.



(B) Structural Aberrations Of Chromosomes

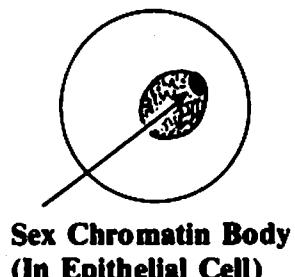
Abnormalities in the morphology of chromosomes may be due to the following: Deletion, Duplication, Inversion, Translocation, Formation of Ring Chromosome and Isochromosome Formation.

- 1– **Deletion**, means detachment and loss of portions from chromosomal arms.
2. **Chromosomal Breaks** in the chromatids which usually heal rapidly and correctly.
3. **Duplication**, It means detachment of a piece from one chromosome, this may be reattached to another chromosome. Duplication may lead to the presence of double dose of genes on one chromosome.
4. **Inversion**, It occurs when a break happens to one chromatid, the broken segments may reattach again but in a wrong manner.
5. **Translocation**, it involves the transfer of a broken piece of one chromatid to be reattached to another chromatid.
6. **Formation of Ring Chromosome**, in which the broken ends of one chromosome may unite to form a ring chromosome.
7. **Isochromosomes**: Sometimes, during cell division, one chromosome may divide transversely instead of longitudinally resulting in the appearance of two unequal chromosomes: one chromosome with two long arms and the other one, with two short arms.



The sex Chromosomes

- Usually the sex of the embryo is determined just after fertilization.
- The sex chromosomes in females are alike XX. The females can give similar ova, each ovum contains only one X chromosome.
- The sex chromosomes in males are unlike XY. The males can give rise to two types of sperms; some of their sperms carry X chromosome and the other carry Y chromosome.

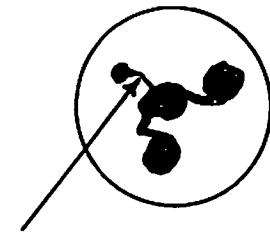


The Sex Chromatin Or Barr Body

Barr (1949) discovered that, the nuclei of female cells contain a darkly stained body and he called it Barr body.

1- Demonstration And Staining Of Barr Body in female epithelial cells:

The examined cells are obtained from female oral cavity.



The cells are then stained by basic stain. The Barr body **Sex Chromatin Body** appears as darkly-stained mass inside the nuclear membrane. (**In Neutrophil**)

2- Demonstration Of Barr Body in blood leucocytes:

The obtained blood leucocytes from a female are stained with Leishman's stain. **The Barr Body** appears as a drumstick-like mass attached to the nucleus of blood neutrophils obtained from female blood.

Clinical Importance Of Sex Chromosomal Studies

1. Diagnosis of sex in doubtful cases of hermaphroditism.
2. Studying the abnormalities of the sex chromosome.
3. Diagnosis of abnormal sexual maturations in males and females.
4. Diagnosis of the cause of infertility, primary amenorrhea and frequent abortions.
5. Identification of sex, either male or female before and after birth.

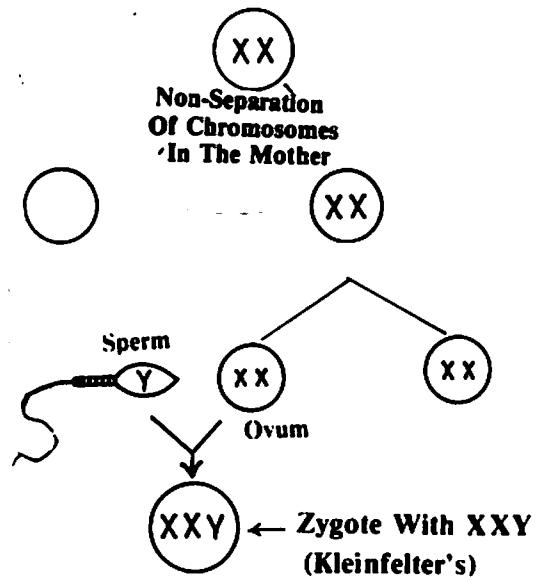
Sex Chromosomal Abnormalities

Kleinfelter's Syndromes

If non-separation of chromosomes occurs in the first meiotic cell division in the mother during the formation of ova, the formed ovum will contain two X chromosomes (XX). If this ovum is fertilized by a sperm with Y chromosome, the resulting zygote will contain XX Y chromosomes. This condition give rise to a male infant with Kleinfelter Syndrome

Characteristics Of a boy with Kleinfelter Syndrome

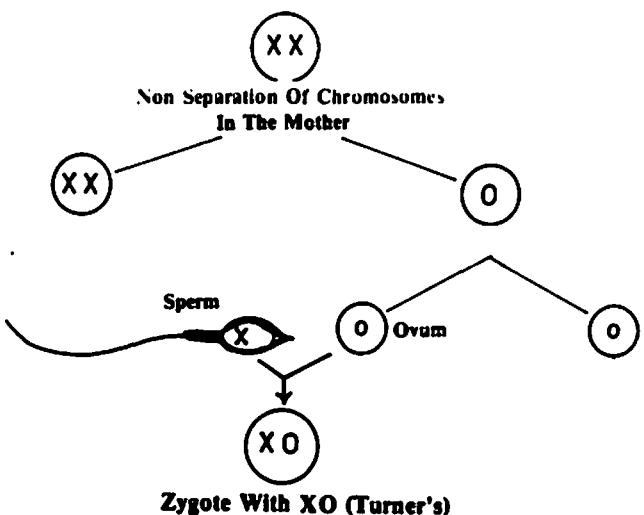
1. Mentally retarded male with small testes and low level of male hormones.
2. The nipples are widely spaced.



3. Barr Body appears in these tall males.
4. The Karyotype of this patient shows the presence of 47 chromosomes.
5. The sex chromosomes of this male infant are XXY.

Turner's Syndrome

As a result of non-separation of chromosomes in the mother during the formation of ova, the X chromosomes may be absent from the ovum. If this ovum is fertilized by a sperm with **X chromosome**. The resulting zygote will contain **XO**. This condition gives rise to a female infant with **Turner's syndrome**. **Barr Body** is not present in these females.



A Femal Infant With Turner's Syndrome Is Characterized By:

1. A female with un-developed ovaries and external genitalia.
2. A short female with widely spaced nipples and oedema of limbs.
3. The females usually have primary amenorrhea.
4. The karyotype of this female is 45 (XO).

The Genome = Distribution Of Genes On Chromosomes

- **The Genome** means the location (position) of the different genes responsible for the normal characters or abnormal diseases on the human chromosomes.
- Each chromosome contains millions of genes.
- **Genes are the units of heredity**, they are formed of **segments of DNA**.
- Genes are arranged in linear order on the chromosomes. They have specific locations on the chromosomes, and each site of gene is called a **locus** or place.
- **Genes are found in pairs like chromosomes**. The 2 genes for a specific character occupy the same loci (the same place) **on the 2 members of the homologous pair of chromosomes**. These 2 genes may be alike (**H H or h h**) and are called **Identical Genes**. On the other hand the genes for a certain character may be unlike (**H h**) and are called **Allelomorphic Genes**.

A Homozygous or Homozygote individual is that individual who carries **identical pair of genes** on the 2 members of the homologous pair of chromosomes. **For example HH or hh .**

A Heterozygous or Heterozygote individual is that individual who carries 2

different genes (Allelomorphic genes) on the 2 members of the homologous pair of chromosomes.

In the heterozygous state, the individual carries two different allelomorphic genes: one being a **dominant gene** and the other is a **recessive gene**.

Example: If the gene of the **Brown colour** of the eye is symbolized **B** and its allelomorphic gene for the **blue colour** of the eye is symbolized **b**.

A homozygous person for brown eyes carries **B.B.**

A homozygous person for blue eyes carries **b.b.**

A heterozygous person carries **B.b.** (his eyes are brown because **brown colour** is a dominant character).

Modes Of Inheritance

The human zygote contains 23 pairs of chromosomes which are as follow:-

- 22 pairs of Autosomal chromosomes.

- One pair of Sex chromosomes.

Thus, there are two main modes of inheritance depending upon which chromosome is carrying the inherited character or disease.

1. Autosomal Inheritance is when the inherited characters or disease are carried by genes present on the autosomal chromosomes. The inherited disease or character may be **dominant or recessive**.

Madness is an example of a dominant autosomal inherited disease.

Brown Eyes is an example of a dominant autosomal inherited character.

Albinism is an example of a recessive autosomal inherited disease. The **albino individual** has a rosy-coloured skin, white hair, red eyes with the absence of tyrosinase enzyme and melanin pigment from his body.

2. Sex-linked Inheritance when the characters or disease are carried by genes present on one of the sex-chromosomes either on the **X or Y chromosomes**.

1- X-chromosome Inheritance Diseases: The diseased genes are present on the X-chromosomes. Examples of these diseases are the **Haemophilia and Colour Blindness**.

2- Y-chromosome Inheritance Disease: The diseased gene is present on the Y-chromosome. Example of this disease is the “**Hairy-Ears**” in male individuals.

Blood Groups

The A,B, O Blood Group System

The blood group of any individual belongs to one of the four major blood groups which are **A,B,AB and O**.

Now there are 6 phenotypes for blood groups among individuals.

These phenotypes of blood groups are: **A₁, A₂, B, A₁B, A₂B, and O**

- The locus (place) of the genes for the A-B-O blood groups are present on the **chromosome number 9**.
- There are at least 4 Alleles for the blood groups which are: **A₁, A₂, B and O**.
- Group **A₂** is considered recessive to Group **A₁**.
- Group **O** is considered recessive to both groups **A** and **B**.

Group A Individuals

- They have antigen **A** on their red blood corpuscles and anti **B** antibodies in their serum (**Antigen A + Antibody b**).
- The major phenotype of group **A** is **A**. while their genotype is either **AA** or **AO**.
- There are two subtypes for group **A** individuals which are the following:-
 1. Subtype **A₁** individuals. (Their blood groups are **A₁**).
 2. Subtype **A₂** individuals. (Their blood groups are **A₂**).

Group B Individuals

- They have antigen **B** on their red blood corpuscles and Anti **A** antibodies in their serum (**Antigen B + Antibody a**).
- Their phenotype is **B**, while their genotype is either **BB** or **BO**.

Group AB Individuals

- They have antigen **AB** on their red blood corpuscles but **no antibodies** in their serum (**Antigen AB + No antibodies**).
- Their major phenotype is **A B**, while their genotype is either **A₁B** or **A₂B**.
- **There are 2 subtypes of group AB Which are:**
 1. Subtype **A₁B** individuals.
 2. Subtype **A₂B** individuals.

Group O Individuals

- They have **no antigens** on their red blood corpuscles, while their serum contains anti A and anti B antibodies (**No antigens + Antibodies a and b**).
- Their phenotype is **OO**, while their genotype is **OO**.

Medical Importance Of Blood Groups

Blood groups are very important to be known. They are essential for blood transfusion and for medicolegal applications.

Blood Transfusion

In blood transfusion the serum of the donor is greatly diluted by the serum of the recipient. The danger in blood transfusion between individuals is supposed to come from the liability of the R.B.Cs of the donor to be agglutinated by the serum of the recipient So **group O** which has No antigens on its R.B.Cs., is a **universal donor**; and **group AB** which has No antibodies in its serum is a **universal recipient**.

The donor's blood must be free from diseases such as: AIDS, Syphilis, Malaria and viruses of infective hepatitis (Liver disease viruses).

Co-Dominant Genes

N.B.: It has been found that the A-B-AB-O blood groups are inherited by **co-dominant genes**.

Example: a gene of group A is dominant for a gene of group O, and a gene of group B is dominant for a gene of group O. Thus a gene of group O is recessive to both genes of group A and B.

However, neither A nor B are dominant to one another, when genes A and B are present together, they produce their effects (**Co-dominant genes**).

Examples: If the father is of group **A** and the mother is of group **B**, one of their children may be of group **AB**.

Medico - Legal Importance Of Blood Groups

Medicolegal applications, of blood grouping is important when the blood groups of the parents and the offsprings are known, it is sometimes possible to prove that these offsprings are not from these parents.

N.B.: There are other less important blood subgroups as: MNSs, P, Kell, Duffy Lewis and the Rh blood group systems.

The Rhesus Factor (Rh Factor)

The Rhesus (Rh) Blood Groups In Man:

- The Rhesus factor is an antigen which was first discovered in special species of monkeys called Rhesus monkeys and was named after them.
- This Rhesus antigen (Rh) is found on the red blood corpuscles of about 85% of human individuals.
- Persons whose blood contains the Rh antigen are called Rh+ (positive) individuals.
- It was suspected that the Rh blood group is determined by a pair of alleles: D and d producing three genotypes: DD, Dd and dd.
- Rh + positive individuals are either homozygous with DD or heterozygous with Dd.
- Persons whose blood is free from these Rh antigens are called Rh – (negative) individuals. They contain dd alleles.
- If an Rh – negative individual is injected (during blood transfusion) with an Rh + positive blood, he will develop anti Rh (antibodies) in his blood plasma.
- An Rh – negative woman may form anti Rh Antibodies in her plasma during her delivery to an Rh + positive foetus.
- If a man with an Rh positive blood, gets married with a woman with an Rh negative blood, the children may inherit the Rh positive blood from their father. The first child will come without complications but during his labour some foetal blood (Rh positive) pass to the mother's circulation. The mother's blood will start to form anti Rh antibodies. In the next pregnancy these antibodies will cross the placenta to be mixed with the foetal blood of the second foetus causing haemolysis of his blood and intra-uterine foetal death. This condition is called Erythroblastosis Foetalis. For the treatment of this case, these pregnant mothers should be injected with a preparation of Anti D (Anti Rh) in the last 2 months of her pregnancy and with another injection immediately after each delivery or each abortion.

The Following are the main types of Haemolytic Diseases OF Newborn (HDN)

- 1– Rh Incompatibility.
- 2– ABO blood group incompatibility.
- 3– Kell blood group system.

Blood

Blood is a viscous fluid, formed of: **Blood Plasma (55%)** and **Blood cells (45%).**

Types of Blood Cells And Their Average Number In The Human Body:-

- 1. Red Blood Corpuscles or RBCs or Erythrocytes:** about 4.5 to 5.5 millions per cubic millimetre.
- 2. White Blood cells or Leucocytes:** about 4000 to 11000 per cubic millimetre.
- 3. Blood Platelets or Thrombocytes:** about 150,000 to 400,000 per cubic millimetre.

The Major Functions Of Blood Are:-

1. Transport of oxygen, nutritive substances and hormones to all tissues.
2. Removal of carbon dioxide and waste products through the lungs, Kidneys and sweat glands.
3. Control of body temperature.
4. Maintenance of acid-base balance.
5. Protect the body against infections through the action of leucocytes.

Red Blood Corpuscles = RBCs

Number Of RBCs

- In males:** The number varies from 5 to 5.5 millions per cubic millimetre:
- In females:** The number varies from 4.5 – 5 millions per cubic millimetre.
The number is less in females due to loss of blood during menstruation.

Abnormalities in the Number of RBCs: Decrease in the number of RBCs is known as **Anaemia**. Increase in their number is known as **Polycythaemia**.

Anaemia: It is either a decrease in the number of RBCs (oligocytosis) or due to a decrease in haemoglobin content of RBCs.

Causes and Types of Anaemias

- 1. Deficiency Anaemia,** deficiency of these elements may result in anaemia: iron, copper, proteins, hormones, vitamin C and vitamin B12.
- 2. Haemorrhagic Anaemia,** as haemorrhage from nose, gums, piles and wounds.
- 3. Haemolytic Anaemia,** when there is an excessive destruction of RBCs as in certain congenital abnormalities of the cell membrane as in **Spherocytosis**; OR deficiency of enzymes as in **Favism**; OR Presence of haemoglobin F as in **Thalassemia**, OR presence of haemoglobin S as in **Sickle cell anaemia**.
- 4. Aplastic Anaemia;** When the bone marrow (in which RBCs are formed) is

congenitally abnormal, or if it is partially destroyed by X-ray or by antibiotics. **Polycythaemia** or increase in the number of RBCs above 6 millions as in hypoxia or in low oxygen tension as in high altitudes, also in heart and lung diseases.

Shape Of RBCs

They are **rounded, non-nucleated biconcave discs**. In slow blood stream and in blood films, RBCs adhere together due to their surface tension showing a **rouleaux appearance**.

Shape Of R.B.Cs



Roundrd

Biconcave

Rouleaux Formation

Abnormal Shapes of R. B. Cs

In certain anaemias RBCs may be pear-shaped (**poikilocytes**) or may be biconvex (**spherocytes**) or may be oval in shape (**ovalocytes**).

Diameters of RBCs

Normal diameter of an RBC is **7.5 microns** and the normal thickness is 1.9 microns at the periphery and 1.1 microns at the centre of **RBC**.

Abnormalities In The Diameters Of RBCs

1. In **Macrocytic Anaemias** there is an increase in the diameters of RBCs.
2. In **Microcytic Anaemias** there is a decrease in the diameters of RBCs.

Structure of RBCs

- RBCs are **acidophilic in staining** because their **Hb** is a **basic protein**.
- RBCs have **no nuclei and no organelles** except their **cell membranes**.
- RBCs have on their surfaces the **antigens of blood groups and of Rh factor**.
- RBCs contain **haemoglobin**, its concentration is about **12-16 gm%** (per 100 cc blood).
- RBCs contain **glycolytic and carbonic anhydrase enzymes**.

Types of Haemoglobins (Hb)

1. **Normal adult Hb. A:** present in 96% of normal individuals.
2. **Foetal (Hb, F) :** present in **Thalathemia** which is a kind of anaemia.
3. **Haemoglobin S:** present in sickle cell anaemia in which Hb form a **crescent** in RBC.

Reticulocytes

- They are **immature RBCs** which contain RNA, Their diameters are large.
- Their percentage in normal blood is **not more than 2%**.
- Their number increase in certain anaemia. They can be stained with cresyle blue.

Colour Of RBCs

- RBCs are **greenish yellow in colour** due to presence of **Haemoglobin (Hb)**. A drop of blood appears red due to overlapping of RBCs. When the **Hb%** is normal, the red blood corpuscles are called **Normochromic**.

Abnormal Colour Of RBCs

- a) RBCs with **less Hb%** than normal are pale and are called **hypochromic**.
- b) RBCs with **more Hb%** than normal are called **hyperchromic**.
- c) **In target cell anaemia**, the Hb is concentrated in the centres of RBCs forming a central coloured mass and a peripheral pale ring (like the target).

Contents Of RBCs

- They are not true cells, they have neither nuclei nor organoids.
- They are surrounded by **plastic cell membranes** formed of **lipoprotein**.
- RBCs contain a cytoskeleton network formed of protein called **Spectrin**.
- The RBCs are filled with **haemoglobin (Hb)**. Haemoglobin combines with oxygen to form oxyhaemoglobin, it goes to the tissues to supply them with oxygen. It also transports carbon dioxide from the tissues to the lung.

Haemolysis

Rupture of the cell membrane and loss of Hb outside the R.B.Cs is known as haemolysis which may be caused by: acids, alkalies, malarial and bacterial toxins, snake venom, hypotonic solution and incompatible blood transfusion.

Osmotic Pressure: normally the osmotic pressure of RBCs is 0.9% saline. If the RBCs are exposed to hypertonic solution (2%) crenation will occur, while if they are exposed to hypotonic solution swelling, rupture and haemolysis will occur.

Life Span Of RBCs

RBCs can live for about 4 months. The life time can be calculated by isotopes. Old RBCs are destroyed by the phagocytic cells in the liver, spleen and bone marrow. Their Hb can be changed to bile pigments and haemosiderin granules.

Adaptation Of The Structure Of RBCs

In Order To Perform Their Functions

1. **The cell membrane of RBCs is plastic.** It allows RBCs to change their shape.
RBCs are in the form of corpuscles with rounded edges which facilitate their passage inside narrow blood capillaries.
2. **The biconcave surfaces of RBCs increase** their surface areas, through these surfaces, gaseous exchange ($O_2 + CO_2$) takes place.
3. **The cell membrane of RBCs is formed of lipoprotein**, it is highly selective, it allows easy exchange of carbon dioxide and oxygen through it.
4. **There is neither nuclei nor cell organoids** in RBCs, this prevents RBCs from

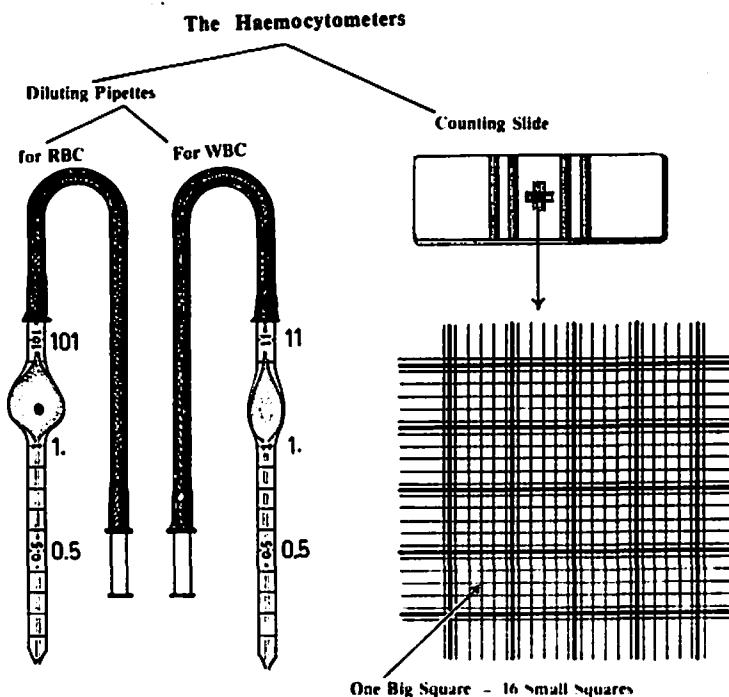
reproduction. Their absence also allows free space for haemoglobin.

5. The main function of RBCs is to enclose haemoglobin, this haemoglobin is formed of a protein (globin) and an iron containing pigment (haem).

Haemoglobin combines easily with oxygen to form oxyhaemoglobin which goes to the tissues to supply them with oxygen. Haemoglobin also plays a role in controlling the hydrogen ion concentration of the blood. Haemoglobin can only do these functions when it is **present inside the RBCs**.

6. RBCs are rich in carbonic anhydrase enzyme which facilitates combination of haemoglobin with CO_2 and to get rid of this CO_2 through the lung.

The Haemocytometer



Red Blood Count

RBCs, leucocytes and blood platelets are counted by the haemocytometer which is formed of: a diluting pipette and a counting slide.

The diluting pipette for RBCs has a large bulb. The pipette is graduated as 0.5 at the middle of the tube, 1.0 below the bulb 101 above the bulb.

The bulb contains a piece of red glass to mix the blood with the diluting fluid.

The counting slide has a depression on its centre with a depth = 1/10mm.

The square area of the base of this depression = one square millimetre which is divided by 20 lines vertically and another 20 lines horizontally, so it contains 400 small squares.

Thus, the surface area of each small square = Length X Width=

$$= \frac{1}{20} \times \frac{1}{20} = \frac{1}{400} \text{ mm}^2$$

The volume of each small square = Length X Width X Depth=

$$= \frac{1}{20} \times \frac{1}{20} \times \frac{1}{10} = \frac{1}{4000} \text{ mm}^3$$

This means that, the volume of one cubic millimeter = 4000 times the volume of each small square

To facilitate counting, each 16 small squares are grouped into one large square.

Steps Of RBCs Counting

1. Clean the thumb with alcohol and leave it to dry in air. With a sterilized needle, **Prick the thumb**, in order to bring a drop of blood.
2. Suck the blood with the diluting pipette till the **mark 0.5** is reached. Rapidly dilute the blood by sucking saline till the mark **101** is reached, and shake well to mix the blood with saline (the blood is now diluted 200 times).
3. Blow out few drops from the pipette, then put a drop of the diluted blood on the depressed area of the counting slide, cover with a cover-glass and count the number of R.B.Cs under the high power of the microscope. They appear as greenish yellow circles.
4. Count the total number of R.B.Cs which is present in **5 large squares** (Each large square contains 16 small squares).
5. Calculate the number of R.B.Cs per cubic millimetre using this equation.

If the total number of RBCs which is counted in one small square = N.

Then, the total RBCs count= $N \times 4000 \times 200 = ?$ millions per cubic millimetre.

But if the total number of RBCs which is counted in 5 large squares = N

So the total number of RBCs= $\frac{N \times 4000 \times 200}{5 \times 16} = ?$ millions per cubic millimetre

N.B. In clinical laboratories, they do the previous steps, they count the number of RBCs in **5 large squares**, this obtained number is then **multiplied by 10.000** in order to get out the number of R BCs per cubic millimetre.

Nowadays, the laboratories use electronic apparatus which counts the different types of blood cells automatically.

Leucocytes

They are called also white blood cells.

They are colourless, but when they are packed together, they appear white.

General Characteristics of Leucocytes

- They are true nucleated cells.
- They contain all cell organoids and cell inclusions.
- They have an amoeboid movements, they can penetrate capillary walls.
- They contain no haemoglobin and they resist changes in osmotic pressure.
- There are 5 types of leucocytes: Neutrophil, Eosinophil, Basophil, Lymphocyte and Monocyte.

Number Of Leucocytes

They vary in number from 4000 to 11.000 per cubic millimetre.

At birth, the total leucocytic count is about 16.000 per cubic millimetre.

Leucocytosis

It is the increase in number of leucocytes above 12.000 per cubic millimetre.

Causes Of Leucocytosis

- 1. Physiological leucocytosis:** Occurs in pregnancy, in newly born infant, after cold bath, after meals, after exposure to sun.
- 2. Pathological Leucocytosis:** Occurs in acute and chronic diseases and in fevers.

Leucopenia

It is the decrease in number of leucocytes below 4.000 per cubic millimetre. This may occur in: **typhoid fever, influenza** and after exposure to **X-ray** or after taking certain **antibiotics**.

Counting Of Blood Leucocytes

Total Leucocytic Count

Leucocytes are counted totally by the **Haemocytometer** which is formed of:

- 1. A diluting pipette.**
- 2. A counting slide.**

The diluting pipette has a small bulb containing a small piece of **white glass** to mix the blood with the diluting fluid. The pipette is graduated 0.5 at the middle of the tube, 1.0 below the bulb and 11 above the bulb (See page 49).

The counting slide is a similar slide to that which is used for RBCs count.

Steps for counting the total number of leucocytes:

1. After pricking the sterilized finger, we suck the blood till the mark 1.
2. Rapidly, we dilute the blood 10 times by sucking till the mark 11, a special diluting fluid formed of equal volumes of: **2% acetic acid** (to haemolyse RBCs) and **1/2% gentian violet** (to stain the nuclei of leucocytes).
3. We shake the pipette to dilute the blood with the diluting fluid, then we throw away few drops, then we put one drop of the diluted blood on the counting slide and we cover it.
4. Under the low power of the microscope we count the number of leucocytes in the all large squares = (16).
5. We calculate the total number of leucocytes by using this equation.

If the total number of leucocytes counted in the 16 large squares = N.

Therefore, The total number of leucocytes per cubic millimetre =

$$\frac{N \times 4000 \times 10}{16 \times 16} = ? \text{ Number per cubic millimetre}$$

Differences Between RBCs And Leucocytes

RBCs	Leucocytes
<ol style="list-style-type: none"> 1. Average number: from 4.5 to 5.5 millions per cubic millimetre. 2. They are of one type. 3. They are corpuscles = not true cells. 4. They have no nuclei and no cell organoids. 5. They have no movements. 6. They are biconcave corpuscles. 7. They appear in rouleaux. 8. Colour: greenish yellow. 9. Diameter 7.5 microns. 10. They are easily haemolysed. 11. They contain haemoglobin. 12. They carry oxygen and Co₂ while they are inside the B.V. 13. They develop in the red bone marrow. 14. Life span about 4 months. 	<ol style="list-style-type: none"> 1. Number : from 4000 to 11.000 per cubic millimetre. 2. They are of 5 types. 3. They are true cells. 4. They contain nuclei and cell organoids. 5. They have an amoeboid movement. 6. They are spherical cells. 7. No rouleaux appearance. 8. They are colourless. 9. Diameter from 8 to 18 microns. 10. They resist haemolysis partially. 11. They have no haemoglobin. 12. They are phagocytic cells but outside the B.V. 13. They develop in red bone marrow and in the lymphatic tissues. 14. Life span from few days to years.

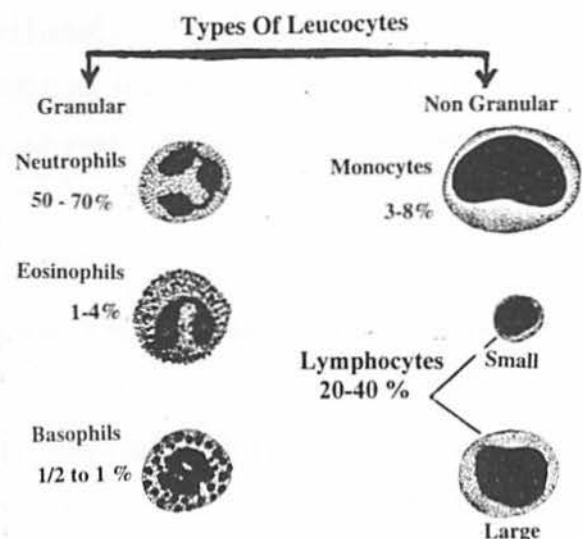
Types Of Leucocytes

There are 5 types of leucocytes which are classified into **granular** leucocytes (neutrophil, eosinophil and basophil) and **non-granular** leucocytes (lymphocyte and monocyte).

Granular Leucocytes

1. Neutrophils (50 - 70 %)

They are Called Polymorpho- nuclear Leucocytes



Neutrophil

- Their **percentage** varies between **50 to 70%** of the total leucocytes.
- Their **diameter** varies from 10 to 12 microns.
- The **nucleus** is single but segmented, it is formed of 2 to 5 segments connected with each other by chromatin threads = **polymorpho - nuclear**.
- Neutrophils have an amoeboid movement, they can form pseudopodia in order to engulf micro- organisms.
- The **E/M of neutrophils** shows few mitochondria, endoplasmic reticulum, glycogen granules, microfilaments and microtubules.

Two Types of Granules Are Present In Neutrophils:

1. Azurophilic Granules: which are few in number and large in size.

They are considered as lysosomes because they are very rich in hydrolytic enzymes.

2. Specific Granules: which are numerous and small in size. They contain collagenase enzyme, alkaline phosphatase and lactoferrin enzymes which kill bacteria.



Neutrophil

Functions Of Neutrophils

1. They are phagocytic to micro - organisms.
2. They secrete **proteolytic** enzymes to dissolve protein around bacteria.
3. They secrete **trophilic substances** which help in healing of wounds.
4. Neutrophils help blood monocytes to migrate to the inflamed areas.
5. During acute infections and in fever conditions, neutrophils stimulate bone marrow to develop more leucocytes.
6. Neutrophils secrete pyrogens which can elevate body temperature.

Neutrophilia

Neutrophilia = increased number of neutrophils. This occurs in acute infections which may produce pus as in = tonsillitis, appendicitis and in any abscess formation.

Neutropenia

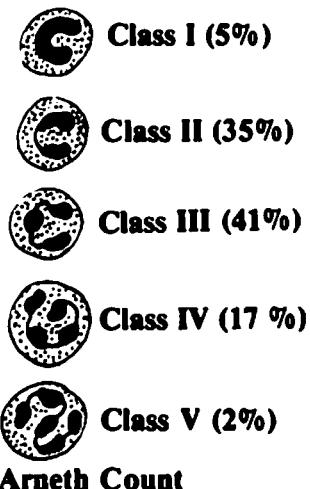
Neutropenia or Neutrophil Leucopenia : It is the decrease in the number of neutrophils. It occurs in typhoid fever, T.B., influenza and in severe poisoning.

N.B. In order to differentiate between typhoid fever and appendicitis: We can do a total leucocytic count and a differential leucocytic count. If the total leucocytic count is above 11.000 with neutrophils more than 75% it means appendicitis. If the total count is less than 4000 with neutrophils less than 60% it means typhoid fever.

Recent Classification Of Neutrophils

a) Arneth Count

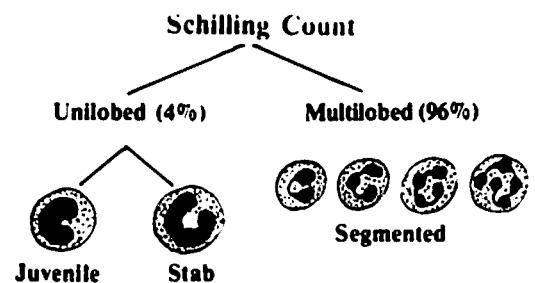
He classified neutrophils into 5 classes according to the number of segments in their nuclei. The number of segments may be one segment which constitute (5%) two segments (35%) three segments (41%), four segments (17%) or five segments (2%). The mature leucocytes are the more segmented ones.



b) Schilling Count

According to Schilling count, neutrophils are classified into:

1. Mature or segmented multilobed neutrophils (about 96%).
2. Immature or unilobed neutrophils (about 4%) which are of two types:
 - a) Stab neutrophils which do not exceed 2% in peripheral normal blood.



- b) Juvenile cells or Metamyelocytes which are normally absent in peripheral blood.

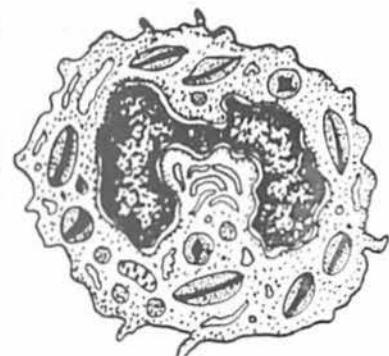
N.B. In severe infections, the bone marrow sends first **many mature neutrophils** to the circulating blood, if infection is continued, the bone marrow then sends **immature neutrophils** to the circulating blood; this condition is called **shift to the left**. In Leukaemia there is also shift to the left. When infection subsides, the blood picture returns to normal, this is called shift to the right.

2. Eosinophil Leucocytes (from 1 to 4%)

- Their diameter varies from 10-14 microns.
- The nucleus is bilobed and is called horse shoe-shaped nucleus. It has non-clear nucleolus.
- By the electron microscope, the cytoplasm contains few mitochondria, small Golgi body and few endoplasmic reticulum. The cytoplasm is rich in oval or ellipsoid shaped granules. These granules are considered as Lysosomes. They contain the following enzymes:
- Histaminase enzyme to destroy histamine substance.
- Sulphatase enzyme to destroy sulphate substances which are secreted by mast cells.



Eosinophil



Eosinophil

Functions of Eosinophils:

1. They can destroy parasites through secretion of cytotoxic proteins.
2. Eosinophils can destroy **allergic substances as histamine and heparin** which are secreted by mast cells and by basophil leucocytes.
3. Eosinophils can phagocytose the antigen- antibody complex in allergic conditions.

Life span of eosinophil: is about 8 hours in the circulating blood. Eosinophil can live about 8 days in the connective tissue.

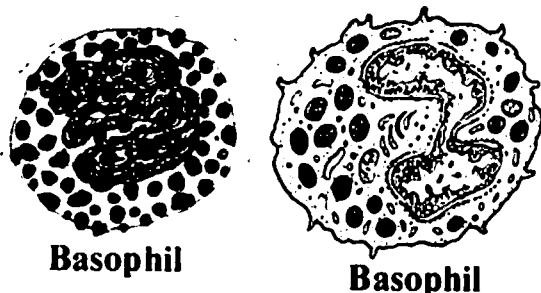
- **Eosinophilia** = increase in the percentage of eosinophils which occurs in:

 1. **Allergic diseases** as urticaria, eczema, bronchial asthma, allergic skin and in allergic blood diseases.
 2. **Parasitic diseases** as ascaris, bilharzia and ankylostoma infestation.

- **Eosinopenia**: = decrease in number of eosinophils which occurs during treatment with **cortisone** because it inhibits their formation in the bone marrow.
- Eosinophils are less motile than neutrophils but they may be present normally: under the skin, in the intestinal, respiratory and in the female genital tracts.

3. Basophil Leucocytes (From 1/2 to 1%)

- Their percentage varies from 1/2 to 1%.
- Their diameter varies from 10-12 microns.
- **E/M of Basophils:** They have few cell organoids and inclusions, they are rich in heparin, histamine and azurophil granules as those of mast cells.
- They have twisted S-shaped nuclei.
- They have surface cell receptors.
- **Their functions** are production and carriage of histamine and heparin.
- They play a role in allergic and parasitic diseases.
- Life span: from 10 - 15 days.
- **Basophilia** = An increase in the percentage of basophils, occurs in: liver cirrhosis, small pox and in allergic and parasitic diseases.



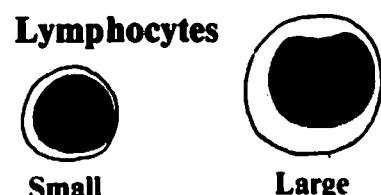
Non Granular Leucocytes

Lymphocytes (20% - 40%)

- Their percentage varies from 20 - 40% of the total number of blood leucocytes.
- According to the diameters of Lymphocytes, they are classified into small, (8 microns), Medium- sized (12 microns), and large Lymphocytes (18 microns)
- Lymphocytes are highly mobile cells, they are present in blood, lymph and lymphatic tissues as spleen, lymph nodes and tonsils.

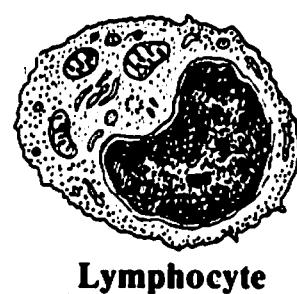
Small Lymphocytes (90%)

- They represent about 90% of the circulating lymphocytes.
- Each lymphocyte is about 8 microns in diameter.
- The cytoplasm is scanty and it contains few organelles and many ribosomes.
- The nucleus is small, darkly stained and filling the whole cytoplasm.



There are 3 types of small lymphocytes

- a) T- Lymphocytes (70%)
- b) B- Lymphocytes (25%)
- c) Null - Lymphocytes (5%)



- **Small T and B Lymphocytes** are covered by microvilli. Their cytoplasm shows many free ribosomes, few endoplasmic reticulum and a pair of centrioles.
- **Null- lymphocytes:** They are **Natural killer cells** to foreign cells

2. Medium- sized Lymphocytes (10%)

- They represent about 10% of the circulating lymphocytes.
- Each lymphocyte is about 12 microns in diameter.
- **The cytoplasm** contains many ribosomes, mitochondria, Golgi apparatus and endoplasmic reticulum.
- The nucleus is indented, pale and is surrounded with large amount of cytoplasm.

Lymphocytosis

Increase in the percentage of small and medium - sized lymphocytes in the circulating blood above 50% is called **Lymphocytosis**.

Causes of Lymphocytosis

- Lymphocytosis occurs normally in children.
- Lymphocytosis occurs in chronic diseases as in: Whooping cough, T.B. (Tuberculosis), Syphilis, Glandular fever and in Leukaemia.

Classifications of Small Lymphocytes

According to the Origin and Functions, Small Lymphocytes Are Classified Into:

1- T- Lymphocytes 2- B- Lymphocytes 3- Null- Lymphocytes

The T- Lymphocytes (70%)

- They are termed as T- Lymphocytes because they are Thymus dependent lymphocytes. They differentiate in the **Thymus**.
- During childhood they require the presence of the **thymus gland** for their development and for their differentiation.
- They contain surface receptors for antigens.
- They have a **long life span**, they can live for years.

T- Lymphocytes develop from mother cells in **bone marrow**. These mother cells migrate from the bone marrow to the thymus. They proliferate in the thymus to be changed into **T- Lymphoblasts** and then to **T- Lymphocytes**. Some T- Lymphoblasts leave the thymus and migrate with the circulating blood to be settled in the **thymus dependent areas** which are present in: **spleen and lymph nodes**. These areas produce **T- Lymphocytes** in the human body throughout life.

Types of T-Lymphocytes

1. **T- Helper Cells** which help B-Lymphocytes to perform their functions.
2. **T-Suppressor Cells** which Suppress (stop) the immune reaction of B-Lymphocytes against body antigens preventing **autoimmune diseases**.
3. **T.Killer Cells** which kill foreign cells and infected cells with viruses.
4. **T-Lymphokines cells**, They secrete Lymphokines which include; chemotactic mitogenic and cytotoxic factors. They secrete also **Interferon**.
5. **T-Memory Cells** which store memories for the future immunological functions.
6. **T-amplifier Cells**, they are present in the thymus and spleen to enhance the functional activities of T-and B-Lymphocytes.

Functions Of T-Lymphocytes

1. **T-Lymphocytes are responsible for cellular immunity.** Any foreign body or bacteria entering our body act as antigens. T-Lymphocytes will come in contact with these antigens and can destroy these antigens, this means that the T-Lymphocytes can kill directly foreign cells and bacteria.
2. **T-Lymphocytes act as Killer Cells:** the T-Lymphocytes can secrete **Lymphokines which include:**
 - a) **Interferon** which inhibits viral replication.
 - b) **Chemostatic Factor;** which attract macrophages to the sites of infections.
 - c) **Cytotoxic Factor** which can kill bacteria as T.B. and foreign cells.
 - d) **Mitogenic Factor:** which stimulate the processes of lymphocyte formation.
3. **T-Lymphocytes may act as Graft Rejection Cells:** They may reject transplanted foreign skin grafts, kidney and heart through their secreted **Perforin**.
4. **T-Lymphocytes act as T-Memory Cells:** If foreign bodies (antigen) enter the body, they activate the newly-formed **T-Lymphocytes** which are then called **T-memory cells**. These memory cells in the future can defend the body against the same antigen if it enters the body again.
5. **T-Lymphocytes are considered as Helper Cells:** to B-Lymphocytes, they can help B-Lymphocytes to perform their immune response against foreign bodies.
6. **T-Suppressor Cells**, they prevent **self auto immune reaction diseases**.
7. **T-amplifier Cells** they enhance the functions of B- and T-Lymphocytes.

The B-Lymphocytes (25%)

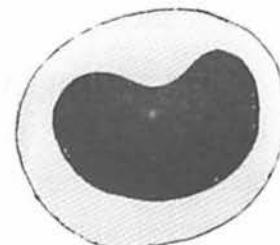
- They are termed as B-Lymphocytes because they develop in the **bursa of Fabricus** in birds.
- They are derived from the primitive stem cells of the bone marrow in mammals.
- They are rich in surface immunoglobulin receptors.
- They have short life span (about 3 months).

Functions Of B-Lymphocytes

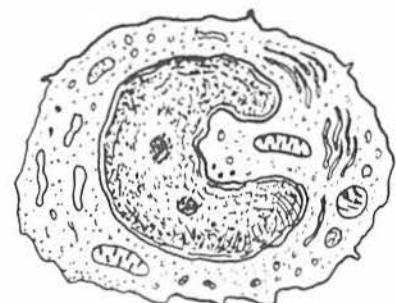
1. B-Lymphocytes are responsible for the development of humoral immunity, as follows: If any antigen enters the body, it is first picked up by the T-Lymphocytes which act as helper cells for B-Lymphocytes. The antigen is then delivered from T-Lymphocytes to activate B-Lymphocytes. These activated B-Lymphocytes are proliferated (changed) in order to form the following 2 types of cells:
 1. Plasma Cells which secrete immune bodies directly in the blood forming **Humoral Immunity**. This process is called **primary immune response**.
 2. B-Memory Cells: which produce **secondary immune response** when they are exposed once again in the future to the same types of antigens.

Null Lymphocytes (5%)

They develop in bone marrow, they have no surface markers, **they are Natural Killer Cells** to foreign and to viral infected cells.



Monocyte



Monocyte

2. Monocytes (3-8%)
 - Their **diameter** varies from 14 to 18 microns.
 - Their **cytoplasm** is non-granular and is not clear.
 - The **cytoplasm** is rich in many Lysosomes (Azurophil Granules), ribosomes and mitochondria.
 - **Mobility:** They can penetrate the capillaries by their pseudopodia to go to C.T.
 - **Nucleus:** The nucleus is pale, large, kidney shaped and with fine chromatin.
 - **Function of Monocytes:** They are highly phagocytic cells in the connective tissue. They can be transformed into **macrophage cells as:** histiocytes in (C.T.), dust cells in (lung) Von-kupffer cells in (liver) and to giant phagocytic cells in (C.T.).

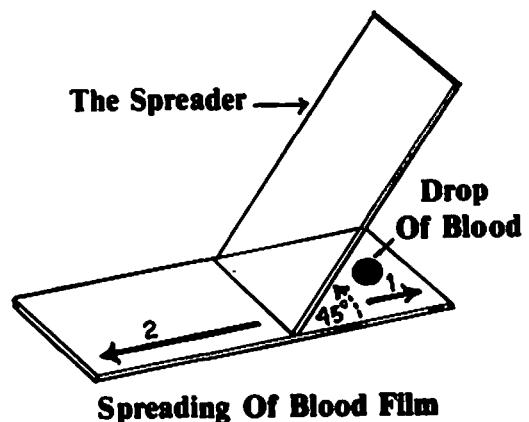
Life Span: It is about 3 days in the blood and 3 months in the tissues.

Monocytosis= increase number of monocytes as in: **Lymphomas, Leukaemia** and in **Chronic Infections** as in: Malaria, T.B., syphilis and Glandular Fever.

The Differential Leucocytic Count

It is the determination of the percentage of each type of leucocytes in the blood.

1. It is done by making a blood film and staining it with **Leishman's stain**.
2. We count the number of each type of leucocytes in different fields of the stained blood film.
3. We record the number of each type of leucocytes in a **table-form**.
4. We find out the percentage of each type of leucocytes in **relation** to the total number counted in all the fields of the blood film.



Leishman's Blood Stain: it is a neutral stain formed of (**eosin**), and (**methylene blue**) dissolved in **methyl alcohol**. It fixes blood on slide. It stains both nuclei and cytoplasm of blood cells.

Spreading And Staining Of a Good Blood Film

1. On a **clean dry slide** we put a medium-sized drop of blood **on its right side**.
2. By means of another slide (**spreader**) which must have a **very smooth and clean** edge, we spread the drop of blood on the first slide.
3. A good blood film must fill **the width of the slide and 3/4 of its length**. It must be **thin, transparent and have a serrated end**.
4. Leave the blood film to be dried in air for 5 minutes.
5. Cover the dry blood film with **15 drops of Leishman's stain** and leave it for **two minutes**. (Concentrated Leishman fixes blood cells on the slide).
6. Dilute the Leishman's stain after the 2 minutes with another **15 drops of distilled water**. Leave the diluted Leishman stain on the blood film for **10 minutes**.
7. After the **12 minutes** we wash the blood film several times in a dish containing **tap-water**.
8. Leave the blood film to dry in air.
9. Put a drop of **Canada balsam** on the serrated end of the film and cover the blood film with a cover slide.

How Can We Do A Differential Leucocytic Count?

1. Examine the stained blood film under the high power of the microscope field by field.
2. Count the number of each type of leucocytes in each field. Differentiate between the various types of leucocytes by the shape of their nuclei and by the type of their granules.
3. Record your results in a table-form, on a sheet of paper.
4. Count the total number of each type of leucocytes seen in the examined fields.
5. Count the total number of the five types of leucocytes seen in the whole examined fields of the stained blood film.
6. To get out the percentage of each type of leucocytes in relation to the total number which is counted in all fields, use the following equation:

The specific number of each type of leucocytes counted in the blood film X 100.

The Total number of leucocytes counted in all the fields of the Blood film.

Importance of Doing the Differential leucocytic Count

By means of the differential leucocytic count we can diagnose certain diseases.
For examples:

- Increase in the percentage of neutrophils, indicates presence of acute infections, as Tonsillitis, Appendicitis and Abscess.
- Increase in the % of eosinophils and basophils, indicates presence of parasitic or allergic diseases.
- Increase in the % of lymphocytes and monocytes indicates presence of chronic infections as: T.B, Typhus and glandular fever.

Blood Platelets

Shape: Blood platelets are not cells, they are small oval non-nucleated bodies, similar to plates, and are found in mammals. In lower vertebrates they are known as thrombocytes because they are nucleated bodies.

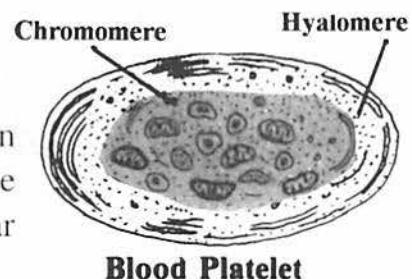
Number of blood platelets varies from 150.000 to 400.000 per cubic millimetre.

The average number = 1/4 million per cubic millimetre.

Diameter: 2-3 microns and have no nuclei.

Structure Of Blood Platelets

Each platelet is covered by cell membrane rich in canalliculi. Each platelet is formed of a peripheral pale clear part called **Hyalomere**, and a central granular basophilic part called **Granulomere**.



The Hyalomere contains microtubules and microfilaments. They have a contractile function.

The Granulomere contains: Lysosomes, Ribosomes, Serotonin, Calcium, Glycogen, Fibrinogen, and Platelet Factor 3.

Life Span of Blood platelets is from 7 to 10 days.

Functions Of Blood Plateletes

1. **Blood platelets aggregate** and adhere together to form a **white plug thrombus** which can close the injured capillaries and can stop bleeding.
2. **Local Blood Coagulation:** platelets deposit fibrin threads around the RBCs forming a **red thrombus** or blood clot which close the injured capillaries.
3. Blood platelets release **serotonin** which is a vasoconstrictor substance to B.V.
4. Blood platelets cause **clot retraction** by means of their microfilaments.
5. Blood platelets help in **removal of blood clot**.

Purpura: It is a congenital disease which results from a decrease in the number of blood platelets. The bleeding time is prolonged in this disease.

Counting Of Blood Platelets

Nowadays new automatic electronic counting apparatus is used to count blood platelets. But: there are two old methods for platelet count: Direct and Indirect Methods.

A) Direct Method For Platelet Count

We use the **haemocytometer** which consists of the same **counting slide** and the same **diluting pipette** used for counting R.B.Cs (See page 49).

1. We suck blood from the punctured skin to the mark 1.0 then we dilute it **100 times** by sucking a special diluting fluid (**Rees and Ecker fluid**) which prevent clotting, prevent adhesion and stain the blood platelets.
2. After few minutes of **shaking** the pipette, we put a diluted drop of the blood on the counting slide, we cover it and then we leave it for **10 minutes**.
3. We count the number of **blood platelets in 5 large squares**.
4. The number of **blood platelets per cubic millimeter** =

The total number of blood platelets counted in five large squares x 4000 x 100

B) Indirect Method For Platelet count

1. We spread a blood film of a non-agglutinated blood.
2. We stain the blood film with Leishman stain.
3. We count the number of platelets and the number of RBCs in several areas of the blood film in order to get the ratio between both numbers (suppose this ratio equals 6 platelets to every 100 RBCs = 6/100).
4. A Proper RBCs count is then made by the haemocytometer from another fresh drop of blood. If we suppose that R.B.Cs count is 5 millions per cubic millimeter.
5. Then we can calculate the number of blood platelets which would be:

$$\text{Number of blood platelets per cubic millimeter} = \frac{5.000000 \times 6}{100}$$

Development Of Blood Cells

The process of development of blood cells is known as **haemopoiesis**.

In adult man, The Haemopoietic Tissues are divided into two main types:

1. **Myeloid Tissue (Bone Marrow).**
2. **Lymphatic Tissue (Lymph nodes, spleen, tonsils and thymus.**

Myeloid Tissue (Bone Marrow)

Kinds of Myeloid Tissue: Yellow and Red Bone Marrow

1. The Yellow Bone Marrow (The Non Active Type)

- It is present in the cavities of long bones in adult. **It is formed of:**
- Many fat cells, reticular cells and some haematopoietic stem cells.
- The yellow bone marrow acts as **reserve areas for haematopoietic tissue.**
- It may change into active red bone marrow in severe blood loss.

2. The Red Bone Marrow (The Active Bone Marrow)

In the foetus, it is present in the bone marrow cavities of all his bones.

In adult man, red bone marrow is found in: the sternum, vertebrae, ribs, pelvic bones and bone marrow cavities of cancellous bone.

Structure Of The Red Bone Marrow (Myeloid Tissue)

The Red Bone Marrow Is Formed Of:

A) Stroma of bone marrow.

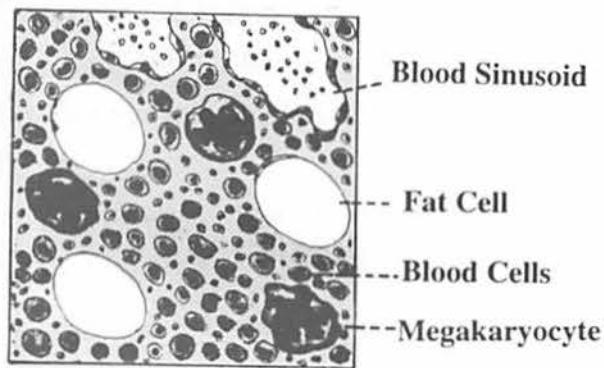
B) Blood sinusoids.

C) Free cells.

A) Stroma of bone marrow.

The stroma is formed of the following fixed cells:

1. **Reticular cells:** They are branched cells with large pale nuclei.



Bone Marrow

- 2. Osteogenic cells** which are the immature mother cells of bone cells.
 - 3. Fat Cells** which are the largest cells in bone marrow.
 - 4. Endothelial Cells** which are the lining cells of blood capillaries, and blood sinusoids.
 - 5. Pericyte Cells:** Present around blood capillaries and can differentiate into smooth muscles.
- B) Blood Sinusoids:** These are wide irregular blood channels lined with fenestrated simple squamous endothelial cells. They are surrounded with **Macrophages** which can phagocytose the extruded nuclei of developing erythrocytes and can transfer iron to the developing erythroblasts.
- C) Free Cells.** They are the developing blood cells which are the immature erythrocytes, mother cells of granular leucocytes, monocytes, lymphocytes and blood platelets.

N.B: If we count the number of immature blood cells in the bone marrow, we find that the number of immature leucocytes is 5 times as many as the number of immature erythrocytes, this is called a **myeloid-erythroid ratio = 5 to 1**. This ratio can be explained by the fact that the life span of leucocytes is about 4 weeks while, the life span of erythrocytes is about 4 months. The bone marrow forms more leucocytes than erythrocytes because the leucocytes are destroyed rapidly in the blood stream, therefore the bone marrow forms and stores many leucocytes.

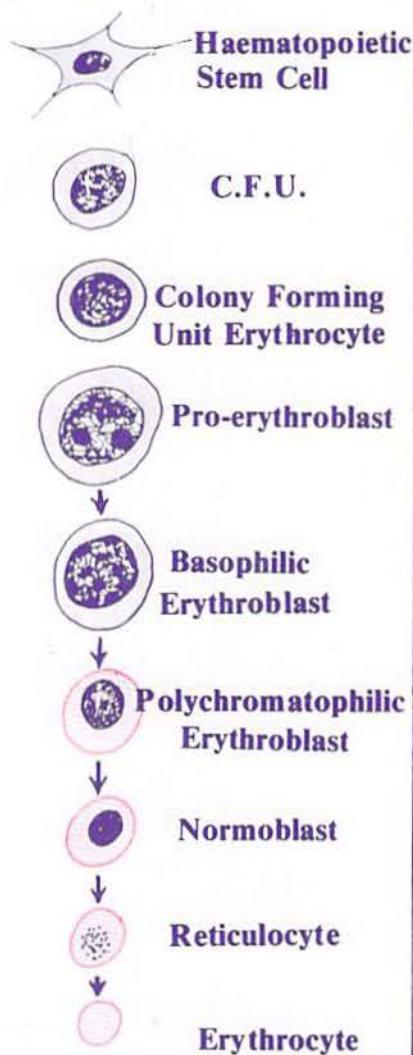
Formation of Blood Cells In The Red Bone Marrow

- The primitive mesenchymal cells which were present in the embryo persist as primitive hematopoietic stem cells in the bone marrow.
- Colony-Forming Unit Cells develop from these hematopoietic stem cells.
- Colony-Forming Unit Cells differentiate into all kinds of blood cells.

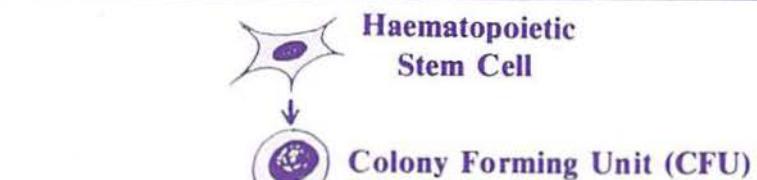
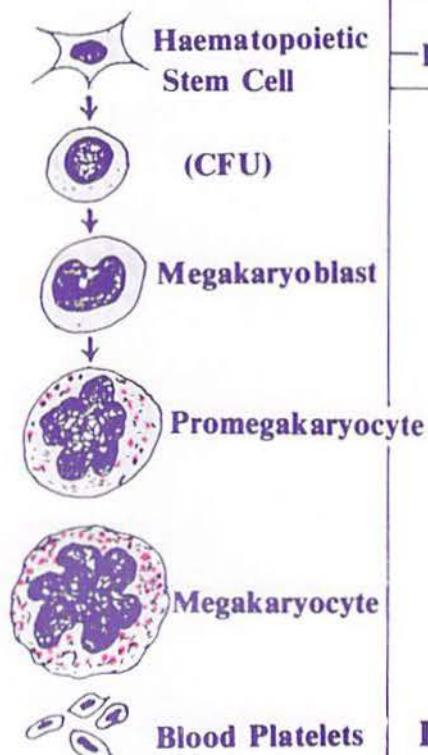
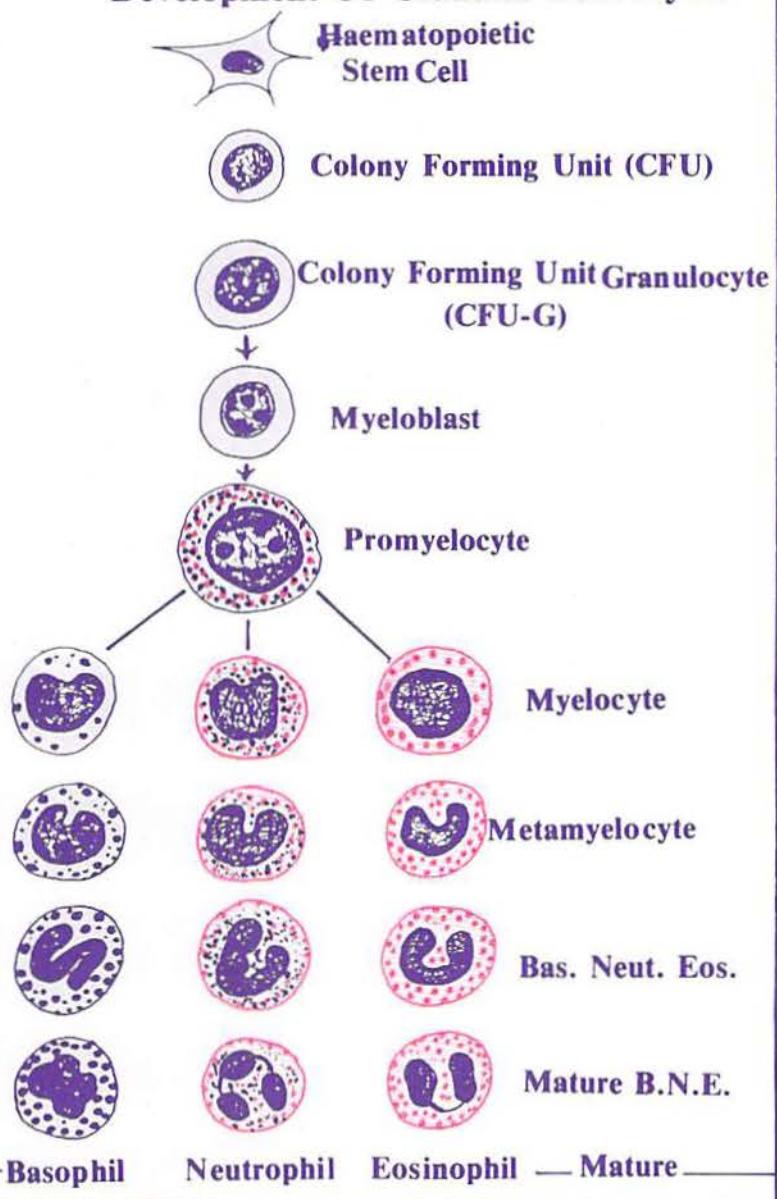
The Colony-Forming Unit Cells:

- They are small cells with pale small nuclei.
- The diameter of each cell ranges from 7- 8 microns.
- The cytoplasm is slightly basophilic with few ribosomes and mitochondria.
- The nucleus is rounded, and it has a fine chromatin network.
- These cells can divide giving rise to:
 - (1) Daughter colony forming unit cells
 - (2) Progenitor cells.
- The Progenitor cells can differentiate to give rise to blood cells which are the erythrocytes, the leucocytes and the blood platelets.

Development Of An RBC



Development Of Granular Leucocytes



Development Of Non-Granular Leucocytes

Stages Of Erythropoiesis Or Stages Of Development Of R.B.Cs.

Erythrocytes are developed in the red bone marrow under the stimulation of kidney Erythropoietin Hormone. These are the stages of development of RBCs:

1. Hematopoietic Stem Cell.

- It is an embryonic branched cell present in the bone marrow.
- It has a large nucleus and few processes.
- It can differentiate into:

2. Colony Forming Unit Cell:

It is a rounded cell from 7-8 microns in diameter. It can differentiate into:

3. Colony Forming Unit (Progenitor)

Erythropoietin stem cell (CFU-E):

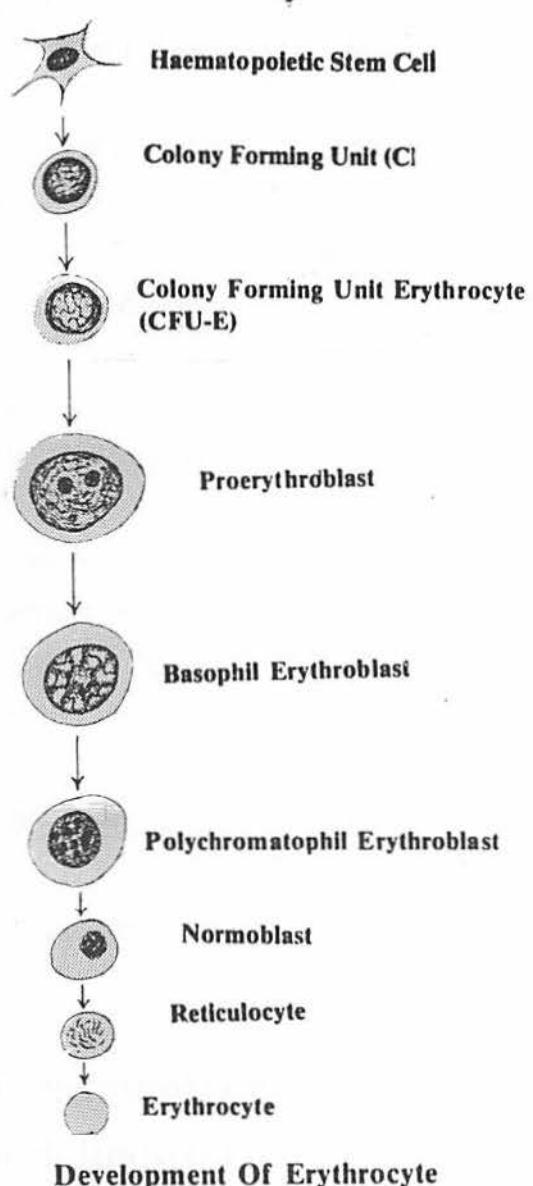
- It is a rounded cell with slightly basophilic cytoplasm.
 - Its nucleus is rounded with fine chromatin granules.
- The erythropoietin hormone secreted from the kidney can stimulate these cells to synthesize haemoglobin.
- This cell can differentiate into:

4. Proerythroblast:

- It is a rounded cell, from 12 to 15 microns in diameter.
- It has a large rounded nucleus with fine chromatin and two nucleoli.
- The cytoplasm is slightly basophilic because it contains few ribosomes.
- The cell can divide and differentiate to give basophilic erythroblast.

5. Basophilic Erythroblast:

- It is about 10 - 13 microns in diameter.
- The nucleus is small with condensed chromatin.
- The cytoplasm is more basophilic and is rich in ribosomes.



Development Of Erythrocyte

- It can divide and differentiate to give **polychromatophil Erythroblast**.

6. Polychromatophil Erythroblast:

- It is about 8-11 microns in diameter.
- Its nucleus is small and without **nucleoli**.
- The acidophilia of the cytoplasm is due to the appearance of **haemoglobin**.
- The basophilia of cytoplasm is due to presence of **ribosomes**.
- **This cell differentiates into normoblast.**

7. Normoblast = Orthochromatophil Erythroblast.

- It is about 8-10 microns in diameter. It cannot divide. Its cytoplasm is acidophilic due to appearance of **more haemoglobin**.
- The nucleus is small, eccentric in position and deeply stained (pyknotic).
- The nucleus is then extruded outside the cell.

8. Reticulocytes:

- It is a small cell, its diameter is about **8 microns**. Its cytoplasm contains **ribosomes** in the form of a basophilic reticulum.
 - Reticulocytes may appear in the circulating blood, but their percentage is not more than 2% Their number may increase after haemorrhage and in haemolytic anaemias.
 - They can be stained with **Supra-vital stain as brilliant cresyl blue**. This can be done by mixing a **fresh drop of blood** with a dried drop from this stain. After a short period of time we spread a blood film from the mixture. From this blood film we can get out the ratio between the counted erythrocytes and reticulocytes .
- Reticulocytes appear as pale cells with central basophilic reticulum of RNA.

9. Mature Erythrocytes:

They are biconcave rounded non-nucleated discs filled with haemoglobin
They can enter through the blood sinusoids of the bone marrow to reach the circulation.

Development Of Granular leucocytes (Neutrophil, Eosinophil And Basophil)

They develop in the red bone marrow through the following stages:

1. Hematopoietic Stem Cells:

They are small embryonic branched stem cells with small nuclei.

2. Colony Forming Unit (CFU)

They are small rounded cells with small rounded nuclei, they differentiate into:

3. Colony Forming Unit (Progenitor)

Granulocytes: (CFU-G): These rounded cells differentiate into myeloblasts.

4. Myeloblast: It is a large rounded cell. Its cytoplasm is basophilic and is devoid of granules. It has a very large nucleus with two or more prominent nucleoli.

5. Promyelocyte: It is a large cell (20 microns) with a large nucleus and prominent nucleolus. Its cytoplasm is basophilic, it contains azurophilic granules. The cell divides and **differentiates into myelocytes.**

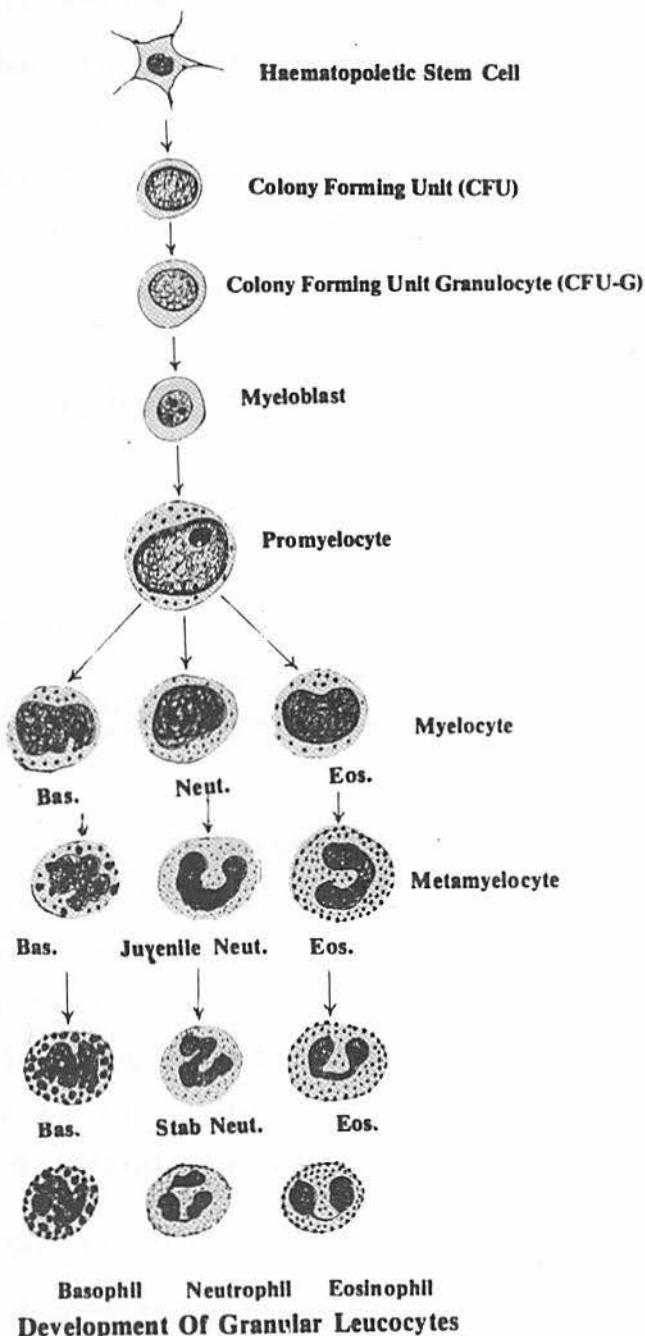
6. Myelocytes: (Neutrophil, Eosinophil and Basophil Myelocytes): In these cells differentiation of granules takes place in order to give **The following three types of cells:**

- **Basophil myelocytes** with basophilic granules.
- **Neutrophil myelocytes** with neutrophilic granules.
- **Eosinophil myelocytes** with acidophilic granules.
- **Myelocytes cannot divide again.** They undergo maturation to be changed into Metamyelocytes.

7. Metamyelocytes: (Neutrophil, Eosinophil and Basophil Metamyelocytes):

N.B. The Neutrophil Metamyelocyte is characterized by the presence of a kidney shaped nucleus and is called **Juvenile Neutrophil.** Continuous maturation of juvenile neutrophils leads to appearance of **Band forms or Stab forms or Staff neutrophils**, these cells have bend-rod nuclei. These cells may appear in the peripheral blood, but their percentage normally is not more than 2%. The metamyelocytes differentiate to give **mature granulocytes.**

8. Mature granular leucocytes with their characteristic nuclei and their specific granules enter the blood sinusoids to go to the circulating blood.



Development Of Granular Leucocytes

Development Of B-lymphocytes

They are developed in the red bone marrow through the following stages:

1. Hematopoietic Stem Cells:

- They are small branched cells with small nuclei.
- They give rise to Colony Forming Unit.

2. Colony Forming Unit:

- They are small rounded cells with small nuclei.
They differentiate into B-lymphoblasts.

3. B-Lymphoblasts:

- They are small cells about 8-10 microns in diameter.
- They divide and differentiate into Prolymphocytes.

4. Prolymphocytes which differentiate into small B-lymphocytes.

5. B-Lymphocytes:

- They are small cells with deeply stained nuclei.
- They leave the bone marrow to enter the blood circulation. They are then filtered in the spleen, lymph nodes, tonsil and in the intestinal lymphatic nodules. In these tissues they are activated by antigens to be changed into plasmablast cells and then into plasma cells. Plasma cells secrete the specific antibodies.

B-Lymphocytes are involved in mediation of humoral immunity.

Development Of T-lymphocytes

The T-lymphocytes develop in the red bone marrow through the following stages:

1. Hematopoietic stem cells: They are branched embryonic cells with small nuclei. They are present in the bone marrow. They divide and differentiate into:

2. Colony Forming Unit (CFU):

They are small rounded cells with rounded nuclei. In foetus and in the new born infants, these cells migrate to the cortex of the thymus gland where they are affected by the thymic hormones. They then develop into T-lymphoblasts.

3. T-Lymphoblasts:

They are small immature rounded cells.

They leave the thymus and are called post thymic cells. They migrate with the circulating blood to be settled in the **thymus dependent zones** in lymph nodes and spleen where they differentiate into Pro-T-lymphocytes then into T-Lymphocytes

4. T-Lymphocytes:

- They are small rounded cells with rounded nuclei circulating in the blood.
- These cells are involved in mediation of cellular immunity.

Development Of Monocytes

Monocytes are developed in the red bone marrow through the following stages:

1. Hematopoietic Stem Cells: They are branched cells, they divide to give:

2. Colony Forming Progenitor cell (CFU)

They are small rounded cells with small nuclei, they divide and differentiate into:

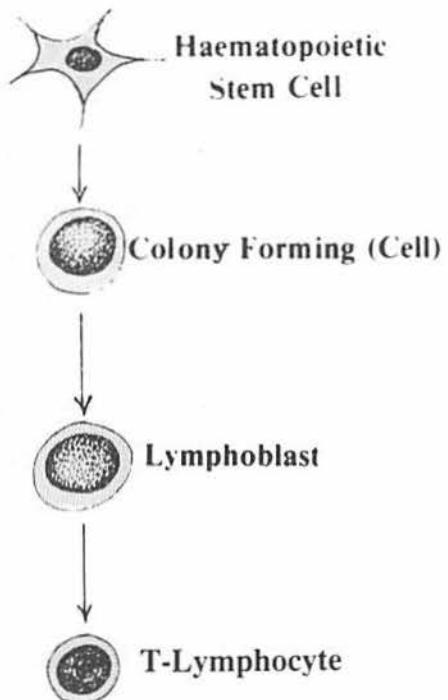
3. Monoblasts: They are large cells with large nuclei.

They divide and differentiate into **Pro-monocytes**.

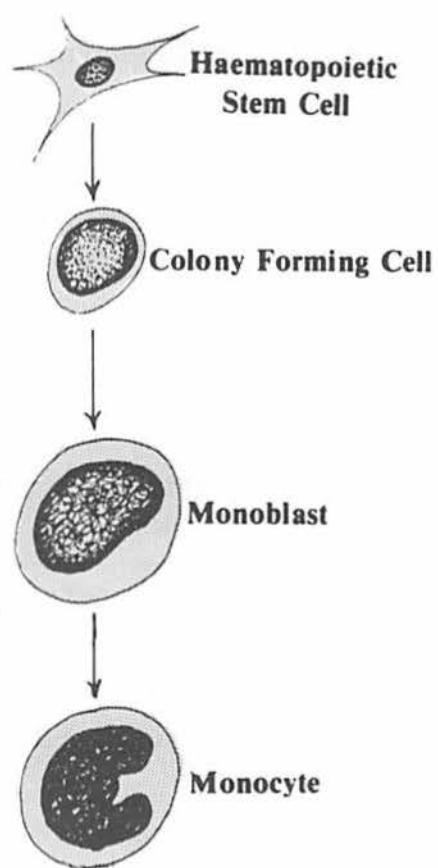
4. Pro-monocytes:

They divide and differentiate to give rise

to: Circulating Blood Monocytes Monocytes which migrate to connective tissue change into phagocytic macrophages.



Development Of T-Lymphocyte



Development Of Monocyte

Development Of Blood Platelets

They are developed in the red bone marrow through the following stages:

1. Hematopoietic Stem Cell: It differentiates into:

2. Colony Forming Unit (CFU): This cell differentiates into megakaryoblast.

3. Megakaryoblast:

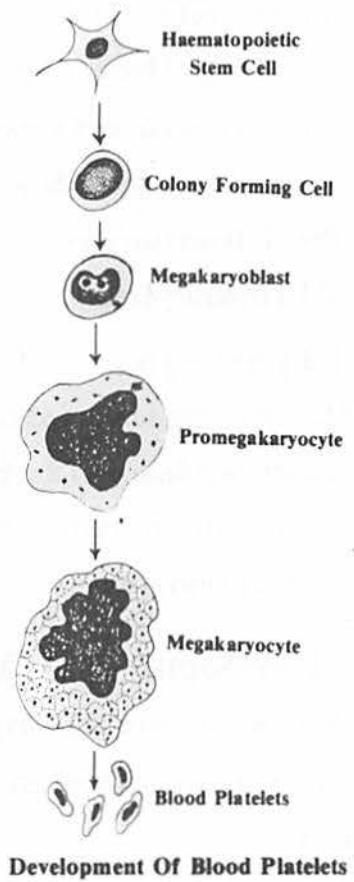
- It is a large cell with a rounded indented nucleus which has two clear nucleoli.
- The cytoplasm is basophilic and is rich in ribosomes.

4. Promegakaryocyte:

- It is a larger cell (about 60 microns in diameter) with a large multilobed nucleus.
- Its cytoplasm is basophilic and contains fine azurophilic granules.
- The cell can differentiate into megakaryocyte.

5. Megakaryocyte: (40 to 60 microns)

- It is a large cell with a large multilobed nucleus.
- With E/M the cytoplasm appears as if it is divided into small areas. These areas are then separated from each other to form blood platelets.



Development Of Blood Platelets

Differences Between Megakaryocyte And Osteoclast

Megakaryocyte	Osteoclast
1. Large cell about 60 microns. It has smooth surfaces 2. Basophilic cytoplasm. 3. It has a single multilobed nucleus. 4. Present in the bone marrow. 5. It forms blood platelets.	1. Its diameter is about 150 microns. has a ruffled (serrated) surface. 2. Acidophilic foamy cytoplasm. 3. Multinucleated cell, it has from 4 to 30 rounded nuclei. 4. Present in Howship's lacuna during ossification near the endosteum. 5. It is concerned in remodelling of bone.

Tissues Of The Body

The human body Organs are formed of the following 4 types of tissues:

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

Epithelial Tissue

Types of epithelial Tissue

- a) **Simple epithelium** (cellular sheets formed of one layer of cells).
- b) **Stratified epithelium** (formed of many layers of cells one above the other).
- c) **Glandular epithelium** (cells are collected to form glands).
- d) **Neuro - epithelium** (epithelial cells act as receptors).
- e) **Myoepithelium** (cells are modified to contract).

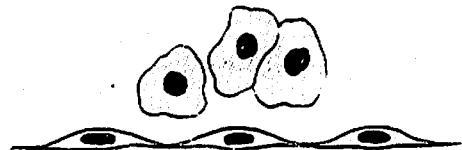
1- Simple Epithelium

Types of Simple Epithelium

1. Simple squamous.
2. Simple cubical (cuboidal).
3. Simple columnar.
4. Simple columnar ciliated.
5. Pseudo stratified columnar.
6. Pseudo stratified columnar ciliated.

1. Simple squamous Epithelium

- It is formed of one layer of flat cells with flattened nuclei.
- It forms a thin smooth lining to blood vessels to allow easy passage of blood.
- It covers the peritoneum to facilitate the movements of viscera.
- It facilitates the active filtration of urine in kidney.



Simple Squamous Epithelium Is Present In The Following Parts of The Body:

- a) The **endothelium** of heart and blood vessels.
- b) The **mesothelium** of serous membranes as: pleura (around the lung), pericardium (around the heart) and peritoneum (around the intestine).
- c) It forms the outer layer of Bowman's capsule of the kidney.
- d) Present in the alveoli of lung.
- e) It lines the anterior chamber of the eye ball.
- f) It lines parts of Henle's loop in kidney.
- g) It covers the adult ovary.

Simple Squamous Epithelium

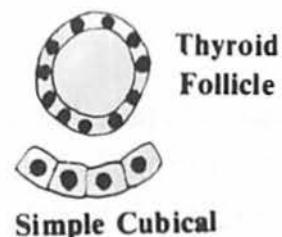
2. Simple Cubical (cuboidal) Epithelium

Simple cubical is formed of one layer of cuboidal cells with central rounded nuclei.

Functions: secretion, excretion, absorption and lining

Simple Cubical Epithelium Is Present In:

1. **Lining the thyroid follicles**, they secrete thyroid hormones.
2. **In kidney**: lining its convoluted tubules and its small collecting tubules. The cells have microvilli for absorption.
3. **In Eye**: Covering the anterior surface of lens and the inner cells of choroid.
4. **In Glands**: Lining the acini and small ducts of glands.
5. **In Ovary**: In newly born infants, it forms the germinal epithelium of the ovary. **N.B.:** **Cuboidal cells** are intermediate forms between cubical and columnar cells.



Some cuboidal cells are covered with **microvilli** and are called **simple cuboidal ciliated epithelium**. This epithelium lines the central canal of the spinal cord and the brain ventricles.

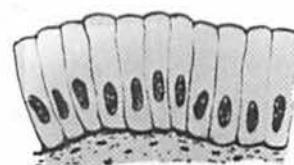
3. Simple Columnar Epithelium

It is formed of one layer of tall columnar cells with basal oval nuclei.

Functions: Columnar epithelium is mainly concerned with secretion, absorption and protection.

Simple Columnar is present in the following areas:

- a) **In the stomach**, **simple columnar** cells secrete mucin, so the cells have clear cytoplasm.
- b) **In the intestine**, they have dark cytoplasm and the surface is covered with microvilli which are rich in **phosphatase enzymes** in order to facilitate absorption processes. **Microvilli** are finger - like processes of the cytoplasm covered with cell membrane and are composed of **microfilaments**.
- c) Lining the gall bladder, the common bile duct and the pancreatic duct.
- d) Lining the large collection tubules of the kidney.



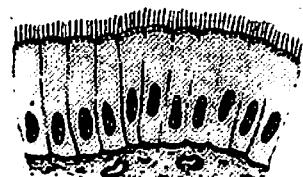
Simple Columnar

4. Simple Columnar Ciliated Epithelium

It is formed of simple columnar cells with basal oval nuclei. The free surfaces of these cells are covered with cilia.

With E/M each cilium is a cylindrical structure covered with a part of the cell membrane.

Each cilium is formed of: A basal body which is formed of 27 microtubules, a shaft which is formed of 20 microtubules and a root which is formed of 7 microtubules which fix the cilium into the cytoplasm.



Simple Columnar Ciliated

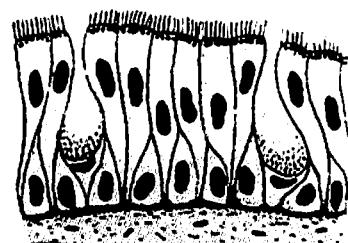
Cilia are responsible for movement of fluid or particles. They also act as sensory receptors.

Sites of Simple Columnar Ciliated Epithelium

- The central canal of the spinal cord and brain ventricles are lined with simple cuboidal ciliated epithelium.
- Fallopian tube and uterus (some of their lining cells are ciliated to facilitate movements of menstrual blood and ova).
- Outer or bony part of Eustachian tube.
- Some bronchioles of the lung.

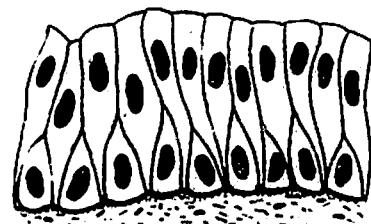
5. Pseudo - Stratified Columnar (Ciliated and Non - Ciliated)

- It is a **simple type** of epithelium formed of one layer of columnar cells resting on a clear wavy basement membrane.



Pseudo Stratified Columnar Ciliated With Goblet Cells

- The basement membrane is formed of:
 - Reticular Lamina** = it is formed of collagen fibrils (of types 3 and 4) and of glycoprotein.
 - Basal lamina** formed of clear and dense layers of glycoprotein and collagen fibrils (types 3+4).
- The columnar cells of this type of epithelium, during their development are crowded over each other, thus they lose their uniformity. the columnar cells are irregularly arranged, therefore their nuclei are arranged at different levels forming false rows.
- All the cells reach the basement membrane but some of them may fail to reach the surface.
- The surface may be ciliated or non - ciliated. Cilia may be motile or non motile (sterile).



Pseudo Stratified Columnar

- Goblet cells may be present between the columnar cells, their upper ends reach the surface, they secrete mucus secretion.

1. Pseudo-Stratified Columnar Ciliated Epithelium with goblet cells and motile cilia, is present in these areas:

- a) The Upper Respiratory Passages as: nasal air sinuses, nasopharynx, lower part of the larynx, trachea and bronchi.
- b) Eustachian tube (in its inner or cartilagenous part).
- c) Lacrimal sac.

Functions: This type of epithelium is responsible for; protection, secretion and transport of particles out of the air passages.

2. Pseudo Stratified Columnar Ciliated Epithelium but the Cilia are non-motile (These are not cilia but are tall solid microvilli).

This type is present only in the epididymis.

3. Pseudo-Stratified Columnar Non-Ciliated Epithelium is Present in:

- a) Upper part of Vas deferens and male urethra.
- b) Large ducts of salivary glands.

2– Stratified Epithelium

Stratified epithelium is formed of many layers of cells (3 or more layers).

Types of Stratified Epithelium: The stratified epithelium is named according to the most superficial cells, So we have the following four types:

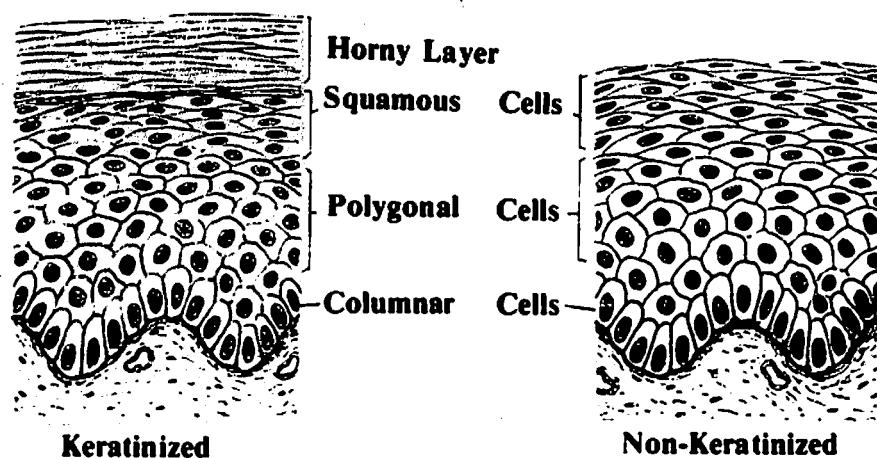
1. Stratified Squamous Epithelium (the superficial cells are squamous).
2. Stratified Columnar Epithelium (the superficial cells are columnar).
3. Stratified Columnar Ciliated Epithelium (the superficial cells are columnar ciliated).
4. Transitional Epithelium (the superficial cells are broad cuboidal cells, therefore it is called stratified cuboidal).

1 - 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 cells rest on a clear wavy basement membrane.
- Under the basement membrane there is C.T. containing blood and lymph vessels.
- The basal cells are well nourished and are formed of columnar cells with oval basal nuclei, from these basal cells, the other layers are renewed.

– The intermediate layers are polygonal cells (have many sides) with desmosomes between their cell boundaries (spiny appearance).

The Superficial layers of cells, are flat squamous cells which may be nucleated or not. They are not-well-nourished and they are exposed to air, so they are gradually shed off. The surface may be covered with fresh non-Keratinizing squamous cells as in the oesophagus. In other areas as in the skin, the epithelium is covered with keratin layer and the epithelium is named keratinizing stratified squamous.



Stratified Squamous Epithelium

Sites:

St. Sq. Epith. has a protective function so it is present in the following areas:

1– Keratinizing Stratified Squamous Epithelium is present in these dry surfaced areas:

a) Epidermis of skin.

b) Openings upon the skin: External ear, External nose, outer surface of the lip and the anal orifice.

2– Non-keratinizing stratified Squamous Epithelium is present in these wet surfaced areas:

a) Oral cavity, inner surface of the lip, gum and palatine tonsils.

b) Oesophagus, Oropharynx and vocal cords.

c) Cornea and exposed parts of the conjunctiva.

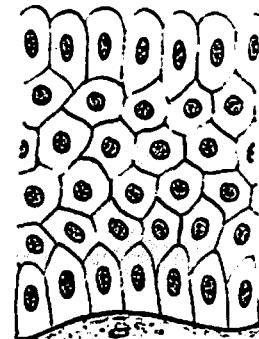
d) Vagina, terminal parts of male and female urethrae and anal canal.

2. Stratified Columnar Epithelium

- It is similar in structure to stratified squamous epithelium but:
- Its layers are less in number.
- The superficial cells are non-keratinizing columnar cells.

It is present in the following areas:

1. Fornices of conjunctiva of the eye.
2. Membranous and penile parts of male urethra.
3. Large ducts of glands.
4. Recto-anal junction.



Stratified Columnar

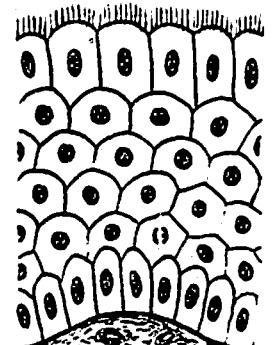
3 - Stratified Columnar Ciliated Epithelium

- It is similar in its structure to stratified squamous epithelium but:

- It is formed of few layers of cells.
- The superficial cells are non-keratinizing columnar ciliated cells.

This type of epithelium is present in:

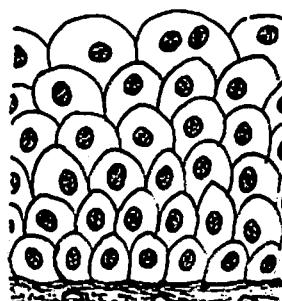
1. Foetal oesophagus.
2. Nasal surface of soft palate.
3. Laryngeal surface of epiglottis.



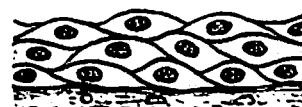
Stratified Columnar Ciliated

4. Stratified Cuboidal Epithelium

When the free surface of the stratified epithelium is covered with cuboidal cells, it is called stratified cuboidal. It is present in the ducts of sweat glands, and in seminiferous tubules of the testes. The transitional epithelium can be considered as a stratified cuboidal epithelium.



Empty Bladder



Full Bladder

Transitional Epithelium

5. Transitional Epithelium

- It is a **stratified type** of epithelium which is present in the **urinary tract**.
- The epithelium rests on **thin basement membrane**.
- Its **superficial cells are cuboidal** in shape with convex outer surfaces and concave inner surfaces. Some of the superficial cells may contain **two nuclei**.
- The **superficial cells** are covered with a **mucous - like substance**, which forms a **protecting membrane**. This membrane acts as an osmotic barrier between urine and tissue fluids. It also protects the epithelium from the high acidity or alkalinity of urine. These superficial cells are called **Facet or Dome-like Cells**.
- The **basal cell layer** is formed of high cuboidal cells.
- The **intermediate cells** which are present between the basal and superficial layers are **polyhedral cells** and are separated from each other by mucous - like substance in their intercellular spaces.
- The presence of mucous substance between the cells, facilitate gliding of cells on each other, so the transitional epithelium may be formed of **3 to 4 layers** only in full distended urinary bladder or **6 to 8 layers** in an empty bladder.
- The superficial cells may change temporarily into squamous cells when the bladder is full of urine.

N.B. Metaplasia means change of one type of epithelium into another type as in **Bilharziasis of bladder** and in **cancer bladder** the transitional epithelium changes into stratified squamous epithelium.

The Transitional epithelium is present in these urinary passages:

1. Minor and major calyces of the kidney.
2. Pelvis of the ureter, the ureter and the urinary bladder.
3. The prostatic part of male urethra and the inner part of female urethra.

N.B. In order to study the sites of the different types of epithelium in the human body you should. remember the following rules:-

Remember The Following Rules:

1. The smooth **endothelium** which is in direct contact with the **blood** as: lining the cavities of heart, blood vessels, lung alveoli and Bowman's capsule of kidney, all these are lined with **Simple Squamous Endothelium**.
2. The **Skin** and its **Openings** as (mouth cavity, tongue, cornea, vagina) and oesophagus, all these are lined with **Stratified Squamous Epithelium**.

3. **The Upper Respiratory Passages** as: Nose, Larynx, Trachea and Bronchi are lined with **Pseudo Stratified Columnar Ciliated Epithelium With Goblet Cells and Motile Cilia**.
4. **The Urinary Passages** as Calyces of Kidney, pelvis of ureter, ureter and urinary bladder are lined with **Transitional Epithelium**.
5. **The Gastro Intestinal Tract** as Stomach, Gall bladder, small and large intestine are lined with **Simple Columnar Epithelium**.
6. **The Acini of Glands** as Salivary glands, Pancreas, Sweat glands and Thyroid Follicles are lined with **Simple Cuboidal**.
7. **The Fallopian tubes and Uterus**, are lined with **Simple Columnar Ciliated Epithelium**.
8. **The central canal of spinal cord** and brain ventricles are lined with **Simple Cuboidal Ciliated Cells**.
9. **The Male Urethra** from inside outwards is lined with: **Transitional, Stratified Columnar** and then **Stratified Squamous Epithelium**.
10. The bony part of **Eustachian Tube** is lined with **Simple Columnar Ciliated**, while its cartilagenous part is lined with **Pseudo-Stratified Columnar Ciliated**.
11. **The Conjunctival Sac** is lined with **Stratified Squamous** at its exposed parts, while its fornices (non-exposed parts) are lined with **Stratified Columnar**.

3– Glandular Epithelium

It is the third type of epithelium which is specialised to produce secretion.

The glands are formed of collections of secretory epithelial cells.

Classification Of Glands

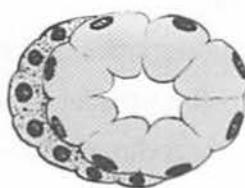
The Different Glands In Our Body Are Classified According To The Following Classifications:

1. **According to presence or absence of ducts, the glands are classified into:**
 - a) **Endocrine or ductless glands**, secreting hormones directly in the blood as: Thyroid, parathyroid, pituitary, suprarenal, pineal body, islets of Langerhan's, placenta, corpus luteum and special cells in the testis and ovary.
 - b) **Exocrine glands**: They have ducts to carry their secretions.
e.g. salivary glands, sweat and sebaceous glands.
 - c) **Mixed glands**: which possess the exocrine and endocrine functions as: pancreas, testis and ovary.
2. **According to changes in the secretory cells, the glands are classified into:**
 - a) **Merocrine gland**: In these glands, there is no cellular changes in their secretory cells; for example: the salivary glands.

- b) **Apocrine gland:** in which the tips of the secretory cells of the gland are detached and come out with the secretory products of the gland e.g. mammary glands and sweat glands of axilla.
- c) **Holocrine gland,** in which the whole secretory **cells** are destroyed and come out with the secretion e.g. the cells of the sebaceous glands may come out with their secretion.



Serous Acinus



Muco-Serous (Mixed Acinus)



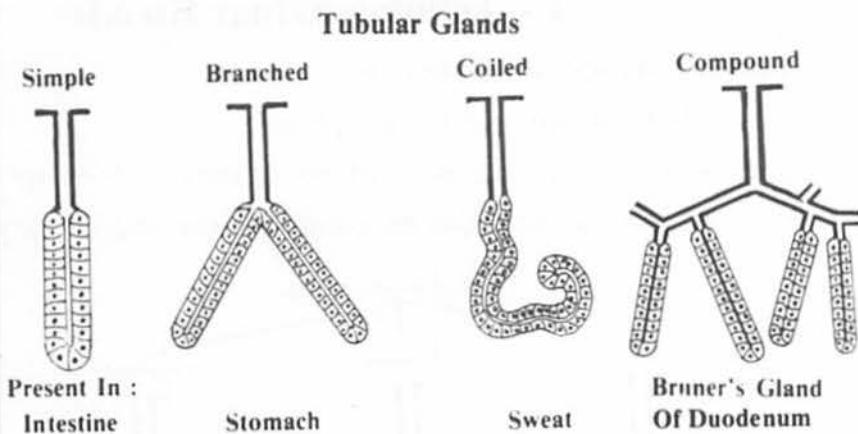
Mucous Acinus

3. The glands are classified according to the kind of their secretion into:

- Serous secretory glands:** as parotid gland and Von Ebner gland of the tongue.
- Mucous secretory glands:** as Brunner's gland and goblet cells.
- Mucoseroous secretory glands:** as submandibular and sublingual glands.
- Fatty secretory glands:** as sebaceous glands.
- Watery secretory glands:** as sweat glands.
- Waxy secretory glands:** as glands of external ear.
- Cellular secretory glands:** as testis and ovary.

4. According to the shape and branching of the secretory part of the glands and the shape and branching of their ducts.

The shape of the glands may be: Tubular, Acinar or Tubulo - acinar.



A - Tubular Glands

Tubular Glands which may be of the following types:

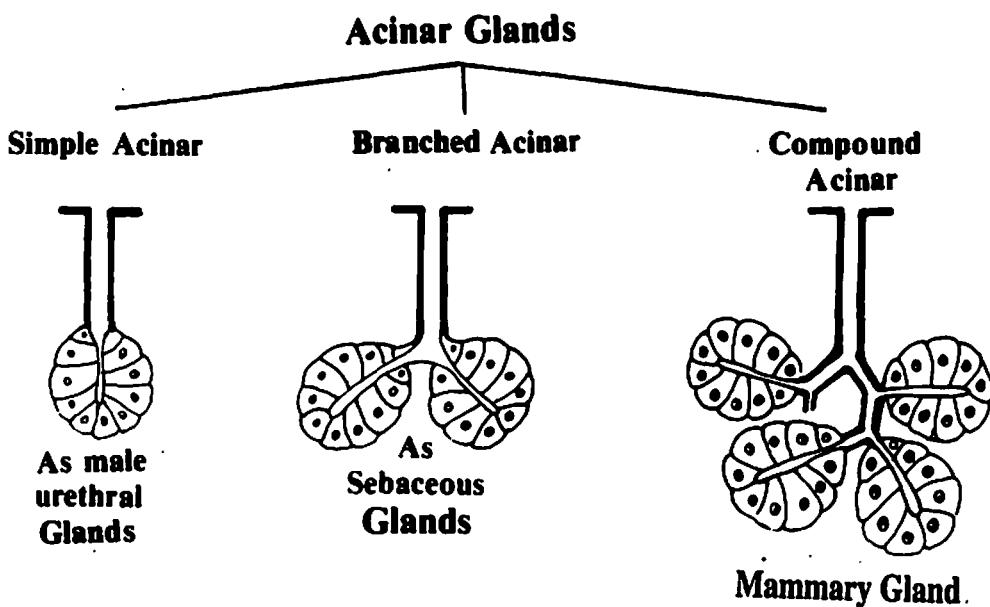
- Simple tubular glands:** as the intestinal glands or the crypts of Lieberkuhn.

- b) Simple branched tubular: as the glands of the stomach.
- c) Simple coiled tubular: as the sweat glands.
- d) Compound tubular glands: as the kidney and testis.

B- Acinar Glands

Acinar Glands are classified into:

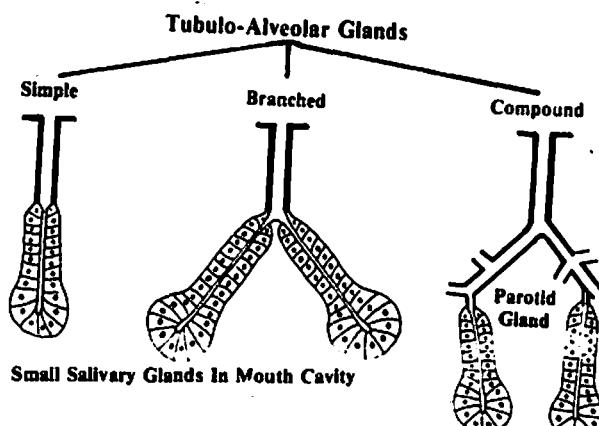
- a) Simple acinar: as male urethral glands and sebaceous glands.
- b) Simple branched acinar: as the sebaceous and tarsal glands of eye lid.
- c) Compound acinar: as the sebaceous gland and mammary gland.



C- Tubulo - Acinar Glands

Tubulo - Acinar Glands: which may be:

- a) Simple Tubulo-acinar: not found in man.
- b) Branched tubulo- acinar: as the glands of the mouth cavity.
- c) Compound tubulo-acinar: as pancreas, prostate and salivary glands.





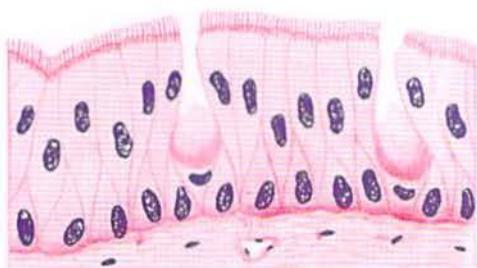
Simple squamous



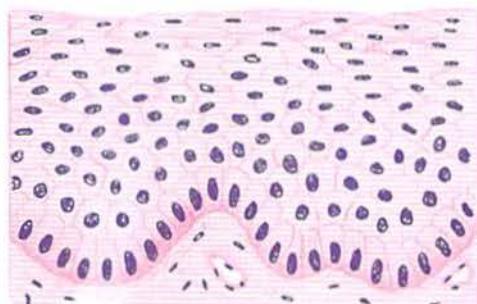
Simple cubical



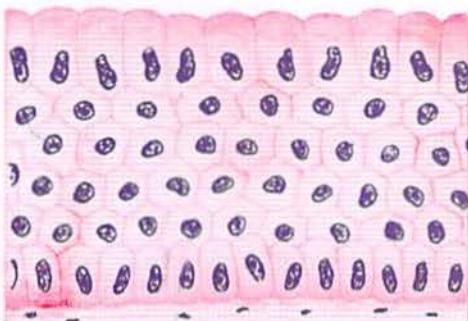
**Simple columnar
With Goblet Cells**



**Pseudo-stratified columnar ciliated
With Goblet Cells**



**Stratified squamous
(non-keratinizing)**



Stratified columnar



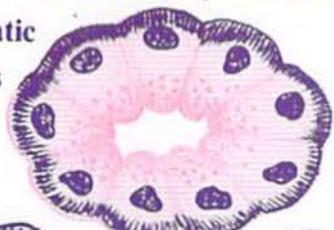
(in full bladder)



Transitional

Glandular Epithelium

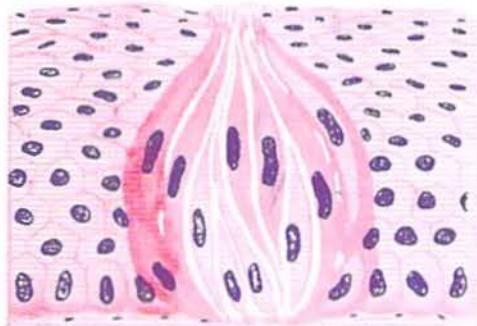
Pancreatic
acinus



Serous acinus



Mucous acinus



Taste bud
(neuroepithelium)



5. The glands can be classified according to their functions into: Secretory and Excretory Glands.

- a) **Secretory Glands:** which synthesize specific substances to be secreted in the body as salivary and endocrine glands.
- b) **Excretory Glands:** which eliminate and excrete the waste products outside the body as kidney and sweat glands.

4. Neuro - Epithelium

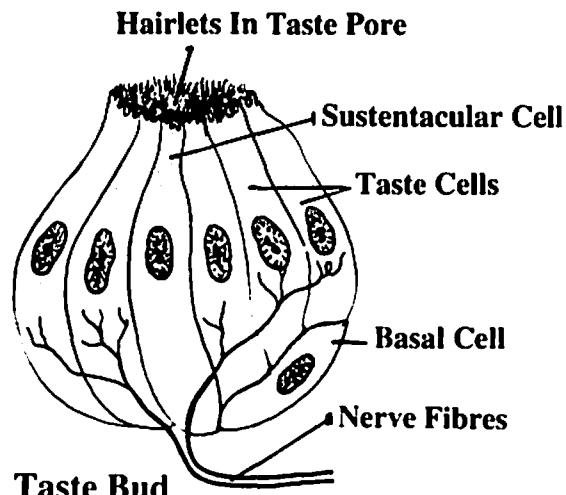
- It is the fourth type of epithelial tissue (Simple, stratified, glandular and neuro-epithelium).
- In this type, the epithelial cells act as **sensory receptors for special stimuli**.
- The neuro - epithelial cells are provided with **small hairs (hairlets)** on their free surfaces, while their bases are surrounded with **sensory nerves**.

Neuro-epithelium is present in taste bud which is formed of the following cells:

1. **Receptor cells** which are also called hair cells or **taste cells** They are concerned with taste sensation.
2. **Supporting cells** or sustentacular cells.
3. **Basal Cells.**

Neuro - epithelium is found in:

- a) **Taste buds** in the tongue.
- b) **Organ of Corti** in internal ear (for hearing).
- c) **Crista Ampularis** in the ampullae of the semicircular canals, in the internal ear (for equilibrium).
- d) **Macula Utriculi and Macula Sacculi** in the utricle and saccule of the interml ear (for equilibrium) .



5. Myo - Epithelium or Basket Cells

Myoepithelial Cells or Basket cells are branched epithelial cells rich in **actin and myosin filaments**. They surround some secretory acini. They contract to squeeze the acini to secrete their products. They are present on the outer surfaces of the acini of: **sweat, salivary and mammary glands**.

General Characteristics Of Epithelial Tissue

1. Epithelium arise during embryological development from **ectoderm** (as skin), from **mesoderm** (as mesothelium of serous membranes) or from **endoderm** (as the epithelium of the intestinal tract).
2. Blood vessels do not penetrate between epithelial cells except in endocrine glands but **nerve fibres can penetrate** between the epithelial cells.
3. Epithelium rests on a **basement membrane** which may be clear or **non clear**.
The non-clear thin basement membrane is present in:
Transitional epith., olfactory epith., thyroid follicles and liver cells.
4. Epithelium can **degenerate** (destroyed) and can rapidly **regenerate** (renewed).
5. Epithelium has a **little intercellular substance** but the epithelial cells may be connected with each other by different types of cellular junctions.
6. **Epithelial tissue** covers a surface or lines a cavity or forms a gland.
7. Epithelial cells may act as special receptors for taste and equilibrium.

N.B.: The endothelium is the simple squamous epithelium which lines the heart and blood vessels.

The mesothelium is the simple squamous cells of the serous membranes (pleura, peritoneum and pericardium).

The mucous membrane is the epithelial lining of any cavity or canal as that which lines the digestive, respiratory and uro-genital tracts.

The Basement Membrane: It is formed of basal and reticular laminae. It binds epithelium to the underlying C.T. It permits the passage of blood and nutrition to the epithelium. In kidney; it acts as filtration barrier.

Functions Of Epithelial Tissues

1. **Protection** against injuries, bacteria, chemicals and water as epithelium of skin and stomach.
2. **Secretion** as glandular epithelium of pancreas, prostate, salivary and endocrine glands.
3. **Absorption** as the cells of intestine and kidney.
4. **Sensation** as the taste buds and organ of Corti.
5. **Reproduction** as the cells of the testis and ovary.
6. **Excretion** as the cells of kidney and sweat glands.
7. **Covering surfaces** (as skin) or **lining cavities** (as stomach).
8. **Respiration** as the epithelium of lung alveoli.

Connective Tissue (C.T.)

The mesoderm of the embryo gives rise to mesenchymal tissue (U.M.C.= undifferentiated mesenchymal cells and homogeneous intercellular substance of proteins).

The mesenchymal tissues are differentiated in the embryo into:

1. Connective tissue = C.T.
2. Vascular tissue.
3. Smooth muscles

The connective tissue is formed of:

- (a) C.T. Cells (b) C.T. Fibres (c) C.T. Matrix

Types Of Connective Tissue

According to the nature of the intercellular matrix we have three types of connective tissue:

1. Connective tissue proper which has a soft matrix.
2. Cartilage which has a rubbery matrix.
3. Bone which has a solid matrix.

Connective Tissue Proper

It is called connective because it supports, binds and connects various tissues and organs.

The Connective Tissue Is Formed Of:

1. C.T. Cells
2. C.T. Fibres
3. Soft matrix or ground substance

Types Of Connective Tissue Proper

The different types of C.T. cells and C.T. Fibres are present in the soft C.T. matrix in order to form the following 6 types C.T. proper:

- | | |
|------------------------|---------------------------|
| 1. Areolar C.T. | 2. Adipose C.T. |
| 3. Yellow elastic C.T. | 4. White collagenous C.T. |
| 5. Mucoid C.T. | 6. Reticular C.T. |

Types Of Connective Tissue Cells

The C.T. Cells Are Of Two Types:

1. **Fixed C.T. Cells As:** Fibroblast, Fixed Macrophages, Fat Cells, Mesenchymal Cells, Pericyte Cells, Endothelial Cells and Reticular Cells.
2. **Free C.T. Cells As:** Mast cells, Plasma cells, Free macrophages, Blood leucocytes and Melanophore cells.

The Fixed C. T. Cells

1. Fibroblast and Fibrocyte Cells

- Fibroblasts develop from mesenchymal cells and from pericytes.
- Its nucleus is faintly-stained.
- It is very numerous in areolar C. T.
- It is a branched cell with multiple processes.
- It has a **dark basophilic cytoplasm**.
- The cytoplasm is rich in RNA, endoplasmic reticulum, Golgi apparatus and mitochondria.
- Fibroblast can divide.
- Fibroblast can change into myofibroblast



Fibroblast



Fibrocyte

Functions Of Fibroblasts:

- They form collagen, elastin and reticulin substances in order to form C. T. fibres.
- They can also form the mucoprotein of the C. T. matrix.
- Their number increases during healing of wounds and in cases of C. T. damage.
- Fibroblasts may change into Myofibroblasts which can close wounds.

Fibrocytes are the mature cells of fibroblasts

- They are small spindle-shaped cells with **darkly-stained nuclei**.
- They have **light basophilic cytoplasm** with few cell organelles.
- They cannot divide. They maintain the function of C. T.

2. Fixed Macrophages or Histiocyte Cells

- They are derived from **blood monocytes** after migration from blood to C. T.
- These cells are more present in the **damaged C. T.**
- They are **branched cells** with many processes.
- They have **irregular cell membranes** due to presence of pseudopodia.
- Their **cytoplasm** is not clear and is rich in lysosomes. It is **basophilic** in staining and is rich in cell inclusions and it contains also phagocytosed particles.
- The **nucleus** is small, it may be indented or kidney-shaped. It is very rich in



Macrophage Histiocyte

chromatin and is **darkly stained**.

E/M: They are rich in lysosomes, Golgi bodies and rough endoplasmic reticulum.

- Histiocyte cells can be stained with vital stain as Trypan blue.

Functions Of Macrophage Histiocytes:

- They are one of the mono-nuclear phagocytic cells which are present all over the body except the brain. They can eat and digest micro-organisms.
- They play a role **in immunity** and in the defensive mechanism of the body.
- They can engulf (eat) foreign bodies, bacteria and old blood cells.
- They can clean wounds from foreign bodies and debris.
- They can **trap (catch) antigens** and transport them to lymphocytes.
- Some **macrophages** may be collected with each other to form a **M multinucleated Giant Cell** known as **Foreign Body Giant Cell** which can surround and destroy bacteria as T. B. They can also destroy old RBCs. in the spleen.

3. Adipose Cell Or Fat Cell Or Adipocyte

- There are 2 types of Fat cells (both originate from UMC.):

1. **Unilocular White Fat cell** contains single large globule of fat and a peripheral flat nucleus.



White Fat cell

2. **Multilocular Brown Fat cell** contains multiple small globules of fat rich in pigments. It has a central nucleus and **pigmented mitochondria**.



Brown
Fat Cell

- Fat cells are **present mainly in** white and brown adipose C.T.

E/M: Fat appear as black areas in fat cells.

- In **HX and E** stained sections, fat cells appear as **empty spaces**.

- Fat cells **cannot divide** but have long life span.

- Fat cells can be stained **orange** with **sudan III** or stained **black** with **sudan black**. Osmic acid stains fat cells with black colour also.

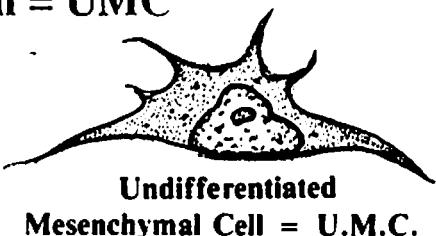
Functions of Fat cells

- Brown Fat cells regulate body temperature in newborn infants.
- White Fat cells release energy during starvation. They support organs as kidney. They give the body its contour. They act as heat insulator.

4. The Mesenchymal Cell = UMC

- It is a stem embryonic branched cell called **Undifferentiated Mesenchymal cell = UMC.**
- It has a large oval nucleus, basophilic cytoplasm and few cell organelles.
- It is present in bone marrow to give blood cells, also in C. T. and around blood vessels.

Function: It can differentiate into other types of C. T. cells.



5. The Pericyte Cells

- They are pale branched cells with long cytoplasmic processes.
- They are present immediately **external** to the endothelium of blood capillaries and small venules, thus they are termed as pericytes (*peri* = around).
- They are considered as mesenchymal cells which **persist in adult life**.

Functions Of Pericyte Cells:

- Pericytes can give rise to both fibroblasts and smooth muscle cells.
- They play an important role in the process of **healing of connective tissue** and blood vessels whenever wounds are present.
- Pericyte cells may be modified to form **myoepithelial cells** which can contract.

6. The Endothelial Cells

- They are present in the **entire surface** of the blood capillaries and blood vessels.
- They **form** the endothelium of blood vessels.
- They **develop from** the embryonic mesenchymal cells.
- In adults, they are considered as connective tissue cells.



Functions Of Endothelial Cells:

1. They synthesize **type 4 collagen**.
2. They can divide to form **new capillaries** in tissue injuries.
3. They play a role in formation of **basement membrane** of endothelium.
4. These cells may divide rapidly giving rise to secretory endothelial cells.
e. g. Endothelial cells of lung capillaries secrete **Angiotensin Enzyme**.

Endothelial Cell

7. Reticular Cells

- They are present mainly in the reticular C. T.
- They are modified fibroblasts which form reticular fibres.
- They are branched cells with small oval nuclei.



- Reticular cells have many processes which are attached with the reticular fibres to form a **network of reticular C. T.**
- **Reticular cells are found in:** the stroma of bone marrow, lymph nodes, spleen, liver, pancreas and other organs.

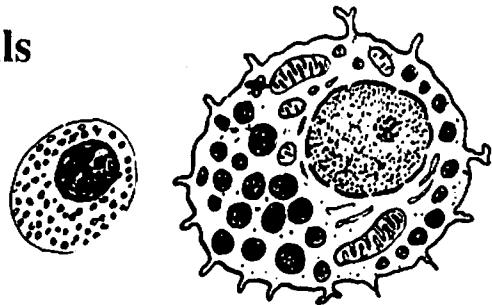
Functions of Reticular Cells: They are supportive cells.

- They form the stroma of glands and bone marrow.
- They remove cellular debris from the lymphatic tissues.

The Free C. T. Cells

1. Mast Cells

- They are small cells.
- They may be oval, rounded or irregular in shape.
- They are usually present around blood vessels, in respiratory and digestive tracts.
- **With The E/M:** The cell membrane is irregular with many cytoplasmic processes.
- Mast cells are very rich in mitochondria, Golgi bodies and ribosomes.
- **Their cytoplasm** is filled with large basophilic granules.
- The granules are the precursor of **heparin and histamine**.
- The granules can be stained metachromatically with **toluidine blue**.
- The cytoplasm is rich in Golgi apparatus, endoplasmic reticulae, heparin, histamin and serotonin granules.
- The nuclei of mast cells are usually present at one side (not central).



Mast Cell

Types Of Mast Cells:

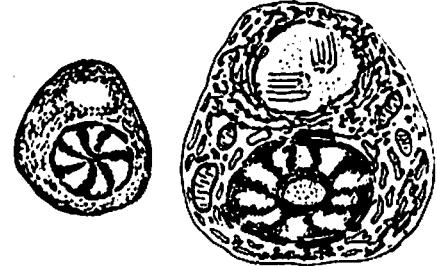
1. **Heparin Secretory Mast Cells** which are present in the C. T. of skin. They secrete **Heparin** which is an anticoagulant.
2. **Histamine Secretory Mast Cells** which are present under the mucosa of respiratory and digestive tracts, they secrete **histamine**. Histamine can contract smooth muscles, dilate blood capillaries and increase the capillary permeability.
- The surface of both types of mast cells contain specific receptors for IgE (Immunoglobulin E).

Functions Of Mast Cells:

- **They are Paracrine Cells.** They secrete heparin, histamine and serotonin.
- They release an **immediate hypersensitivity factors** which activate the defense system of the body.

2. Plasma Cells

- These cells are present mainly in the C.T. of the peritoneum, submucosa of digestive and respiratory tracts, in lymph nodes and spleen.
- They originate from **plasmablast** cells which develop from B-lymphocytes.
- Plasma cell is small and rounded, with homogeneous **basophilic cytoplasm**.
- Around the nucleus there is a pale area which is the space of Golgi apparatus.
- **With the E/M**, its cell membrane shows finger-like processes.
- Plasma cells are rich in granular endoplasmic reticulum and **RNA**.
- Rounded acidophilic bodies known as **Russell bodies** are present in the cytoplasm of mature plasma cells. These bodies represent the **immunoglobulin granules**.
- **The nucleus** is small and eccentric, its chromatin materials are arranged in radiating masses, giving the appearance of **cart-wheel shape** or the shape of **clock-face**.



Plasma Cell

Functions of Plasma Cells:

- They **secrete specific antibodies** against organisms and foreign bodies. These antibodies circulate in the blood and are termed **humoral antibodies** and the process is called **humoral immunity**.
- Plasma cells **cannot divide** and have **no phagocytic activity**, but they increase in certain inflammatory conditions to secrete specific antibodies.

3. Free Macrophages

- These cells are derived from blood monocytes after their migration to C.T.
- They are branched cells with multiple processes.
- Their cytoplasm is rich in lysosomes and rough endoplasmic reticulum.
- They have oval eccentric nuclei.

– Functions of Macrophages:

1. They participate in the immune system of the body.
2. They are highly phagocytic cells.
3. They secrete collagenase and elastase enzymes and lysozyme.
4. They can kill certain viruses through secretion of **interferon**.



Mesenchymal Cells



Fibroblast Cells



Fixed Macrophage



Reticular Cell



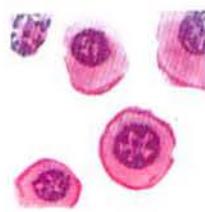
Two Fat Cells



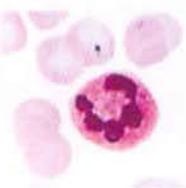
Mast Cell



Pigment Cells



Plasma Cells



Neutrophil
Leucocyte



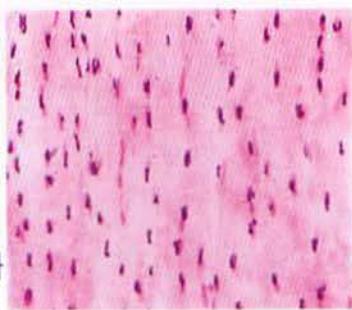
Eosinophil
Leucocyte



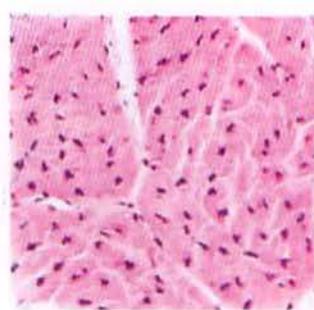
Lymphocyte



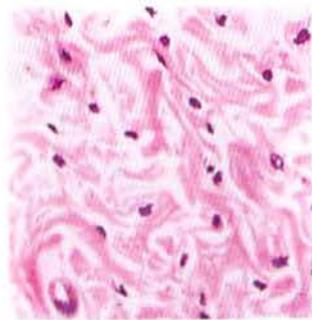
Free Macrophage
Monocyte
Engulfing RBC.



Regular White
Collagenous C.T.
(L.S. In Tendon)



White Collagenous C.T.
(T.S. In Tendon)



Irregular White
Collagenous C.T.

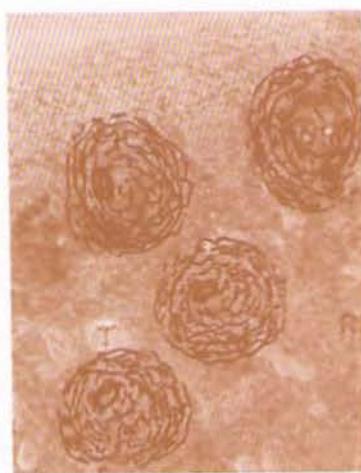
Zakaria d

plate 4





Reticular C.T.



Reticular C.T. In Spleen



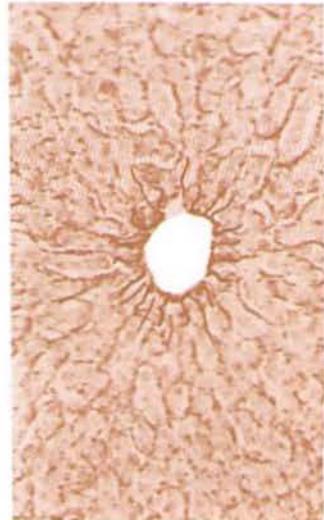
Reticular C.T.
In Lymph Node



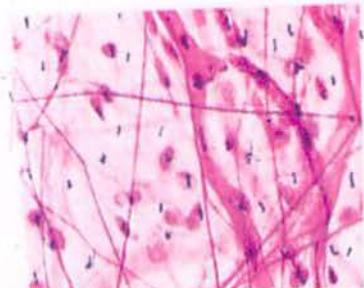
Reticular C.T.
In Suprarenal Gland



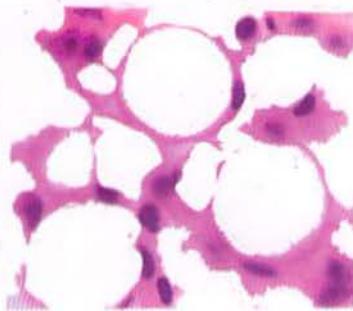
Elastic C.T. In Aorta
(Orecein Stain)



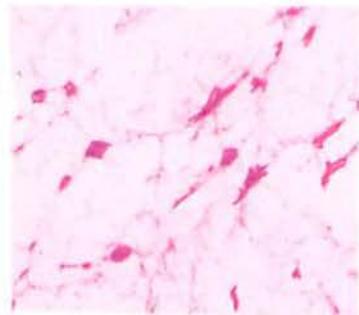
Reticular C.T. In Liver



Areolar C.T.



Adipose C.T.



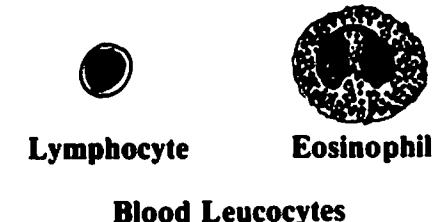
Mucoid C.T.

zakaria



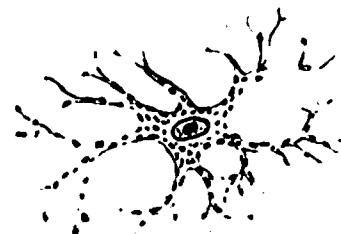
4. Blood Leucocytes

- Some Blood Leucocytes may appear normally in the C. T. of the following body organs:
- **Eosinophils and Basophils:** They are found in the C. T. of respiratory, intestinal and female genital tracts. They increase in allergic conditions.
- **Lymphocytes and Monocytes:** They are present in the C. T. of many organs and their number increases in chronic infections.
- **Neutrophils:** They migrate from blood vessels to C. T. where acute infection is present in order to phagocytose micro-organisms.



5. Melanophore Pigment Cells

- They are C. T. Macrophages which phagocytose melanin pigments. Melanin pigments are formed by the melanocytes.
 - They are branched cells with small rounded nuclei and are rich in melanin pigments.
 - They are present in C. T. of skin and eye.
- Functions:** Their melanin pigments protect skin from sun and facilitate eye vision.



Pigment Cell

Types Of Connective Tissue Fibres

There are three types of C. T. fibres.

1. White collagenous fibres.
2. Yellow elastic fibres.
3. Reticular fibres.



Collagenous Bundle

1. White Collagenous Fibres

Shape: They are colourless wavy branching bundles formed of non-branching small fibrils. The fibrils run parallel to each other in the bundles. They appear white as in tendons.

Character: They are soft, strong and flexible, but not elastic in nature.

Structure: They are formed of a protein known as collagen. Fibroblast first synthesize the **tropocollagen** which is then changed into collagen.

Staining: Collagenous fibres are acidophilic; they stain pink with **Eosin**, red with **Van Gieson** and blue with **Mallory** stain.

E/M: They are formed of **tropocollagen** **microfibrils** which have **cross striations** due to overlapping of the tropocollagen molecules.

Types Of Collagen

There are many types of collagen which are classified according to the **chain of amino acids** present in each type, also according to thickness and origin of each type.

1. **Type 1 Collagen** Present in: loose connective tissue, white fibro-cartilage, bone and teeth. This type is formed by: fibroblasts, osteoblasts, and odontoblasts.
2. **Type 2 Collagen:** Present in hyaline and elastic cartilage and is formed by chondroblasts.
3. **Type 3 Collagen:** Present in skin, smooth muscles and reticular fibres. It is formed by fibroblasts and by smooth muscle cells.
4. **Type 4 Collagen:** Present in the basement membranes of epithelial tissue and in the lens of eye. It is formed by the **fibroblasts and by endothelial cells**.
5. **Type 5 Collagen:** Present in the placenta. It is formed by **fibroblasts**.

2. Elastic Fibres

Shape: They are fine, straight branching fibres. They are not made up of fibrils.

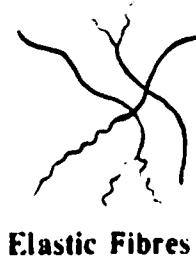
Character: The fibres branch and anastomose with each other. They run singly and not in bundles. They are **stretchable** fibres and appear yellow in fresh state.

Structure: They are formed of protein known as **elastin** which is resistant to boiling and to some chemicals. They are formed by fibroblast cells and by some smooth muscles from a protein called **tropoelastin**.

Staining: They can be stained **brown with orcein and black with Verhoeff**.

Sites: Present in elastic tissues as arteries and lung.

E/M: Each fibre is formed of a central homogeneous area of elastin substance surrounded by peripheral microfibrils of glycoprotein material.



Elastic Fibres

3. Reticular Fibres

Shape: They are very thin fibres, they branch and anastomose to form a network or **reticulum**.

Structure: They are formed of **type 3 collagen**, glycoproteins and proteoglycans.

Staining: They can stain black with silver.

Sites: In **Stroma of glands and bone marrow**.



Reticular Fibres

Matrix Of C. T. Proper Or Ground Intercellular Substance

It is an amorphous jelly-like substance in which the C. T. cells and fibres are embedded. It is stained red with PAS and blue with toluidine blue.

The Matrix is Formed of Two Components:

1. Viscid substance formed of Hyaluronic acid, heparan sulphate, chondroitin sulphate and Glycoproteins as: fibronectin, laminin and integrin.
2. Tissue Fluid which may increase in some diseases to form oedema.

Types Of C. T. Proper

There are 6 types of C. T. Proper which are distributed allover the human body. They are named according to the most abundant C. T. fibres or C. T. cells or C. T. matrix.

The 12 types of C. T. cells and the 3 types of C. T. fibres are present in a soft matrix of glycoproteins to form **The Following 6 Types of C. T. Proper:**

- | | |
|-------------------------|----------------------------|
| 1. Areolar C. T. | 4. White collagenous C. T. |
| 2. Adipose C. T. | 5. Reticular C. T. |
| 3. Yellow elastic C. T. | 6. Mucoid C. T. |

1. Loose Or Areolar Connective Tissue

- It is the most common type of C. T. in the human body. It contains all types of C. T. fibres and C. T. cells (see plate 4).

Functions: It acts as packaging material for other tissues.

Structure:- It is formed of a loose matrix rich in glycoproteins and hyaluronic acid. It contains areolae (spaces) usually filled with air or fluid.

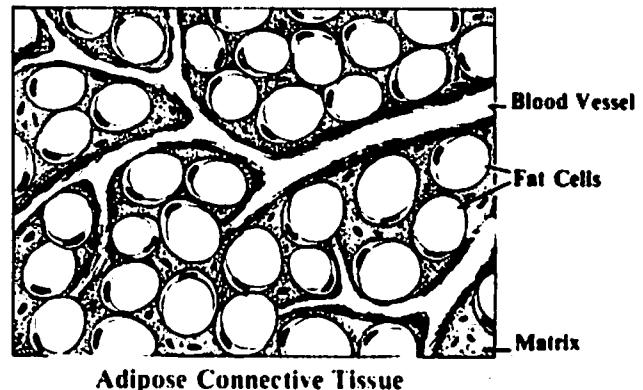
- **The C. T. Cells and C. T. fibres are embedded in a loose C. T. matrix.**
- **The C. T. Cells are mainly; Fibroblasts, Macrophages, Fat and Mast Cells.**
- **The C. T. Fibres are mainly collagenous which are condensed in certain areas as in dermis of skin.**

Sites: Present allover the body except between Brain Cells. **It is present in:**

1. Under the skin.
2. Submucosa of digestive tract.
3. In the serous membranes as pleura, peritoneum and pericardium.
4. Under the epithelial lining of organs.
5. Around the organs and blood vessels.

2. Adipose Or Fatty Connective Tissue

- It is one of the largest tissues in the body.
- It is formed of a loose matrix, few C. T. fibres and cells, with many fat cells.
- The fat cells develop from undifferentiated mesenchymal cells which are transformed into lipoblasts then into fat cells.
- There are Two types of Adipose C. T. **White and Brown.**



a) White Or Yellow Adipose Tissue Or Unilocular Adipose Tissue.

It is composed of large fat cells (each is over 100 microns in diameter). The bulk of each cell is occupied by a single large globule of **non-pigmented** fat. This type is affected by hormones and by the restriction of diet (regime).

- These fat cells have **eccentric flat nuclei**.
- The rim of cytoplasm around the nuclei contains few cell organelles.
- The fat cells appear empty after alcoholic stains.
- Fat cells stain **orange** with **sudan 3** and black with **osmic**.

Functions of White Adipose C. T.

- It acts as heat insulator and as fat storage areas.
- It gives the body its normal shape. It supports organs as kidney.

Sites of White Adipose C. T.

It is present in the following fatty areas:

1. Under the skin especially in females, it is more condensed in the mammary glands and gluteal regions.
2. Around the kidney and blood vessels.
3. In the mesentery, omentum and in the abdominal wall.

b) Brown Adipose C. T. Or Multilocular Adipose Tissue.

- It is formed of **small fat cells** which are filled with **many droplets of fat** (not a single mass of fat). It appears brown because their mitochondria are rich in pigments and is surrounded by **many blood capillaries**.
- It develops mainly in the embryo from U. M. C. It persists for few months after birth. It supplies newly-born infants with heat to protect them from cold.

Functions Of Brown Adipose C. T.:

- It regulates body temperature in newborn infants.

Sites of Brown Adipose C. T.

- Interscapular region, axillary region and mediastinal region, especially in infants.
- Around the thoracic aorta.

Adipose C. T. is not present in the following skin areas.:

Eye lid, penis, labia minora, clitoris, nipples, ear pinna and scrotum.

3. Elastic Connective Tissue

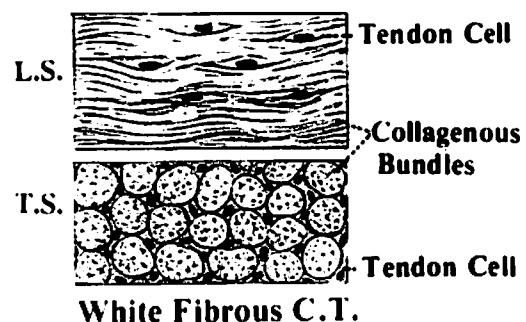
- It is an elastic type of C. T. which appears yellow in fresh conditions.
- It can be stained brown with orcein stain.
- It is formed of condensed **elastic fibres** separated with areolar C. T.
- In certain areas the elastic fibres are condensed to form elastic C. T. sheets which are surrounded with loose C. T. and flattened fibroblasts.
- The elastic tissue is stretchable i. e. **elastic in nature**.
- Elastic tissue is present in the form of elastic membranes as in aorta or in the form of elastic ligaments as in vocal cords.

Sites Of Elastic Tissue: It is present in the following elastic areas:

1. Aorta and large arteries. (to maintain continuous blood flow).
2. Bronchi, bronchioles and around alveoli of lung (to facilitate respiration).
3. Ligamentum flavum (between the vertebrae) and ligamentum nuchae (in the back of the neck) to facilitate movements of trunk and neck.
4. Suspensory ligament of penis (to facilitate erection of the penis).

4. White Collagenous Or Tendonous Connective Tissue

- It is a very **dense type of C. T.**
- It is formed mainly of collagenous fibres.
- In fresh state, it appears **white in colour**.
- The collagenous fibres are present in bundles, the bundles are separated from each other by areolar C. T. containing B. V., nerves and lymphatics.
- It has a small amount of matrix and it is poor in blood supply.
- The arrangement of the collagenous bundles in the white fibrous C. T. may be **regular or irregular** but usually pressing between them modified fibroblast cells which are known as **tendon cells**.



- The fibroblast cells are triangular in shape with basophilic cytoplasm and their nuclei are oval in shape.
- The tendon cells and fibres are connected with each other by areolar C. T.

Types Of White Collagenous Connective Tissue

1. Regular White Collagenous C. T. Which is formed of regular collagenous bundles.

Sites: It is present in the cornea of eye and in the tendons of muscles.

2. Irregular White Collagenous C. T.: Which is formed of irregular collagenous bundles.

Sites: It is present in the following white structures:

1. **Sclera** of the eye ball (through which eye muscles are attached).
2. Capsule and septa of glands and organs.
3. **Dura mater** which forms the covering and protecting membrane to the brain.
4. **Perichondrium** (around cartilage) and **Periosteum** (around bone).

5. Reticular Connective Tissue

- It is a very fine type of adult C. T.
- It forms the stroma or background of glands.

Reticular C. T. is formed of:

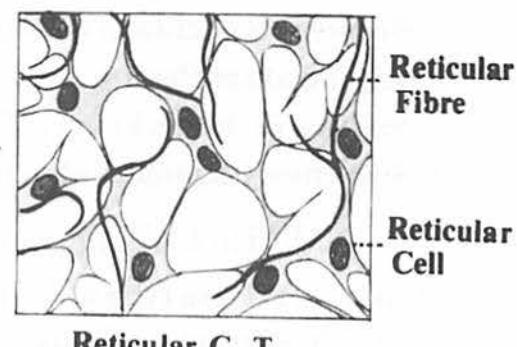
- a) **Reticular fibres** which are thin fibres.
- b) **Reticular cells** which are stellate-shaped cells.
- c) **Mononuclear phagocytic cells**.

The reticular cells and fibres form a network.

Staining: It can be stained Brown with silver.

Sites of reticular C. T.:

1. Present in the stroma of bone marrow.
2. In the stroma or frame-work of the spleen, lymph node, liver, testis, ovary and endocrine glands.
3. In the kidney, lung and gastro-intestinal tract.



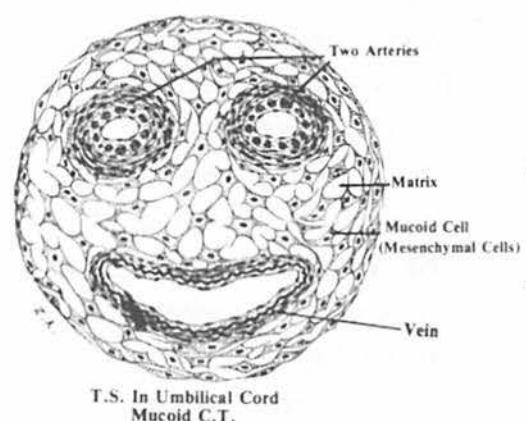
Reticular C. T.

6. Mucoid Connective Tissue

- It is called also as Mucous C. T.

It is formed of:

1. **Mucoid cells** which are young fibroblasts.
2. **Matrix** which is soft and formed of hyaluronic acid, reticular and collagenous fibres.



Sites of Mucoid C.T.

1. In the umbilical cord of the embryo, (between the blood vessels of the umbilical cord where it is called **Warton's jelly**).
2. In adult, it is present in the vitreous humour of the eye ball and in the pulp of growing teeth.

The Embryonic Mesenchymal Connective Tissue

- It is present in the embryo.
- It is formed of undifferentiated Mesenchymal Cells (UMC), Inter-cellular soft substance and fine reticular fibres.

The Pigmented Type Of C.T.

The Pigmented type of C.T. is an adult type of C.T. proper similar to areolar C.T. but it is very rich in pigment cells.

It is present in the iris, ciliary body and choroid of the eye.

Functions Of C.T. Proper

1. It supports and connects the different organs and tissues together.
2. Through the C.T, B.V., nerves and lymph vessels reach the organs.
3. C.T. Plasma cells secrete antibodies, mast cells secrete histamine and heparine.
4. C.T. is important in regeneration and healing of wounds.
5. Some C.T. cells are important for body defence and immune response.

Preparation and Staining Of a C.T. film

1. Cut a very small piece of areolar C.T. and spread it on the centre of a slide.
2. The film should be thin, transparent and should contain fat cells.
3. Cover the film with 10% formaline for 5 minutes.
4. Wash it in distilled water for one minute.
5. Cover the film with sudan 3 for 15 minutes.
6. Wash it in distilled water for one minute.
7. Cover the film with hematoxylin for 10 minutes.
8. Wash the film in tap water for 3 minutes.
9. Dry the film and cover it with a drop of glycerine and cover glass.
10. Examine the film under the microscope, demonstrate that the fat cells are stained orange yellow and the nuclei of C.T. cells are stained blue.

Cartilage

Definition: It is a firm, rigid, flexible and dense type of C. T. It is poor in blood supply.

Structure: It is formed of:

1. **Cartilage Cells:** Chondrogenic cells, Chondroblasts and Chondrocytes.
2. **C. T. Fibres;** Collagenous and elastic C. T. fibres.
3. **Matrix;** formed of collagen, chondroitin sulphates and glycoproteins.

Cartilage Cells

1. **Chondrogenic Cells,** spindle-shaped cells with oval nuclei. They change to **chondroblasts**.
2. **Chondroblasts:** They have basophilic cytoplasm with all organoids and inclusions.
 - They are present mainly under the perichondrium of cartilage.
 - They form type II collagen, They change into mature chondrocytes.
3. **Mature Chondrocytes:**
 - They are oval or rounded cells with rounded nuclei.
 - Their cytoplasm is basophilic, it contains all organoids and inclusions. It is rich in glycogen, fat and phosphatase enzymes.
 - Chondrocytes are present in groups called **Cell Nests**.
 - The groups of cartilage cells are surrounded with a space called **lacuna**, outside this lacuna the matrix is condensed to form the **capsule** of cell nest.

Function Of Mature Chondrocytes: They synthesize (form) type II collagen, proteoglycans, hyaluronic acid and chondroproteins of the matrix.

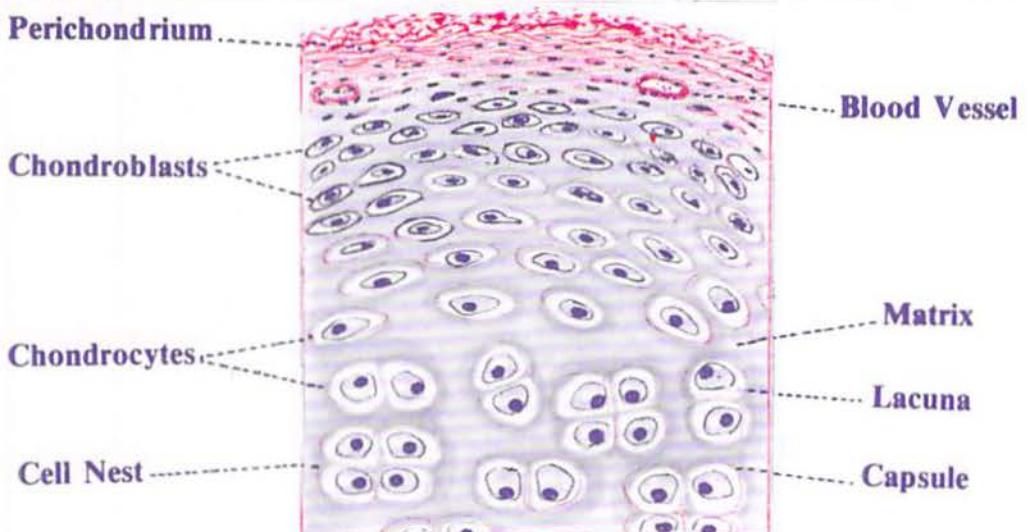
Matrix Of Cartilage

- It is rubbery in consistency. It is formed by chondroblasts and chondrocytes.
- It is formed of proteoglycans, hyaluronic acid, glycoprotein and type II collagen.
- It is rich in very thin collagenous fibres.
- It is **basophilic** in staining, it can be stained blue with hematoxylin.
- It has no blood vessels, no lymph vessels and no nerves.

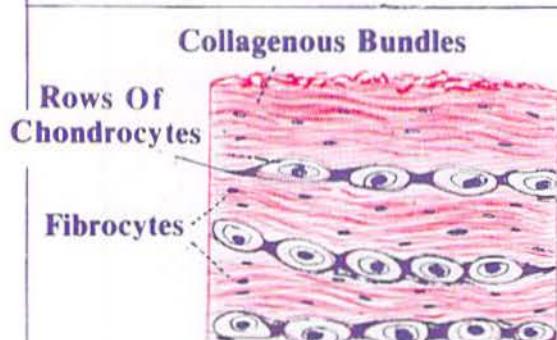
Types Of Cartilage

The cartilage cells and the C. T. fibres are embedded in a rubbery matrix in order to form **the following three types of cartilage**.

1. **Hyaline cartilage** (it appears glassy).
2. **Elastic fibro-cartilage** (contains elastic fibres).
3. **White fibro-cartilage** (contains white collagenous bundles).



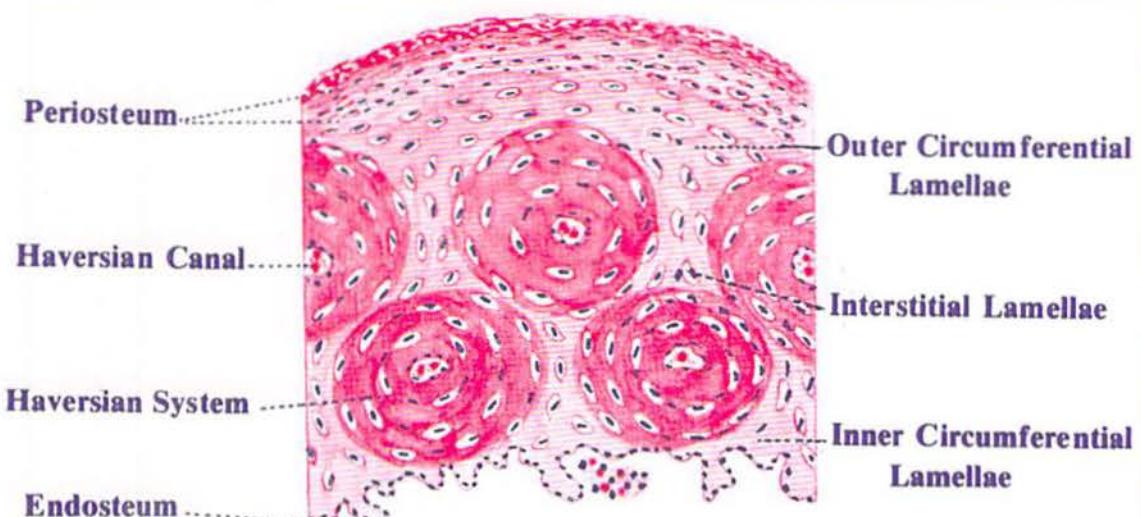
Hyaline Cartilage (T.S. In Costal Cartilage)



White Fibro-Cartilage



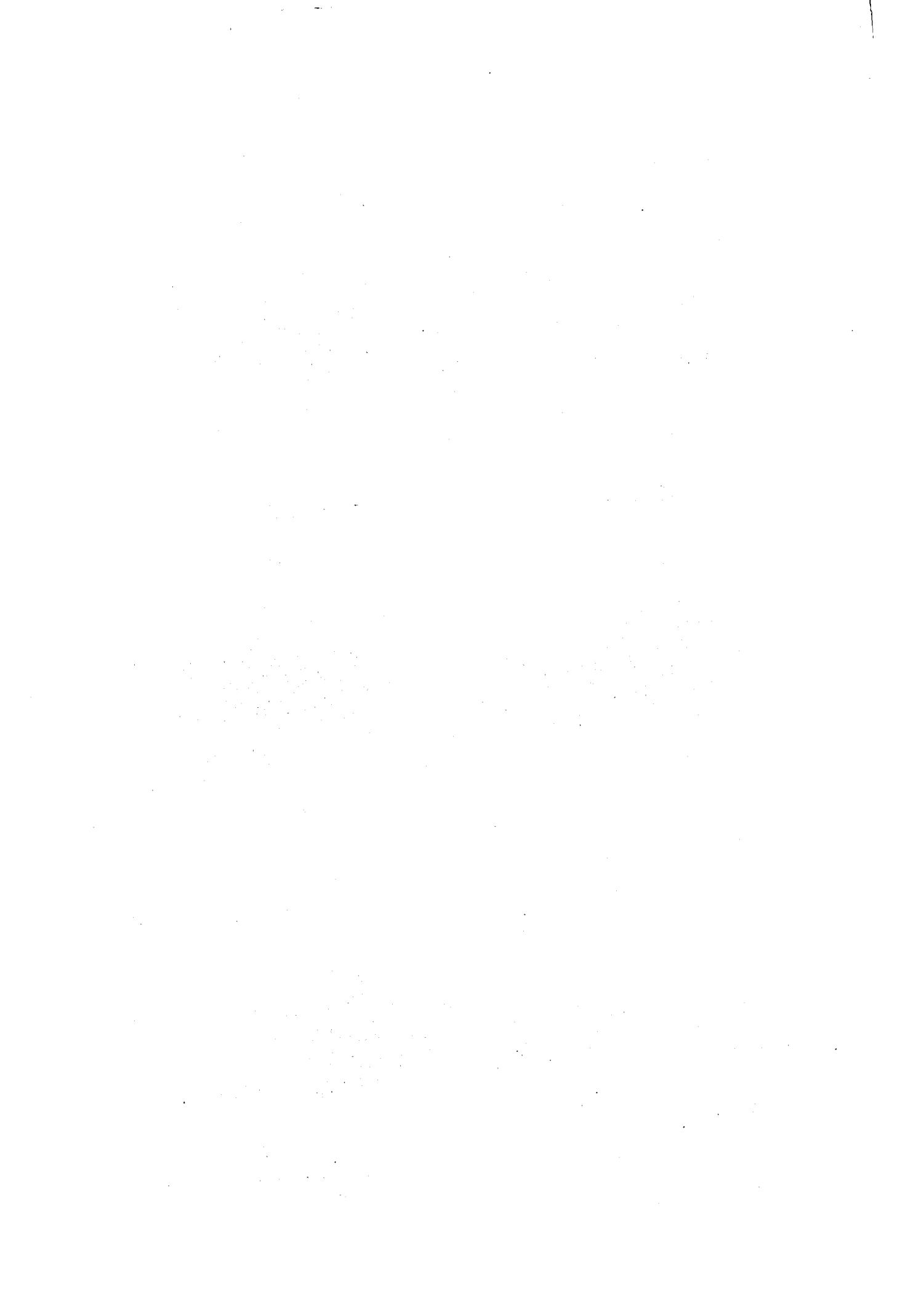
Elastic Cartilage (Ear Pinna)



Compact Decalcified Bone (T.S. In Long Bone)

Zakaria

[Plate 6]



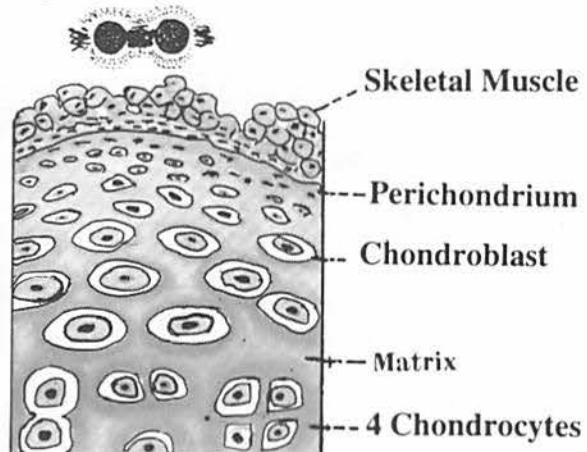
Hyaline Cartilage

- It is the commonest type of cartilage. It appears, when fresh, translucent and pale blue in colour. Therefore it is called hyaline (See plate 6).
- The matrix is poor in blood supply. The blood vessels which appear in the matrix pass through it on their way to supply other tissues.
- Hyaline cartilage is covered by a vascular membrane or **perichondrium**, which is not present over the cartilage which covers the articular surfaces of joints.
- **The perichondrium is formed of:**

- a) **Outer Fibrous Layer** of collagenous bundles, rich in B.V. and fibroblasts.
- b) **Inner Chondrogenic Layer** formed of chondroblasts which can be changed into chondrocytes. These chondroblasts can divide and can secrete new matrix, this process will result in growth of cartilage at its periphery.

Functions of perichondrium:

1. It supplies cartilage with blood.
 2. Its chondroblasts form the matrix of cartilage.
 3. It provides an attachment for muscles.
- Under the perichondrium there is a basophilic matrix formed of glycoprotein (proteoglycan) and fine collagenous fibres.
 - **Embedded in the matrix there are:**



Two Types of cartilage cells:

Hyaline Cartilage

- a) **Young Chondrocytes or Chondroblasts.** They are flat cells surrounded by spaces or lacunae. They have flat nuclei and basophilic cytoplasm. They are present as single cells under the perichondrium. With growth of cartilage, chondroblasts are transformed into mature **Chondrocytes**.
- b) **Mature Chondrocytes:** They are spherical cells with rounded nuclei and basophilic cytoplasm rich in phosphatase enzyme. Each cell is present in a space called **lacuna**. During growth, chondrocyte can divide giving rise to 2 or 4 or 8 chondrocytes. These groups of chondrocytes are surrounded with lacuna and capsule and are called **Cell Nests**.

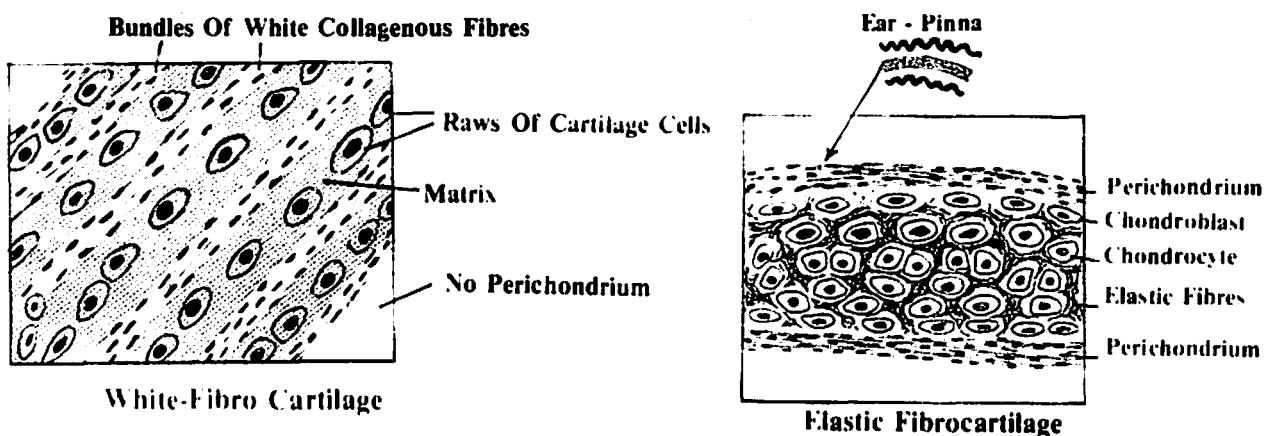
Sites Of Hyaline Cartilage:

1. Costal Cartilages which are present in the thoracic cage.
2. Cartilage of respiratory passages as in: nose, trachea, bronchi, thyroid and cricoid cartilages of the larynx.
3. Long bones of the skeleton of foetus.
4. Articular surfaces of joints (cartilage here is not covered with perichondrium).

2. Yellow Elastic Fibro-Cartilage

This type of cartilage is similar in its structure to hyaline cartilage BUT:

- a) The matrix is rich in elastic fibres which surround cartilage cells.
- b) Presence of small cell nests of chondrocytes and few collagen fibres (Type 2).
- c) This cartilage is flexible and yellow in colour due to presence of elastic fibres.



Sites Of Elastic Fibro-Cartilage

1. Ear Pinna, External Ear and Eustachian tube.
2. Epiglottis, arytenoid, corniculate and cuneiform cartilages of the larynx.

3. White Fibro-Cartilage

Characteristics Of White Fibro-Cartilage:

1. It is similar to hyaline cartilage but it is very rich in **type I collagen** fibres.
2. Its matrix is acidophilic due to presence of type I collagen fibres.
3. It has less abundant matrix.
4. It is formed of **chondrocytes** similar to those of hyaline cartilage.
5. The cartilage cells are arranged in **rows or in columns**.
6. The cartilage cells are present in a **single form** or in groups of two cells.
7. The rows of cartilage cells are separated by acidophilic **collagenous bundles**.
8. The white fibro-cartilage is **not covered by perichondrium** but it is surrounded by dense fibrous tissue rich in blood capillaries from which it is nourished.

Sites Of White Fibro-Cartilage In The Body

1. Present in the intervertebral discs.
2. In the semilunar cartilages of knee joints.
3. In the symphysis pubis, acetabulum and in the glenoid cavity.
4. In the discs between sterno-clavicular and mandibular joints.
5. In the terminal parts of the muscle tendons and in the tendon grooves.

Functions Of Cartilage

1. Cartilage helps in maintaining the patency of respiratory passages.
2. Cartilage and bone form the skeleton of the body.
3. Cartilage forms a smooth firm surface for the articular surfaces of joints.
4. Cartilage is essential for growth of bone before and after birth.
5. Cartilage and bone protect essential organs as lung, brain and bone marrow.

Growth Of Cartilage

Young cartilage can grow out by The following two different methods:

1. **Interstitial Growth:** The cartilage cells in the centre divide to form groups of young chondrocytes. These chondrocytes secrete the matrix resulting in growth of the cartilage from its centre.
2. **Appositional Growth:** The chondroblasts of the perichondrium become transformed into chondrocytes which can secrete the matrix. They cause growth of cartilage at its periphery resulting in an increase in its width.

The Intervertebral Discs

- Present between the bodies of all vertebrae.
- Formed of an outer ring of white fibro cartilage called **Annulus Fibrosus** and a central soft jelly like mass called **Nucleus Pulposus**.
- **Disc Prolapse = Herniation:** It is the disease in which separation of nucleus pulposus from annulus fibrosus occurs in the inter-vertebral disc.
- This disc prolapse cause pressure on the **Spinal nerves** which result in severe pain in the back and limbs of patients.

Bone

Bone is a calcified osteoid tissue. It is rich in blood supply. It has a solid matrix.

Functions Of Bone

- It forms the skeleton of the body.
- It protects the vital organs (as brain, heart, lungs and bone marrow).
- It acts as a reservoir for calcium.

Shape: The bones may be **Long** as the bone of limbs, **Short bone** as the bones of hand and foot, **Irregular bone** as vertebrae and **Flat bones** like skull, scapula, sternum, iliac bones and ribs.

Types Of Bone

1. **Compact or ivory solid bone** which is present in: the shafts of long bone and in the **outer thin layer** of the spongy bone in old age.
2. **Spongy or Cancellous bone** which is present in: the epiphyses of long bones, ribs, vertebrae, **flat bones** as: skull, scapula, sternum, and sacrum.

Histological Slides taken from compact bone can be prepared by two methods:

1. **Decalcified Compact Bone:** Bones are treated with nitric acid to remove their calcium. The cut bone sections are stained with **Hx** and **Eosin** to demonstrate: Periosteum, endosteum, osteocytes and bone marrow cells,
2. **Ground Compact Bone:** The dry bone is ground to demonstrate: Haversian canals, Volkman's canals, lacunae and canaliculi.

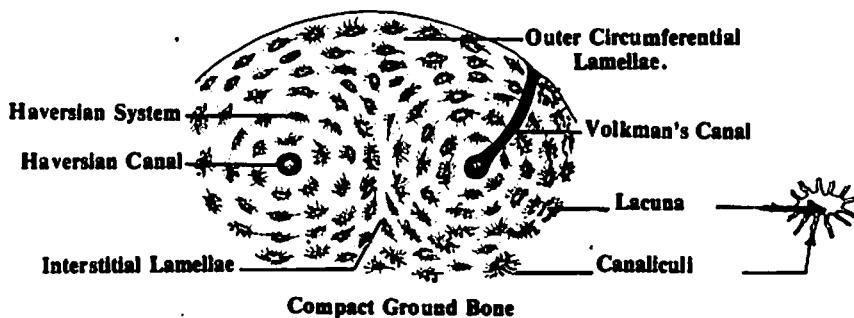
Structure Of Bone

Bone is formed of:

1. **Bone Matrix** formed of calcified lamellae of type I Collagen.
2. **Bone Cells** Which are: Osteogenic Cells, Osteoblasts, Osteocytes and Osteoclasts.
3. **Periosteum** which is the covering layer of bone from outside.
4. **Endosteum** which is the lining layer of bone from inside.

The Bone Matrix Is Formed Of:

1. **Organic Substances:** Type I collagen, glycoprotein and proteoglycans.
2. **Inorganic Substances:** Calcium phosphate, Ca carbonate and Ca citrate.



Types Of Bone Cells

There are Four Types of Bone Cells:-

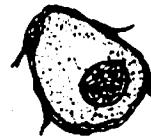
1. **Osteogenic Cells:** They can differentiate into osteoblast cells.
2. **Osteoblast Cells:** They are responsible for calcification of bones and formation of the organic materials of the bone matrix.
3. **Osteocyte Cells:** They are mature cells which maintain the bone matrix.
4. **Osteoclast Cells:** They are responsible for bone resorption during ossification.

1. Osteogenic Cells or Osteoprogenitor Cells

- Osteogenic cells develop from embryonic **mesenchymal cells** or from **pericyte** cells. They are rich in ribosomes.
- They are present in **periosteum and bone marrow cavities**.
- They are **spindle-shaped** cells with basophilic cytoplasm and flat nuclei.
- By cell modulation they change into **osteoblast cells**.
- They can divide during growth of bone and during healing of fractured bone.

2. Osteoblast Cells

Origin: They arise from osteogenic cells.



Osteoblast

- They are oval cells with eccentric rounded nuclei.
- The cell membrane has few cytoplasmic processes.
- The cytoplasm is deep basophilic.
- Around the nucleus there is an unstained area which is the space of Golgi apparatus.
- The cytoplasm is rich in RNA, endoplasmic reticulum and Golgi body.
- **Osteoblasts cannot divide, they are bone building cells.**

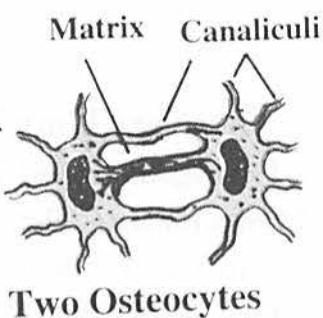
Sites: Osteoblasts are found in: **periosteum, endosteum and in bone marrow cavities.**

Functions:

1. **They synthesize the protein of bone matrix to form the osteoid tissue of bone.**
2. **Osteoblasts secrete Matrix Vesicles which are rich in these enzymes:-**
 - a) **Alkaline phosphatase enzymes** which facilitate deposition of calcium.
 - b) **Pyrophosphatase Enzymes** which inhibit the action of pyrophosphate substances (these pyrophosphates retard the process of calcification).
3. **Osteoblasts change into osteocytes** when they are surrounded by lacunae and by calcified matrix.

3. The Osteocyte

- It is a mature **non-dividing** bone cell, present inside lacuna.
- It is surrounded by calcified matrix.
- Its cytoplasm is slightly **basophilic**.
- It is rich in **phosphatase** enzymes.
- Its nucleus is **oval** and central.
- **Each cell is surrounded** by a space or **lacuna** from which canaliculi arise. The canaliculi of the neighbouring osteocytes are connected with each other.
- **Cytoplasmic Processes** of osteocytes pass through the surrounding canaliculi.
- Tissue fluids pass through the canaliculi and lacunae in order to conduct nourishment to all osteocytes and to remove the waste products from them.



E/M Of Osteocytes: Each cell contains few endoplasmic reticulum and ribosomes. Many cytoplasmic microtubules are present in their cytoplasm. The cytoplasmic processes of osteocytes are rich in actin filaments.

Origin: Osteocytes are considered as mature osteoblasts which are surrounded by calcified matrix.

Functions:

1. **They Form The Bone Matrix Vesicles:** These Vesicles are rich in enzymes which maintain the hardness of bone matrix.
2. They maintain the bone matrix by formation of its glycoproteins.

4. Osteoclast Cells

Origin: They are formed by fusion of **blood monocytes**.

- It is a large cell with irregular cell membrane.
- Each cell contains from 4 to 50 **nuclei**.
- Each cell is about **150 microns** in diameter.

Multiple Nuclei



With the E/M: Osteoclast shows **the following 4 zones:**

1. **Ruffled or striated** cell membrane rich in actin filaments.
2. **Clear Zone** under the striated part of the cell membrane.
3. **Zone of lysosomal vesicles**.
4. **Basal zone** of cytoplasm which contains the nuclei, cell organelles and cell inclusions.
 - The cytoplasm of osteoclast is **foamy acidophilic** and is rich in acid phosphatase enzymes, with many lysosomes, mitochondria and vesicles.
 - Osteoclasts secrete osteolytic enzymes which destroy bone matrix, therefore, they are surrounded by spaces called "**Howship's lacunae**".
 - **Sites:** They are present in bone marrow cavities and endosteum of bone.

Functions Of Osteoclasts

1. They are concerned in bone resorption during ossification.
2. They secrete **Enzymes** that dissolve bone matrix during ossification.
3. They secrete **acids** which play a role in decalcification of bone matrix.
4. They remove bone debris during ossification. They are bone eating cells.

Microscopic Structure Of Compact Bone

– Transverse section in the shaft of adult long bone is formed of:

1. **Haversian Systems** or osteons.
2. **Interstitial lamellae** between Haversian systems.
3. **Outer and Inner circumferential lamellae** under periosteum and endosteum.
4. **Periosteum**: cover the bone.
5. **Endosteum**: line the bone.

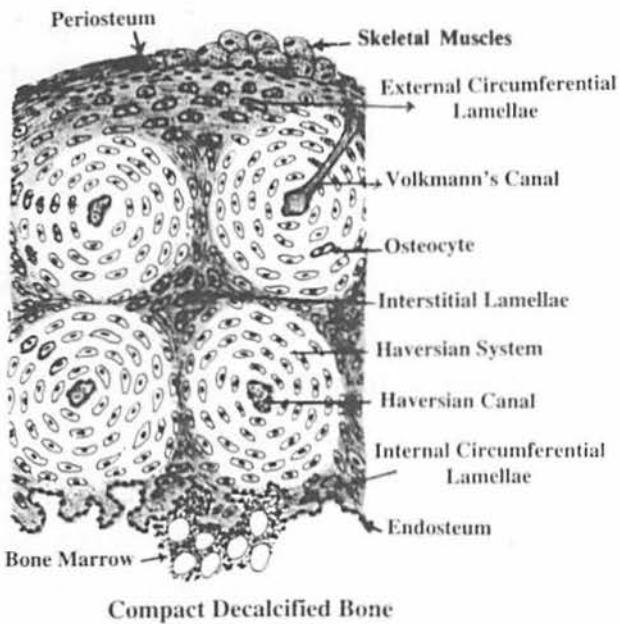
The Periosteum

- It is a vascular C.T. membrane.
- It is formed of two layers:-

- a) **Outer fibrous layer** which is formed of collagenous fibres, fibroblast and fibrocyte cells, nerve fibres and blood vessels.
- b) **Inner osteogenic layer** which is formed of osteogenic spindle-shaped cells.

Functions of periosteum:

- It provides an attachment for muscles, tendons and ligaments.
- It provides the bone with blood supply and nourishment.
- It is important for formation of bone during its growth and after its fracture.



Compact Decalcified Bone

The Endosteum

- It lines the internal surface of bone, bone marrow cavities and Haversian canals.
- It is formed of a vascular C.T. membrane rich in osteogenic cells, osteoblast and osteoclast cells.

Functions Of Endosteum:

1. It supplies bone with blood supply and nutrition.
2. Its osteogenic cells, osteoblast cells and osteoclast cells are concerned with bone formation during growth of bone.

Volkmann's Canals

- These are transverse or oblique canals. They connect the Haversian canals together.
- They also connect the Haversian canals with the periosteum or endosteum.
- They are lined by endosteum and contain blood vessels.

The Perforating Fibres Of Sharpy.

These are calcified collagenous bundles which arise from the deep surface of the periosteum to be embedded like nails into the bone. They are present at the sites of attachments of tendons and ligaments of muscles to fix them more into the bone.

The Haversian System Or Osteon

- It is the structural unit of compact bone.

It is formed of:-

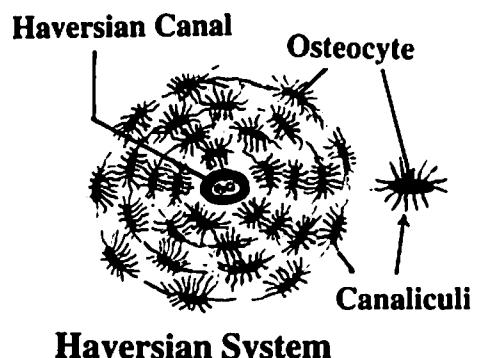
- a) **Haversian Canal:** It runs parallel to bone.

It contains C.T, B.V. and osteogenic cells.

- b) **Concentric Bone Lamellae:** formed of 4 to 20 layers of bone lamellae.

Osteocytes are present between these lamellae.

- c) **Osteocytes:** These are the mature bone cells which are present inside their lacunae. From these lacunae, canaliculi arise. Cytoplasmic processes of the osteocytes pass through these canaliculi to be connected with the processes of other osteocytes.



The External Circumferential Lamellae:-

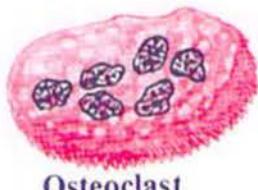
These lamellae are formed of calcified osteoid tissue in which osteocytes are embedded. They are present under the periosteum and are arranged parallel to it.

The Internal Circumferential Lamellae:-

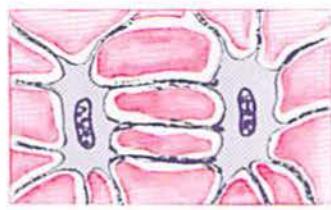
These lamellae are formed of calcified osteoid tissue present adjacent to the endosteum. Osteocytes are embedded in these lamellae and are arranged parallel to the endosteum.

The Interstitial Or The Inter Haversian Lamellae:-

These are formed of calcified osteoid tissue present between the Haversian systems. Osteocytes in these interstitial lamellae are irregularly arranged.



Osteoclast



Osteocytes



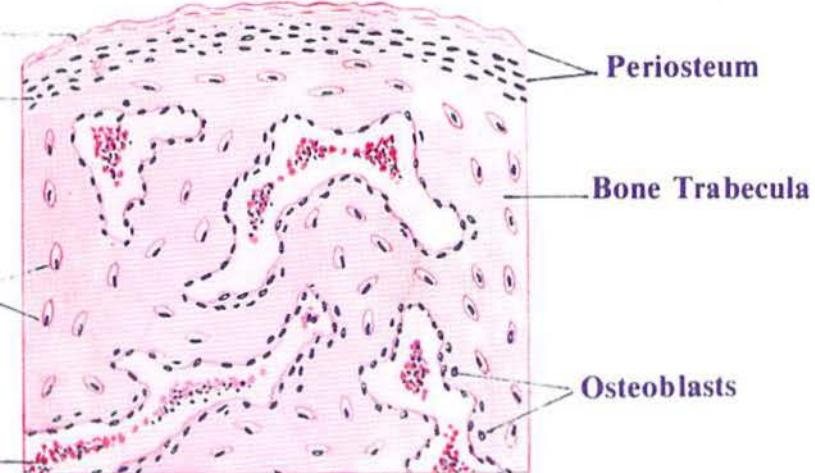
Osteogenic Cell
Osteoblast

Outer Fibrous Layer

Inner Osteogenic Layer

Osteocytes

Bone Marrow



Spongy (Cancellous) Bone

Resting Cartilage

Proliferating Cartilage

Hypertrophied Cartilage

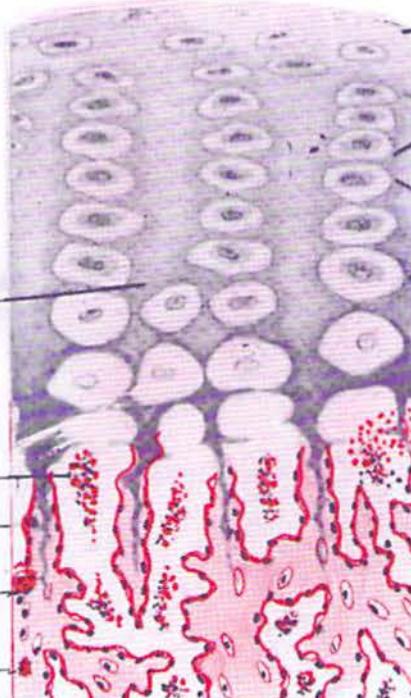
Calcifying Cartilage

Bone Marrow

Osteoblast

Osteoclast

Osteocyte



Invasion

Bone Trabecula

Spongy Bone

Zone Of Ossification

Intracartilaginous Ossification

Zakaria

[Plate 7]



Spongy Or Cancellous Bone

- The long and short bones are formed externally of compact bone, but their endosteums are irregular due to presence of **spongy bone**.
- **Cancellous Bone looks spongy**, with many vascular channels (See Plat7).
- It is formed of irregular bars or plates of bone separating between them multiple **bone marrow cavities** which are rich in blood vessels.
- The multiple bone marrow cavities are filled with **active red bone marrow**.
- **Sites of Spongy Bone:** In the centers of: vertebrae, ribs, flat bones as: skull, scapula, sternum and in the centre of the epiphyses of long bones.

Differences Between Cartilage And Bone

Bone	Cartilage
<ol style="list-style-type: none">1. It is a solid inflexible tissue.2. There are 2 types of bone: compact and spongy (cancellous).3. It has a solid matrix rich in calcium. type 1 collagen and osteocalcin.4. Bone cells (osteocytes) are present singly inside lacunae.5. Osteocytes intercommunicate by the canaliculi arising from their lacunae.6. Bone is a vascular tissue, its haversian canals, Volkmann's canals and the canaliculi carry blood to all parts of bone.7. Osteocytes cannot divide.	<ol style="list-style-type: none">1. It is a rigid flexible tissue.2. There are 3 types of cartilage: Hyaline, elastic and white fibro cartilage.3. It has a rigid matrix rich in chondroitin sulphate and hyaluronic acid.4. Cartilage cells (chondrocytes) are present singly or in groups (cell nests).5. Chondrocytes do not communicate because there are no canaliculi.6. Cartilage is a none - vascular tissue but its chondrocytes receive nourishment from B.V of the perichondrium.7. Chondrocytes can divide.

Ossification

Ossification is the process of formation of bone which leads to its growth . There are two methods for bone development or bone ossification:

- 1.**Intramembranous**
2. **Intracartilagenous.**

Intramembranous Ossification, occurs in Mesenchymal Membranes.

Intracartilagenous Ossification, occurs in cartilage models.

Mechanism of Ossification: Bone development occurs as a result of the following two processes: **Bone Formation and Bone Resorption**.

(1) Intramembranous Ossification

It occurs in: Flat bones of the face, skull and also in the clavicle.

The site of the future bone is occupied by a **mesenchymal membrane** which is formed of matrix, blood capillaries and mesenchymal cells. This membrane is transformed into spongy bone **through the following steps:**

1. A **centre of ossification** appears in the middle of the mesenchymal membrane. At this centre, the blood supply increases and the mesenchymal cells are transformed into **osteogenic cells** which are then transformed into **osteoblasts**.
2. The newly formed osteoblasts synthesize the organic components of the matrix. They are rich in phosphatase enzymes which can deposit calcium on the newly formed matrix forming trabeculae of calcified osteoid tissue. The osteoblasts which are now surrounded by a solid matrix are then transformed into **osteocytes**. Fusion of blood monocytes form **osteoclast cells**.
3. The trabeculae of the newly-formed spongy bone extend from the centre of ossification outwards in a radial manner.
4. The **osteogenic cells** of the outer and inner surfaces will form the periosteum and the endosteum of spongy bone.
5. **Growth and remodelling** of bone occurs by deposition of new bone by the osteoblasts and resorption of irregular bone by osteoclasts.

(2) Intracartilagenous Ossification

This type of ossification occurs in the long bones which were originally formed of **hyaline cartilage** in the foetus. These cartilage models will be replaced by bone.

Ossification starts as **primary centre of ossification** in the middle part of the long bone (**at its Diaphysis**). Then **secondary centres of ossification appear at both ends of long bone (at its Epiphysis)**.

The epiphyseal disc and the part of the diaphysis near to it are called the **Growing Zone**; If we examine a longitudinal section in the growing end of a long bone, we can demonstrate the different stages of intracartilagenous ossification.

Stages Of Intracartilagenous Ossification

The following steps are the stages of **replacement** of Hyaline cartilage by **Compact bone**. The growing zone of the future bone shows the **following stages**: (See plate 7).

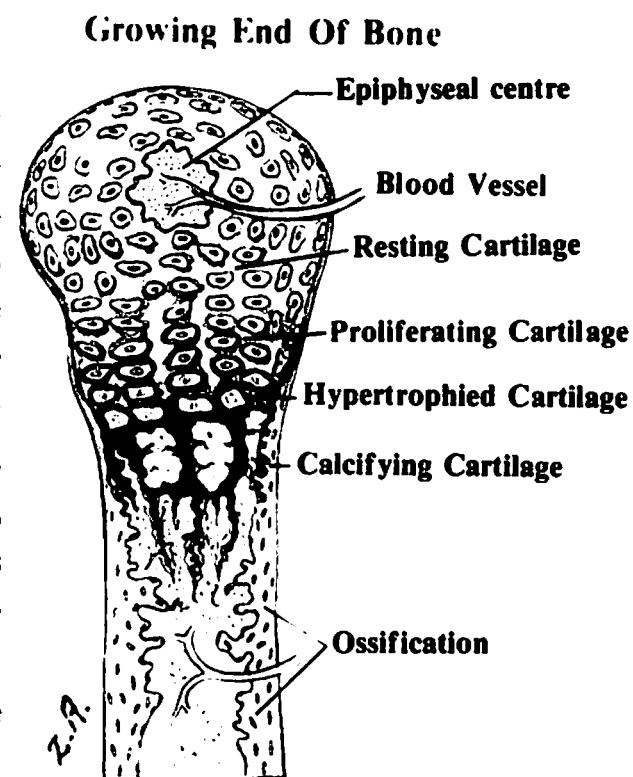
1. Resting stage of hyaline cartilage which is present in the region of the growing zone of the long bone. It is formed of cartilage cells embedded in their matrix. This growing zone acts as reserve area for the next stages.

2. **Proliferative stage of cartilage cells** or stage of increase in number of young cartilage cells. The chondrocytes divide to give many small chondrocytes, which will be arranged in rows.
3. **Maturation or hypertrophy stage of cartilage Cells:** The small chondrocytes grow in size and become mature cells.
4. **Calcification stage of cartilage:** The alkaline phosphatase enzyme in the mature cartilage cells deposit calcium phosphate and carbonate in the matrix. At the same time, some of the osteogenic cells under the perichondrium change into osteoblasts which can form a layer of calcified tissue around the perichondrium forming **Periosteal Collar**. The calcified matrix around the cartilage cells as well as the collar of calcified tissue under the perichondrium will prevent nutrition and blood supply to reach to the central mature cartilage cells which will then die. Death of the mature cartilage cells will result in appearance of empty spaces which are separated from each other by thin trabeculae of calcified matrix.

5. Stage of invasion of the previous empty spaces by **vascular mesenchymal** tissue which is rich in B.V. and osteogenic cells. Some blood monocytes change into osteoclasts which form a hole through which the mesenchymal cells and B.V. (**Vascular Bud**) will proceed to fill the empty spaces. Now the dead cartilage cells are replaced by blood capillaries, osteogenic cells, blood monocytes and mesenchymal cells. These invading cells can be changed into: osteoblasts, osteoclasts and bone marrow cells.

6. Stage of sponge bone formation:

Some osteogenic cells which are now filling the central empty spaces can be changed into osteoblasts. These osteoblasts start to form the trabeculae of spongy bone by depositing calcium to form the calcified trabeculae of spongy bone.



Cartilagenous Ossification

7. Stage of internal reconstruction or stage of Remodelling:

It is the process by which spongy bone is transformed into compact bone. Some blood monocytes change into osteoclasts, these osteoclasts will destroy the central irregularities of the spongy bone forming regular endosteum.

8. Stage of complete ossification: The Haversian systems are formed as follows:

The osteoblasts will arrange themselves concentrically around B.V. taking from them calcium and nutrition. Osteoblasts by this way can form concentric calcified bone lamellae around the central B.V. This formed longitudinal canal around B.V. is now called **Haversian canal**. This process goes on several times until mature Haversian systems are formed.

Facts about ossification:

Ossification goes on at both ends of the long bone but two parts of the epiphysis are not ossified and remain cartilagenous for a certain period of life; these two parts are:

- a) **The articular surfaces of joints.** (remain as such through-out life).
- b) **The epiphyseal discs** between the ends of bone and their shaft. These epiphyseal discs remain as cartilage during the growth of bones, their cartilage cells divide and give new daughter small cells resulting in an increase in the length of the shaft from its both ends. This process continues until the epiphyseal discs disappear at a specific age (16-20 years).

Growth of Bone in Length: Bones grow in length by the proliferation of more cartilage cells at both epiphyseal discs.

Growth of Bone in Width: Bones grow in width (diameter) by deposition of subperiosteal bone under the periosteum.

Growth of bone is affected by: Genes, Hormones, and Nutrition.

Joints Of Bone In the Body Are Classified Into:

1. Synarthrosis Joints: They have little degree of movement as in symphysis pubis and in the joint of the first rib.

2. Diarthrosis Joints with free movements as in all synovial joints of the body. The **Synovial Joint** is formed of an outer fibrous **capsule** and an inner **synovial membrane** which is formed of cubical cells which secrete **synovial fluid** rich in hyaluronic acid.

Muscular Tissue

There are three types of muscles:

1. Smooth
2. Skeletal
3. Cardiac

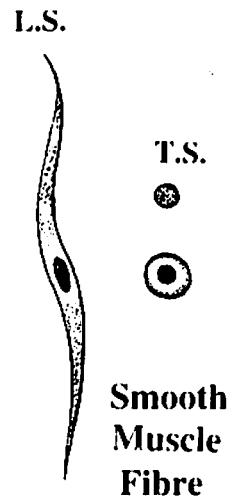
General Characteristics of Muscles.

- The structural and functional units of muscles are formed of special elongated cells known as **muscle fibres**.
- The **cell membrane** of these muscle fibres is known as **sarcolemma**.
- The **cytoplasm** of these muscle fibres is known as **sarcoplasm**.
- The **sarcoplasm** contains all cell organoids and cell inclusions.
- The **cytoplasm** is rich in: fat, glycogen, pigments, mitochondria, and **myofibrils**.
- **Myofibrils** are responsible for muscle **contractions**.
- The muscle fibres may have **transverse striations** as the skeletal and cardiac muscle fibres, or they may show **no striations** as the plain or smooth muscles.

1. Smooth Muscles

Characteristics of smooth or plain or involuntary muscles:

- Smooth muscles are covered by **thin sarcolemma**
- **Dense Bodies** are present under the sarcolemma.
- Smooth Muscles are arranged singly as in skin
- They are arranged in layers as in the wall of stomach.
- They are spindle-shaped **non-striated** cells.
- Their cytoplasm is acidophilic rich in mitochondria. Golgi body, ribosomes and glycogen.
- Their cytoplasm is poor in **granular endoplasmic reticulum**.
- They have no **satellite cells** outside their sarcolemma.
- The **nucleus** is single, oval and is central in position.
- The **cytoplasm** contains **longitudinal myofibrils**.
- The **myofibrils** of the cytoplasm are of three types: **Actin, Myosin and Intermediate** filaments. The intermediate filaments are of 2 types: **Dysmin and Vimentin Filaments**.
- **Contraction** of smooth muscles starts by gliding of myosin filaments over the actin filaments. Then, the actin filaments pull on the intermediate filaments and both pull on the dense bodies. This cause twisting and shortening of muscles.
- Smooth muscles have **no triad of the T-tubular system**.
- Smooth muscles can form collagen, elastin and proteoglycans.
- The length of a smooth muscle ranges from 30 microns as in the wall of B.V. up to 500 microns as in pregnant uterus.



Smooth Muscle Fibre

- The diameter of each smooth muscle fibre ranges from 4 to 10 microns.
- All smooth muscles originate from the mesoderm except: the muscles of the iris and the myoepithelial cells around the acini of certain glands which are ectodermal in origin.
- Smooth muscles are involuntary in action. They are innervated with sympathetic and parasympathetic nerves.
- The number and size of smooth muscle fibres may increase during life as in pregnant uterus and in certain arteris. Smooth muscles regenerate from Pericytes.
- Smooth Muscles Replacement occurs by division of healthy smooth muscles Formation of new smooth muscles occurs also through modification and changes of the Pericyte Cells (present around blood vessels) .
- All smooth muscles are involuntary except the ciliary muscles of the eye and special muscles in the urinary bladder which are partially voluntary.

Sites Of Smooth Muscles

1. **Digestive System:** Muscles in the wall of the lower third of oesophagus, the wall of stomach, intestine, gall bladder, salivary and pancreatic ducts.
2. **Respiratory system:** Wall of trachea, bronchi and bronchioles.
3. **Urinary system:** Wall of ureter, urinary bladder and urethra.
4. **Male genital system:** Epididymis, vas deferens, prostate and penis.
5. **Female genital system:** Fallopian tube, uterus and vagina.
6. **All the media** (middle part) of blood and lymph vessels.
7. **Capsule of glands and of spleen.**
8. **In the eye:** in the ciliary muscles and iris.
9. **In the skin:** As the arrector pili muscles of the hairy skin.

2. Skeletal Muscles

Sites: The skeletal muscles are attached to the skeleton: They form the muscles of the limbs, neck and trunk. They are present also in: the diaphragm, tongue, muscles of the face, external muscles of the eye ball, pharynx and upper third of oesophagus.

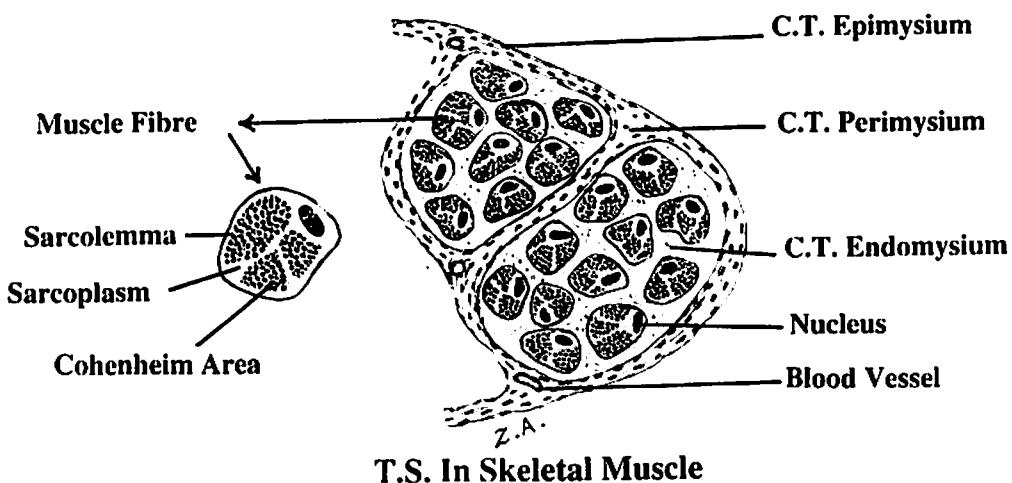
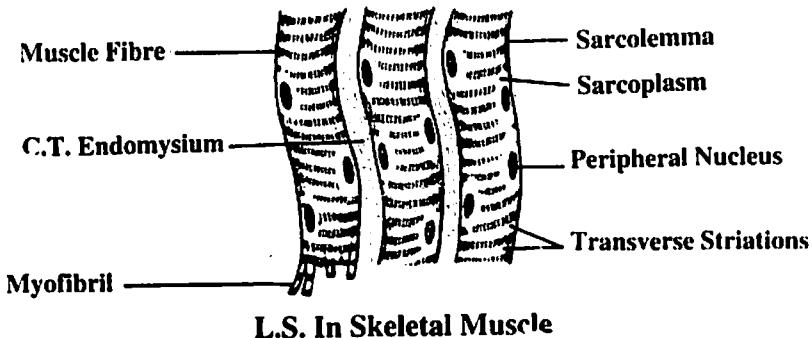
Skeletal muscles are voluntary muscles except those in: the upper third of oesophagus, some muscles of the pharynx and the cremasteric muscles of the spermatic cord.

Connective Tissue Around Muscle Fibres And Muscle Bundles:

If we cut a section in skeletal muscle, we can see the C.T. fascia or the epimysium around the whole muscle. The perimysium is the C.T. septa between

the muscle bundles, while each muscle fibre is surrounded by C.T. endomysium.

In the connective tissue of the muscles, B.V., nerves and lymph vessels are present. C.T. also firmly attach the muscle bundles together.

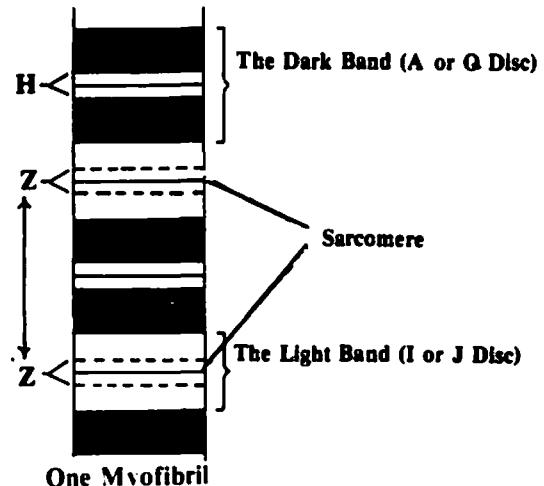


Characteristics Of Skeletal Muscles:

- Skeletal muscles are attached to bone forming the muscles of limbs, abdomen, head, neck, face, eye ball, diaphragm and tongue.
- They are formed of **striated muscle fibres**. Each muscle fibre is a single cell which varies in length from 1mm up to 40 mm.
- The muscle fibres **do not branch** except in the tongue and face muscles.
- Each muscle fibre is a multinucleated cell, it has many rod - like nuclei.
- The cell membrane of the muscle fibre is known as **Sarcolemma**.
- The Nuclei are **peripheral** in position, present under the sarcolemma.
- The cytoplasm of the muscle fibre is known as **Sarcoplasm**.
- The sarcoplasm is acidophilic rich in glycogen and myoglobin.
- The myoglobin is formed of pigmented protein.
- The sarcoplasm (cytoplasm) contains many ribosomes, many mitochondria and many smooth endoplasmic reticulum which is called **Sarcoplasmic Reticulum**.
- The sarcoplasm contains also longitudinal fibrils known as **Myofibrils** or **Sarcostyles**.

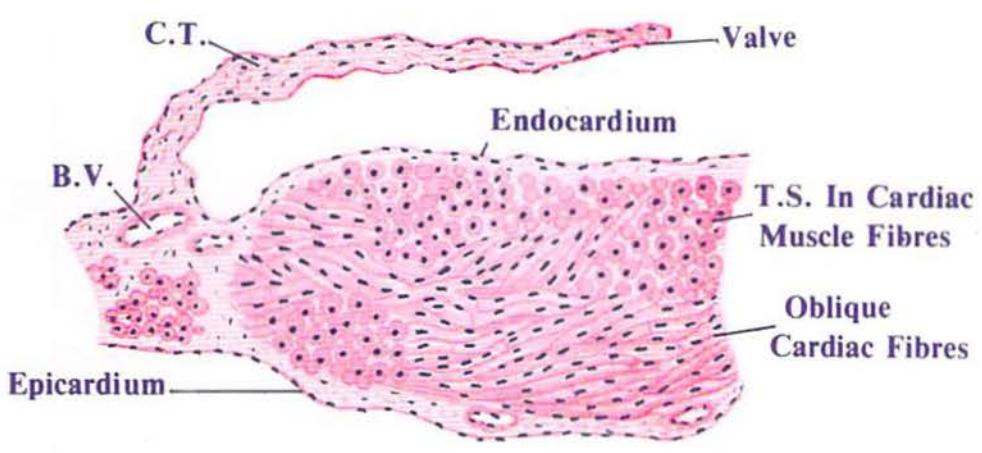
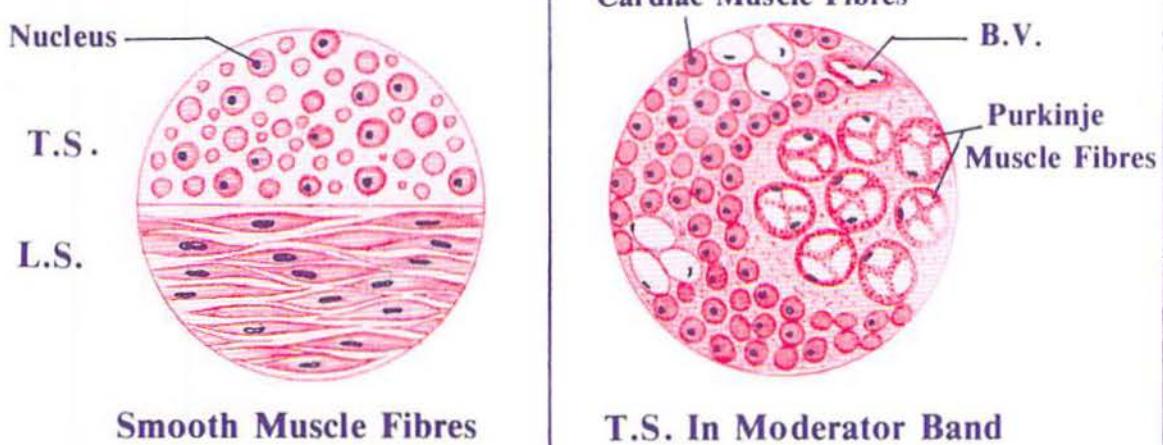
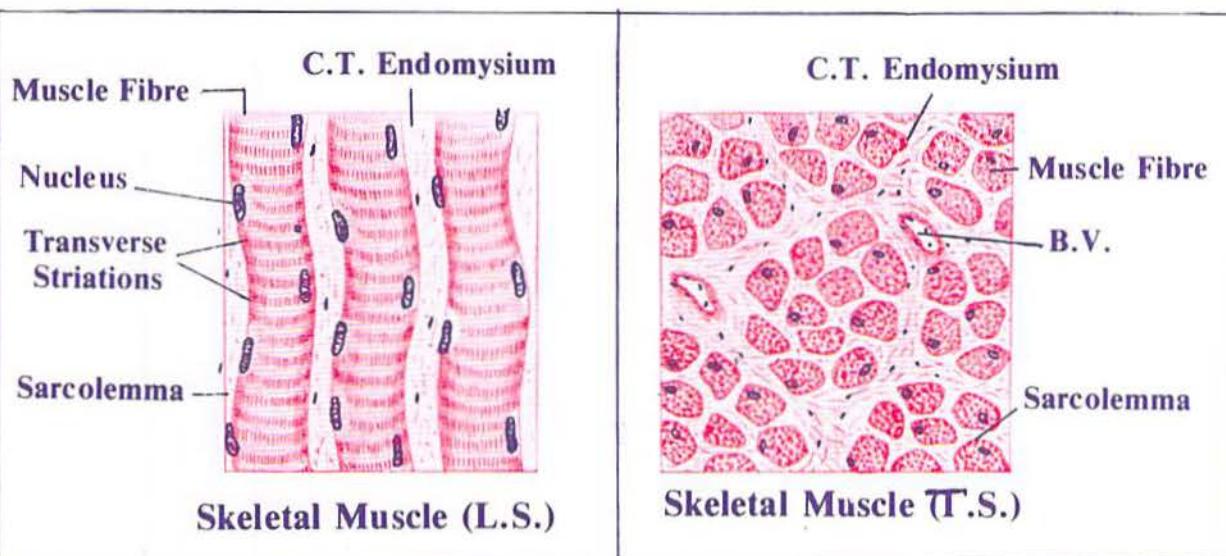
The Myofibrils Of Skeletal Muscles

- The myofibrils are the contractile fibrils which are arranged longitudinally in the sarcoplasm of each muscle fibre.
- The arrangement of myofibrils near each other shows transverse striations.
- The transverse striations in the muscle fibres are due to presence of alternating dark and light bands on each myofibril.
- Each dark band of one myofibril is present beside the dark band of the adjacent myofibril. This arrangement of dark and light bands is the cause of transverse striations.
- The dark bands: They do not reflect light equally. They are called Anisotropic bands or A-Bands.
- The light bands: They reflect light equally. They are called Isotropic bands or I-Bands.
- Each dark band is further subdivided by a pale area in its centre called Hensen's zone or H-Disc.
- Each light band is also further subdivided by a darkly-stained zone present at its center and is called Z-Disc= Z-Zone or Z-line.



The Sarcomere

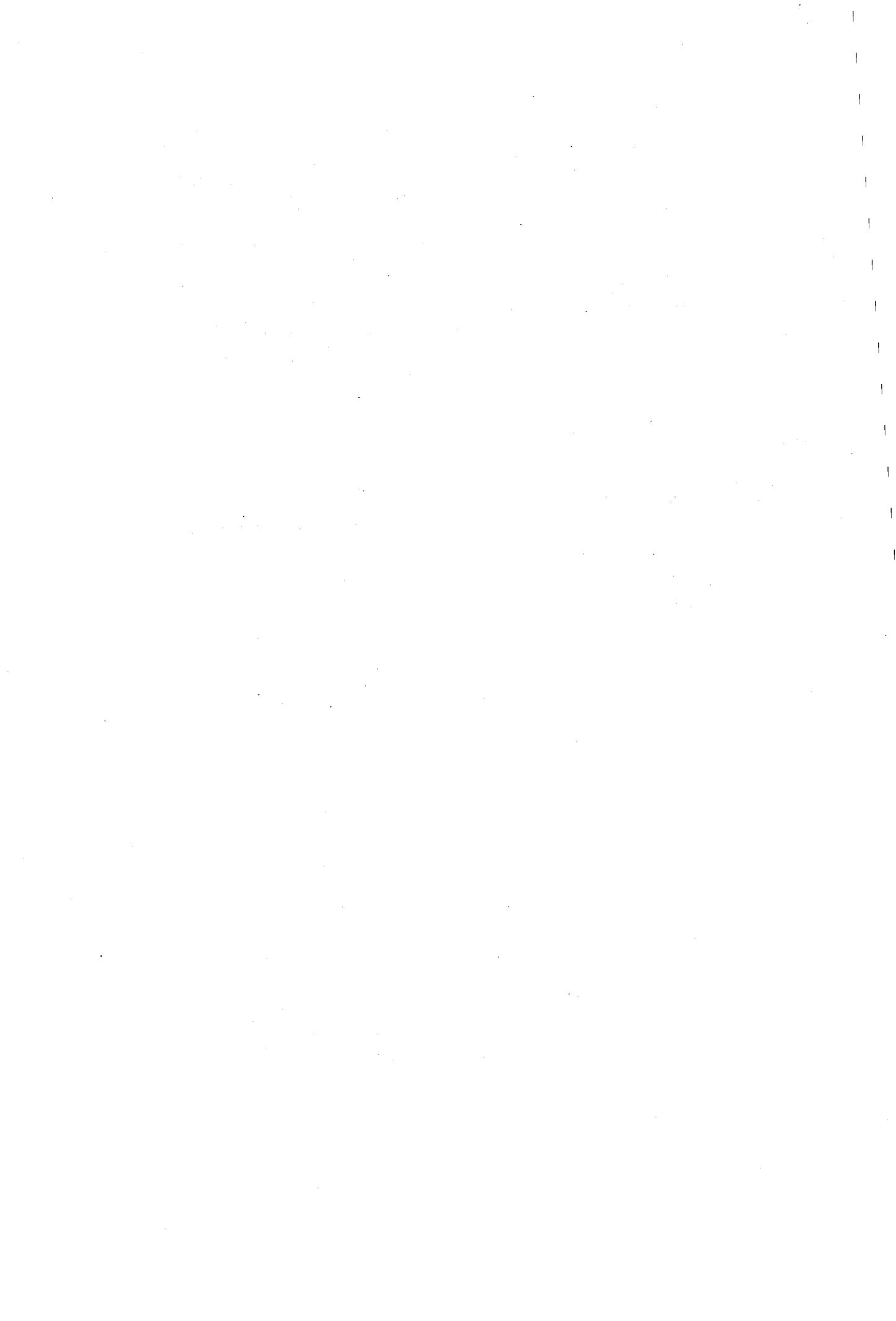
- The area of the muscle fibre enclosed between two-Z-Discs is called Sarcomere.
 - The sarcomeres are the functional contractile units of the muscle fibre.
 - Each Sarcomere includes the whole dark band and the two halves of the two light bands on both sides.
 - The sarcomeres of each muscle fibre contract and relax as one unit. Their contractions are due to the presence of longitudinally arranged very fine electron microscopic filaments known as Myofilaments.
 - The Myofilaments are of 2 types: Thin and Thick Myofilaments.
1. Thin Filaments or Actin filaments are formed of the Following proteins: Actin, Troponin and Tropomyosin, They extend from the Z line till the middle of the dark band (They terminate just before, the middle of the dark band therefore, the middle of the dark band appears light and is called H-zone).



Wall Of Heart (Cardiac Muscle And Valve)

Zakaria

[Plate 8]



2. Thick Filaments or Myosin
filaments which are formed of protein known as **Myosin**. They extend in the **dark bands only**.

Each myosin molecule has a head called **Heavy Meromyosin** and a tail called **Light Meromyosin**.

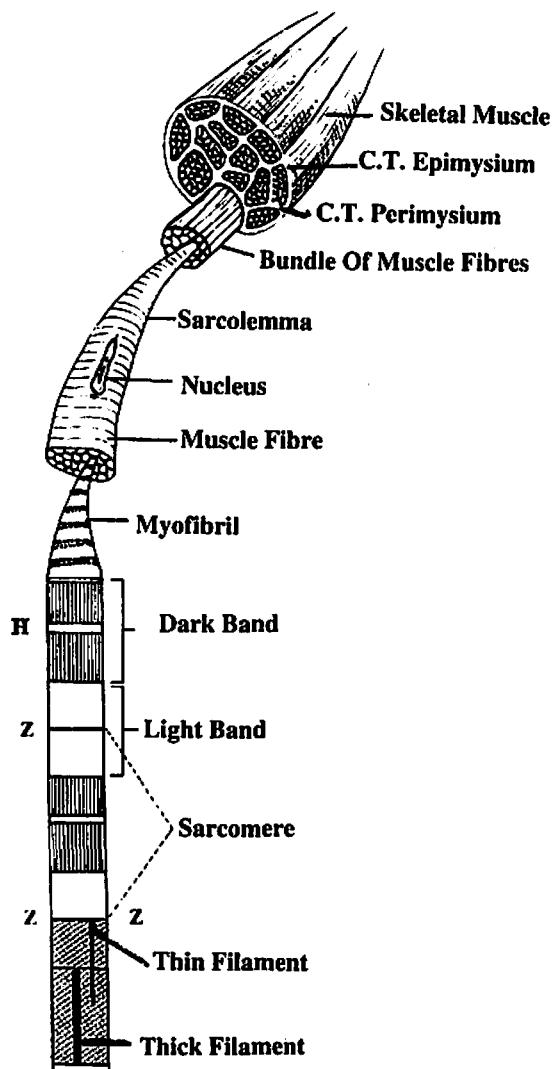
Both ends of the thick filament are free, while the thin filament has only one free end and the other end is attached to the **Z-line**.

N.B The dark band, therefore, appears darker because it contains the two types of filaments (the thick and thin filaments). The light band appears light, because it contains one type of filaments (the thin filaments).

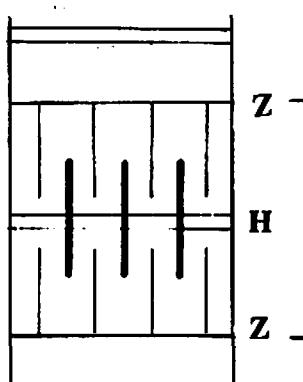
Contraction Of Muscles

When a nerve impulse reaches the muscle, acetylcholine is released at its motor-end plate. Acetylcholine cause depolarization of sarcolemma and T-tubules.

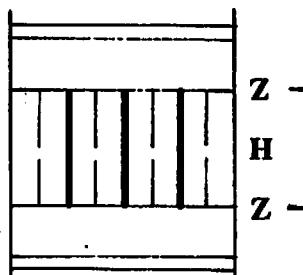
Depolarization of T-tubules causes release of calcium ions from the sarcoplasmic reticulum. The released calcium causes gliding of the thin filaments over the thick filaments. The thin filaments thus slide towards the middle of the sarcomere. This will result in pulling the two Z-lines behind them during contraction. During relaxation, calcium ions return again to the sarcoplasmic reticulum.



Structure Of Skeletal Muscle



Sarcomere During Relaxation



Sarcomere During Contraction

Electron Microscopic Structure Of Sarcolemma

The Triad of Tubular System

- The sarcolemma is the cell membrane of a muscle cell (muscle fibre).
- It plays an important role in conducting the wave of excitation to the myofibrils through the presence of three types of tubules called The Triad of Tubular System.

The Triad Of Tubular System
Includes: One Transverse T. Tubule Surrounded By Two Sarcoplasmic Tubules:

1. **The T-Tubule:** It is a transverse tubule which runs transversely in the muscle fibre. These T-tubules encircle the myofibrils like collars.
- **The T-tubules** are formed by invagination of the sarcolemma. They extend transversely through the sarcoplasm. The cavity of each T-tubule is continuous with the exterior.
2. **Two Sarcoplasmic Tubules:** These tubules are the modified longitudinal parts of the smooth endoplasmic reticulum of each muscle fibre.
- They run transversely in each muscle fibre and each two sarcoplasmic tubules surround **one transverse T-tubule**. The three tubules (one T-tubule and the surrounding two sarcoplasmic tubules) are called **triad tubular system**.

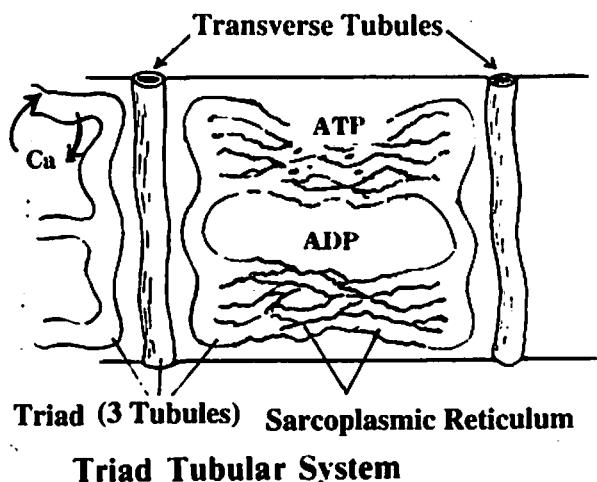
The Role of Tubular System in Muscular Contractions:

- The T-tubules and the surrounding Two Sarcoplasmic Tubules control muscular contractions by regulating the concentration of calcium ions within the myofibrils of skeletal muscles. Calcium ions facilitate the interaction between actin and myosin filaments.

Types of Skeletal Muscle Fibres

Muscles contain pigmented protein called **myoglobin**. Myoglobin is red in colour similar to haemoglobin of RBCS.

According to the amount of **myoglobin**, the type of innervation and the mode of contraction, the muscle fibres of skeletal muscles are classified into:



- Type I: Red Muscle Fibres:** They have large amounts of myoglobin, mitochondria and cytochrome. They have **small diameters**. They can sustain contraction for a long time without fatigue. Their energy is derived from oxidation of fatty acids.
- Type II: White Muscle Fibres:** They have small amounts of myoglobin and few mitochondria. They have **wide diameters**. Their contractions are quick, but they become fatigued easily. Their energy is derived from glycolysis.
- Type III Intermediate Muscle Fibres:** They have intermediate characters between red and white fibres.

N.B.: Human Muscles contain the three types of muscle fibres.

Cohenheim's Areas: These are formed by the collections of myofibrils inside the sarcoplasm forming groups of myofibrils separated with the sarcoplasm.

Development and Regeneration of Skeletal Muscles

In the embryo muscle fibres develop from **Mesodermal Myoblast Cells**.

In adults, they regenerate from satellite cells present **outside** the sarcolemma. **Growth of muscles and repair of torn muscles** occur by the proliferation of **the satellite cells** which are stem cells present outside the sarcolemma and can differentiate into myoblast cells then into new muscle fibres.

Changes at the Musculo-Tendonous Junctions:

- The C.T. epimysium, perimysium, and the sarcolemma are firmly attached and continuous with the C.T. of the tendon.
- The muscle fibres stop abruptly at the junction of the muscle with its tendon.

3. Cardiac Muscles

The heart is formed of two thin atria and two thick ventricles. **The cardiac muscle** forms the main wall of the heart and is known as **myocardium**.

The wall of the heart is formed of the following 3 layers:

1. Epicardium 2. Myocardium 3. Endocardium

1.The Epicardium: It is the visceral layer of the pericardium. **It is a serous membrane formed of: Simple squamous epithelium and a layer of C.T.** which contains; fat cells and the branches of the coronary vessels.

2.The Endocardium which lines the heart from inside. It is formed of the following four layers from inside outwards:

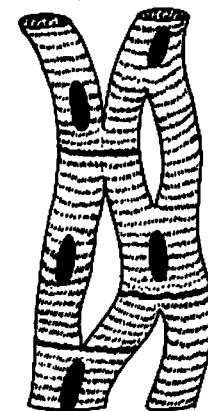
- Simple squamous endothelial cells joined together by tight junctions.**
- Subendothelial layer of loose connective tissue.**

- c) Dense elastic and collagenous membranes.
 - d) Loose C.T. layer containing blood capillaries and Purkinje muscle fibres.
- 3. The Myocardium:** It forms the main walls of the heart. It is formed of continuous joined chains of cardiac muscle fibres.

Characteristics Of Cardiac Muscle Fibres

Cardiac Muscle Fibres are formed of individual muscle cells joined together end to end by cell junctions. The fibres are surrounded by connective tissue **endomysium** which contains blood capillaries and lymphatics.

- Cardiac muscle fibres have **small diameters**.
- They branch and join each other forming a **continuous sheet**.
- They contract spontaneously (**involuntary** in action).
- **Striation:** They have **irregular** striations.
- **Nuclei are large, central** in position and **oval** in shape. Most of the cardiac cells contain **one nucleus**, but some of them may have two nuclei.
- **The Sarcolemma:** It is the covering cell membrane of muscle fibres, it is **thin**.
- **The Cytoplasm:** It is granular acidophilic sarcoplasm and is **rich in:** glycogen, mitochondria and **lipochrome granules**. These lipochrome granules increase in number in **old age** as well as in brown atrophy of the heart (Aging Granules).



Cardiac Muscle Fibres

E/M Picture of the Cardiac Muscle Fibres:

- They are rich in myofibrils which are of variable diameters.
- The myofibrils branch and anastomose with each other.
- The myofibrils are surrounded with many mitochondria, glycogen granules, lipid droplets and with many Golgi saccules.
- **Cardiac Muscle Fibres** are characterized by the presence of a **Diad System** instead of the presence of a **triad system**.
- **The Diad System** is formed of one transverse T-tubule surrounded with **One** tubule of the endoplasmic reticulum. **The T-diad Tubules** are present at the level of Z-lines
- The cardiac muscle fibres are traversed at intervals by **dark staining discs** which extend across the fibres and are called **Intercalated Discs**.

The Intercalated Discs

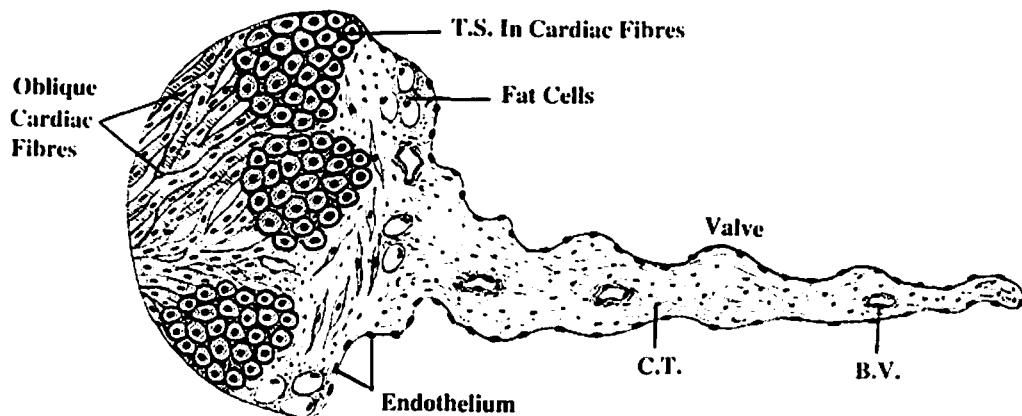
- Individual cardiac muscle fibres are composed of several elongated cells.
- Each cell has a central nucleus, therefore, the cytoplasm of the cardiac muscle fibres is not syncytium (the cytoplasm of each cell is isolated from the other).
- The cardiac muscle fibres are joined end to end by the intercalated discs.
- These discs are cell membranes, they prevent cytoplasmic continuity between the different segments. They are present at the level of Z-lines of cardiac fibres.
- Each Disc has longitudinal and transverse portions (Stepwise).
- There are three types of junctional complex at the intercalated discs which are:
 1. Desmosomal junction, to prevent separation of cardiac muscle cells.
 2. Adherens junction, to connect myofibrils of cardiac muscle cells.
 3. Gap junction, to transmit impulses to all cardiac muscle cells.
- Cardiac muscles of the ventricles are larger in diameter than those of the atria.
- More T-diad system are present in the atrial than in the ventricular muscles.
- The atrial muscle fibres secrete Atrial Natriuretic Diuretic Factor which regulates the electrolytes and can lower the blood pressure.

N. B.: Cardiac muscle fibres have no satellite cell, they cannot divide, nor regenerate after injury. They heal by fibrous tissue.

Cardiac Muscles are mesodermal in origin. They are innervated by autonomic nervous system and are involuntary in action following "the all or non law". They have the ability to undergo rhythmic contraction.

Valves of The Heart are formed of dense C.T. rich in elastic and collagenous fibres and are covered by simple squamous endothelium. Phagocytic histiocyte cells are present in its C.T. to engulf micro-organisms.

The Fibrous Skeleton Of the Heart is formed by dense fibrous tissue. It is present at the junctions of the two atria with the two ventricles. Cardiae muscles and valves are attached to this fibrous skeleton.



Cardiac Muscle And Valve

The Conducting System Of The Heart

It is formed of modified cardiac muscle cells that are specialized to generate and to conduct cardiac impulses to all heart muscles.

The Conducting System Of The Heart Consists of:

1. Sino - atrial node in the right atrium. It is the pace maker of the heart.
2. Atrio - ventricular node present in the inter - atrial septum.
3. Atrio - ventricular bundle of His: It branches into right and left bundles.
4. Right and left bundle branches: The right branch is called Moderator Band.

Each of The previous parts of The conducting system is formed of:

- Cardiac muscle fibres with few myofibrils and many mitochondria.
- They are surrounded with vascular connective tissue.
- Nerve fibres are present between these muscle fibres.

The Moderator Band

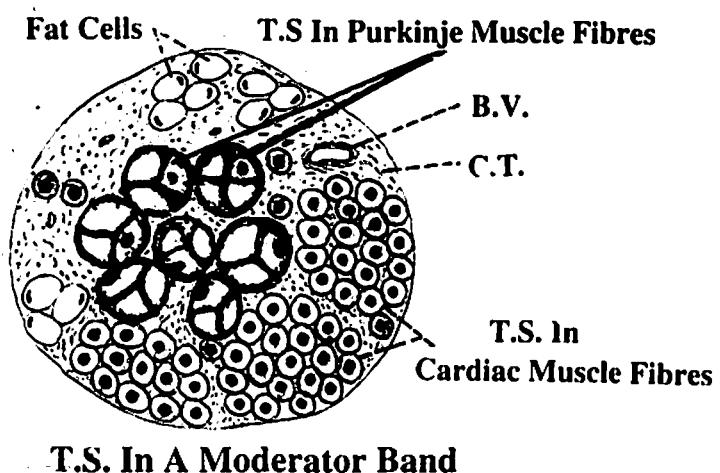
It is a bundle of cardiac muscle fibres through which the right branch of the atrio - ventricular bundle traverses the cavity of the right ventricle to reach the lateral wall of the heart. It is well - developed in the heart of the sheep.

The Moderator Band is formed of:

Cardial muscle bundles, some fat cells, blood capillaries, Purkinje Muscle Fibres and bundles of nerve fibres. Delicate branches from the nerve fibres come in contact with the Purkinje muscle fibres, but nerve cells are not present in the moderator band.

Characteristics Of Purkinje Muscle Fibres

- The atrio - ventricular bundle and its branches are composed of elongated cells called Purkinje cardiac muscle fibres.
- These Purkinje fibres branch in the ventricular wall under the endocardium transmitting the cardiac impulses 5 times faster than the cardiac muscle fibres.



- They are **larger in diameter** than the cardiac fibres.
- They are **paler in colour** than the cardiac fibres.
- They are usually **grouped into bundles** which are surrounded by C.T. sheath.
- **Each Purkinje fibre is formed of separate, short, thick, elongated cylindrical cells.**
- **The sarcolemma of Purkinje fibres is thin and irregular.**
- **The cytoplasm of the Purkinje muscle is granular and rich in glycogen.** It has few myofibrils which are peripherally situated. The myofibrils are arranged parallel to the sacolemma.
- **Purkinje fibres have no Diad or Triad tubular systems.**
- **The intercalated discs are absent in the Purkinje muscle fibres.**
- **Purkinje muscle fibres have eccentric nuclei and many gap junctions.**
- **Purkinje fibres are richly supplied with nerves and with non-anastomosing end arteris.** The fibres are **non-striated**.

The following table shows the differences between the three types of muscles:

The Differences Between The Three Types of Muscles Smooth, Skeletal and Cardiac

	Smooth Muscles	Skeletal Muscles	Cardiac Muscles
Action	involuntary	voluntary	involuntary
Site	in the viscera	Attached to bone	in the heart
Shape of fibres	spindle-shaped	cylindrical	cylindrical
Striations	non-striated	well striated	non-clear striations
Sarcolemma	very thin	very thick	very thin
Sarcoplasm	pale cytoplasm	red and pale cytoplasm	red cytoplasm
Size	small in size	large in size	medium-sized
Branching	non branching fibres	branch in face and tongue	branching and anastomosing
Length of fibres	from 30-500 microns	variable	form continuous sheet
Diameter of fibres	Up to 10 microns	up to 100 microns	up to 25 microns
Nuclei	single and central	multiple and peripheral	central nuclei
Intercalated Discs	absent	absent	present
Myofibrils	with no sarcomeres	regular sarcomeres	irregular sarcomeres
Triad of tubular system	absent	present	presence of diad system
Satellite cells	absent	present	absent
Regeneration	from the pericytes	from satellite cells	cannot regenerate

Nervous Tissue

The nervous system of the body includes:

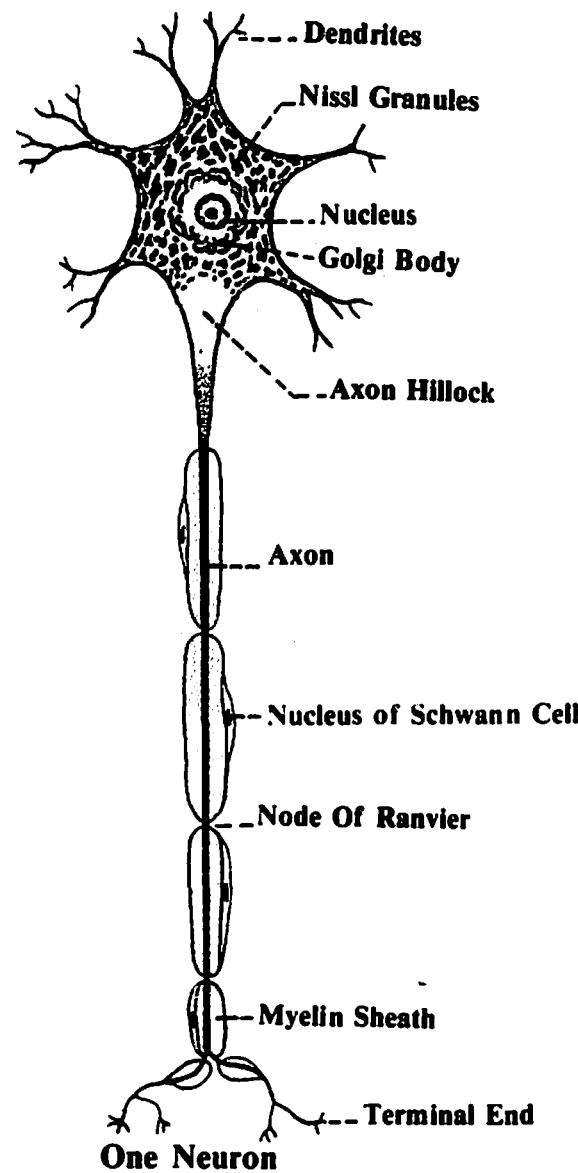
1. **Central nervous system:** It consists of the brain and the spinal cord.
2. **Peripheral nervous system:** It consists of cranial nerves, spinal nerves, ganglia, nerve endings and glial cells.

The Neuron

The neuron is the structural and functional unit of the nervous system. It is formed of a **nerve cell** with all its **processes** which are the **dendrites** and the **axon**.

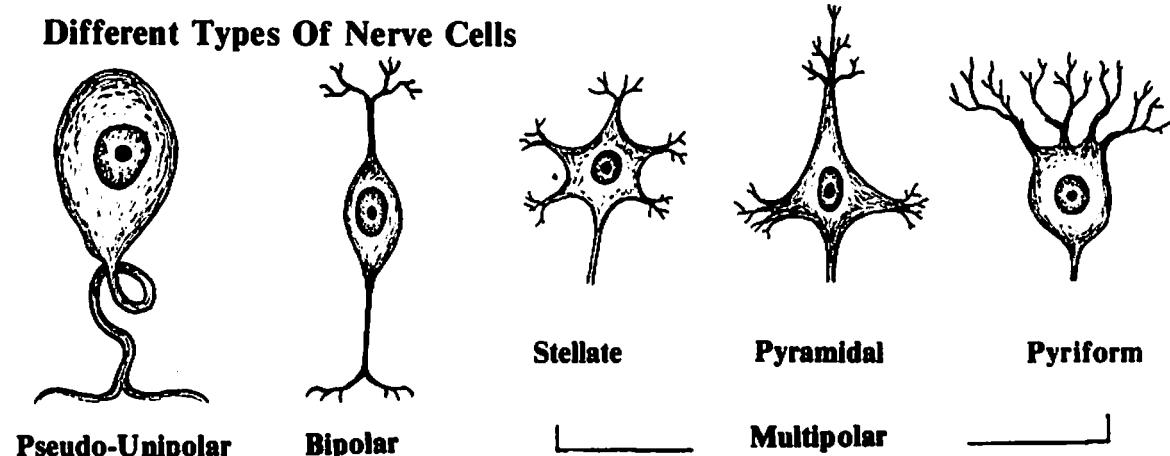
Characteristics Of A Nerve Cell:

- **The size of nerve cells** ranges from 4 microns as the granular cells of the cerebellum and up to 100 microns as the pyramidal cells of the cerebrum.
- **The cell membrane** of the nerve cell is very thin.
- **The nucleus** of the nerve cell is vesicular (open-face type). It is very rich in **nuclear fluid**. It is spherical in shape and central in position. It has a very thick nuclear membrane and very clear nucleolus.
- **The cytoplasm** of the nerve cell contains all cell organoids and cell inclusions, **but with no centrioles**.
- **The cytoplasm** is rich in microtubules, neurofilaments and microfilaments.
- The cytoplasm of nerve cell is rich in **Nissl Granules** or Nissl Bodies.
- **Nissl Granules** are specific basophilic bodies consisting of masses of rough endoplasmic reticulum with their attached **ribosomes**.
 - They are known as chromophil substance because they like certain stains.
 - They may disappear from their nerve cells during degeneration of neurones and the condition is known as **chromatolysis**.



- Nissl granules are not present in axon and not present near the nuclear or cell membranes.
- Nissl granules share in the formation of protein of the nerve cells.
- They help in nutrition and in carrying the memory of nerve cells.
- They can be stained by toluidine blue or by hematoxlin stains.
- Golgi Apparatus in nerve cell is well-developed, it surrounds the nucleus.
- Mitochondria are present in the body and processes of nerve cell.
- Centrioles: They are not present in mature nerve cells, therefore they cannot divide.
- Centrioles may be found in young nerve cells to form neurofilaments.
- The cell inclusions of the nerve cells are:
- Glycogen granules which are important for the function of nerve cells.
- Melanin Pigments and fat droplets may be present in some nerve cells.
- Yellowish lipofuscin granules are also present and may increase in old age.

Classification Of Neurones



I. Neurones Are Classified According To The Shape Of Their Nerve Cells Into:

1. The Unipolar Neurones:

- They have only one process which branch to act as dendrites.
- They are found in the amacrine cells of the retina.

2. **Pseudo-unipolar Neurones:** These neurones are bipolar, but their two processes form a T-shaped division. One branch act as an axon and the other act as dendrite. These neurones are present in: the spinal ganglia and in the mesencephalic nucleus of trigeminal nerve.

3. **Bipolar Neurones:** These neurones are spindle-shaped cells. They have an axon at one pole and a dendrite at the other pole. **Bipolar Nerve Cells are Present in:**

- Bipolar nerve cells in the retina of the eye.
- In the spiral ganglia of the internal ear.
- In the vestibular ganglia of the internal ear.
- In the olfactory epithelium of the nose.

- 4. Multipolar Neurones:** They are subdivided into the following 3 subtypes.
- Stellate-shaped or polygonal neurones:** which are present in the anterior horn cells of the spinal cord and in the **sympathetic ganglia**.
 - Pyramidal neurones:** They are Pyramidal in shape, present in the cerebral cortex.
 - Pyriform neurones:** Are flask-shaped as **Purkinje cells of cerebellum**.

II. Neurones Are Classified According To Their Functions Into:

- Sensory Neurones** as neurones of dorsal root ganglia.
- Motor Neurones** as neurones of anterior horn cells.
- Inter Neurones** which connect neurones together as in Retina.

III. Neurones Are Classified According To The Length of their Axons Into:

Golgi Type 1 Neurones: They have long axons as neurones of **cerebral cortex**, their axons form the tracts in the brain and spinal cord.

Golgi Type 2 Neurones: They have short axons as neurones of **Retina**.

The nerve cell processes are the **axon (efferent)** and the **dendrites (afferent)**.

Differences Between Axon and Dendrites

The Axon	The Dendrites
<ol style="list-style-type: none"> It is a single process. Usually it is thin and long. It has a uniform diameter along its length. It branches at its end but may give also collateral branches which arise at right angles. It contains neurofibrils but no Nissl granules. Two types of axonal transport exist: Antegrade and Retrograde. 	<ol style="list-style-type: none"> Usually multiple processes. Usually short and thick. Thier thickness decreases gradually towards its end. Have many fine side projections called spines or gemmules. They contain Nissl granules and neurofibrils. They receive impulses from other neurones via their synapses.

The Axon

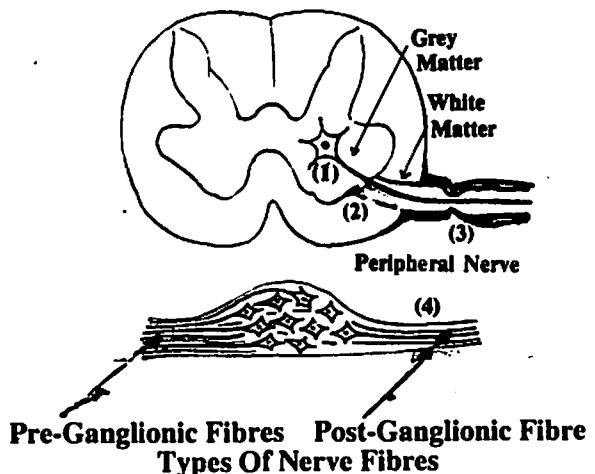
It is formed of a cytoplasm known as **axoplasm** containing mitochondria, neurofibrils and neurotubules: It is surrounded with a membrane known as **axolemma**.

The **axon hillock** is the conical expansion of the axon at its origin from the nerve cell, it has no **Nissl granules** but it is rich in neurofibrils.

Types Of Nerve Axons According To Their Covering Sheathes

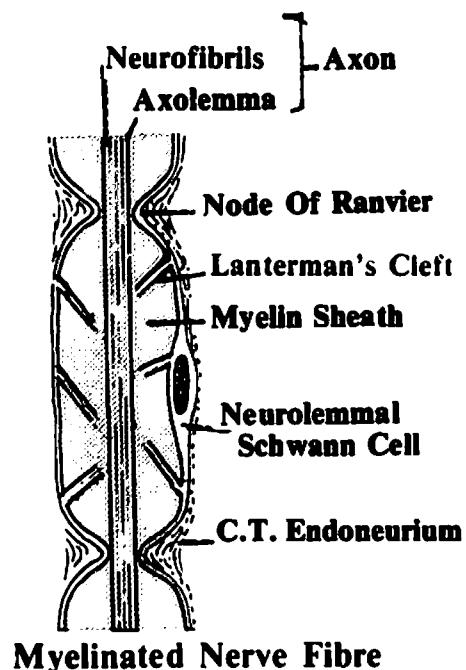
The axons may be naked or may be covered with: myelin sheath or with neurolemma or with both. On tracing any axon of an anterior horn cell of the spinal cord from origin to its termination, we can notice the following types of nerve axons:

1. Naked nerve axons without a myelin sheath and without a neurolemma as those axons in the grey matter and the terminal parts of axons at its motor-end plate in the muscles.
2. Nerve fibres which are covered with myelin sheath but without neurolemma e.g. the nerve axons in the white matter and also the optic nerve.
3. Nerve fibres which are covered with myelin sheath and are covered also with neurolemma e.g. the peripheral somatic axons outside the spinal cord.
4. Nerve fibres which are covered with neurolemma but are not covered with myelin sheath, e.g. the post ganglionic sympathetic nerve axons.



The Myelin Sheath

- It is a fatty tubular covering around the axon.
- It is formed by neurolemmal cells which surround the peripheral nerves. In the brain it is formed by neuroglia cells (oligodendroglia).
- It is composed of cholesterol, fatty acids and phospholipids.
- The myelin sheath is white in colour.
- It is interrupted at intervals by the nodes of Ranvier and by Lantermann's clefts.
- At the node of Ranvier, the axon is not covered by myelin sheath.
- Lantermann's clefts are the areas of discontinuities in the myelin sheath. These clefts facilitate the passage of nutrition from Schwann cells to the myelin sheath.



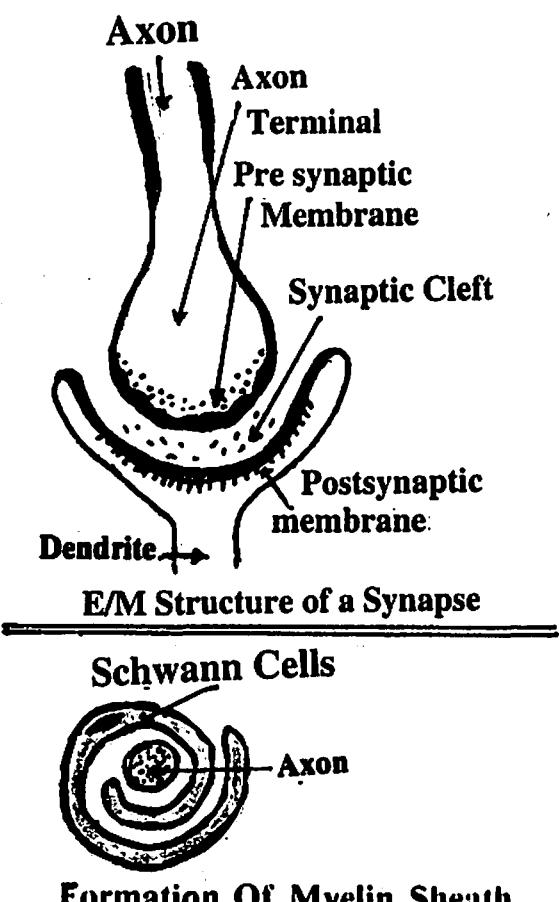
Functions of Myelin Sheath: It protects the axon. It accelerates conduction of nerve impulse. It also isolates nerve impulses.

The Neurolemmal Cells Or Schwann Cells

- They are formed of a chain of Schwann cells around the myelin sheath.
- Each cell corresponds to an internodal segment and it comes in contact with the axon at the **nodes of Ranvier**.
- Each cell has an oval nucleus and a basophilic neuroplasm.
- The Schwann cell in order to form the myelin sheath around the axon, it encircles the axon and rotates several times around it forming a series of rings of phospholipids. These rings will be the myelin sheath.

Function of Neurolemmal Cells:

1. They **isolate** nerve impulses.
2. They help in **regeneration** of neurones after injuries.
3. They **form** the myelin sheath around axons.



Formation Of Myelin Sheath

The Synapse

- **Definition:** It is the point of **contact** between the processes of the neurones.
- In the synapse, there is no cytoplasmic continuity between neurones.
- Synapses may be **Excitatory** (facilitatory) or **Inhibitory**.
- **Chemical synapse** transmit impulses through **neurotransmitters**.
- **Electrical Synapse** transmit ionic signals very rapid as in retina.

Types of Synapses

- a) **Axo-dendritic Synapse:** In which there is a contact between the **axon** of one neuron and the **dendrites** of another neuron.
- b) **Axo-somatic Synapse:** In which there is a contact between an **axon** of one neuron and a **cell body** of another neuron.
- c) **Axo-axonic Synapse:** Contact between the **axons** of 2 neurones.
- d) **Dendro-dendritic:** Contact between **dendrites** of 2 neurones.

E/M Structure of a Chemical Synapse: It is formed of the following:

1. **Terminal Bouton:** It is the terminal end-bulb of the axon. It is rich in these neuro-transmitters: Acetylcholine, Catecholamine and Dopamine.
2. **Pre synaptic Membrane:** is the membrane of the terminal end bulb of axon.
3. **Synaptic Cleft:** is the distance between Pre and Post-synaptic membranes.
4. **Postsynaptic membrane:** It is the cell membrane which belongs to the dendrites of the other neuron. It contains neurotransmitter receptors.
5. **Gemmules or Spines:** They are small projections which arise from the pre and post synaptic membranes.

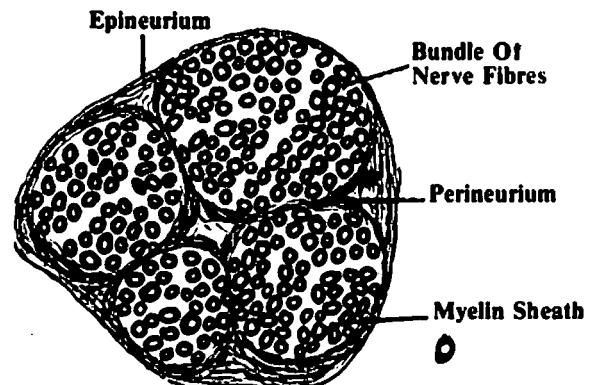
Functions of the Synapse: The arrival of a nerve impulse at the synapse will cause the discharge of the chemical transmitter into the synaptic cleft which either excites or inhibits the post-synaptic membrane.

The Structure Of A peripheral Nerve Trunk

The nerve trunk is formed of collections of axons arranged in bundles bound together by C.T. The whole nerve trunk is surrounded by C.T. fascia called **epineurium**. The C.T. around each axon is called **endoneurium** or **Henl's sheath**.

In a T.S. of a nerve trunk stained by hematoxylin and Eosin, alcohol will dissolve the myelin sheath. Each nerve fibre shows a centrally stained axon surrounded by an empty space of the dissolved myelin, then a rim of Schwann cell cytoplasm stained pink (see plate 9).

In a T.S. of a nerve trunk stained with **osmic acid**, the myelin sheaths will appear as **black circles** (Osmic acid stains only the myelin sheath).

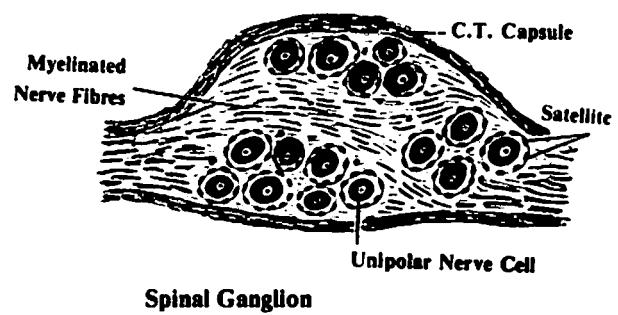


T.S. In A Nerve Trunk (Osmic Acid)

Nerve Ganglia

A nerve ganglion is formed of nerve cells and nerve fibres surrounded by C.T. There are two types of ganglia: **spinal and autonomic ganglia**. The autonomic ganglia are of two types: sympathetic and parasympathetic ganglia.

- **The Spinal Ganglia are present** beside the spinal cord at its both sides.
- They act as relay for sensations.



Spinal Ganglion

- They are formed of pseudo-unipolar nerve cells. The axon of each nerve cell forms a convolution called a **glomerulus**.

- Each nerve cell is surrounded by many supportive **satellite cells**.

- The ganglion is covered by thick capsule.

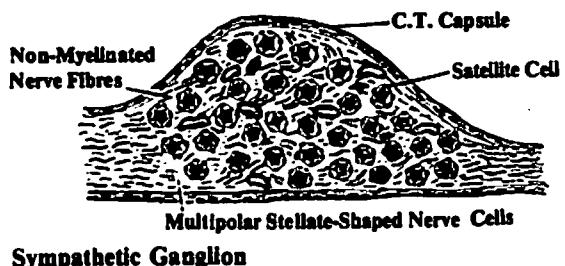
- **The Sympathetic Ganglia** are present as

sympathetic chain or as isolated ganglia in the different regions of the body.

- They act as relay for the different motor functions arising from the spinal cord in order to distribute the autonomic orders to the different body organs.

- They are formed of **multipolar stellate-shaped nerve cells**.

- The nerve cells are surrounded by few satellite cells.



Sympathetic Ganglion

Differences Between Spinal And Sympathetic Ganglia

Spinal Ganglia	Sympathetic Ganglia
<ol style="list-style-type: none"> Present mostly at the dorsal roots of the spinal cord. Covered by thick C. T. capsule. Formed of pseudo-unipolar nerve cells. The cells may be large or small (20-120 microns). The cells are arranged in groups or rows. The groups of cells are separated by myelinated nerve fibres. The cells are rounded in shape in cross section. Each ganglion contains few nerve cells. The axon of each nerve cell is convoluted at its beginning in the nerve cell forming a glomerulus in its cytoplasm. There are more satellite cells around each nerve cell. There is no synapse between the neurones. It is poor in blood supply. 	<ol style="list-style-type: none"> Present mostly at the sympathetic chain. Covered by thin C. T. Capsule. Formed of multipolar stellate shaped nerve cells. All the cells are mostly of the small size (30 microns). The cells are scattered. (not present in groups). The nerve cells are separated by non-myelinated nerve fibres. The cells are irregular in shape in cross section. Each ganglion contains many nerve cells. There is no intra cellular glomerulus because the nerve cells are multipolar and their axons are not convoluted. Less number of satellite cells around each nerve cell. Synapse is present between the neurones. It is rich in blood supply.

The Neuroglia

There is no C. T. in the central nervous system; instead there are the neuroglia.

They form the supporting tissue between the neurones of the C. N. S.

Neuroglia can be stained with silver or with gold chloride

Neuroglia Are Classified Into:

1. The Neuroglia Proper, they are of 3 types:

- Macrogelia or Astrocytes (protoplasmic and fibrous).
- Microglia or mesoglia (mesodermal in origin).
- Oligodendroglia (with few dendrites).

2. Other Types of Supporting Neuroglia-like Cells Present In Nervous Tissue:

a) Ependymal Cells:

These are the simple cuboidal ciliated cells which line the central canal of the spinal cord and brain ventricles. They are derived from the spongioblast cells. They form the **Cerebro Spinal Fluid (C. S. F.)**.

b) Satellite Cells: They are the small cells which surround the nerve cells of the brain and of the ganglia. They are of nutritive functions to nerve cells.

c) Schwann or Neurolemmal Cells.

They are present around the axons of the peripheral nerves, they form the myelin sheath. They help in regeneration of cut nerves.

d) Spongioblast Cells: They are primitive embryonic cells which can differentiate into neuroglia cells.

e) Tanacyte cells which surround the neurones of Hypothalamus.

The Neuroglia Proper

1. Macrogelia or Astrocytes = Star-Shaped Cells

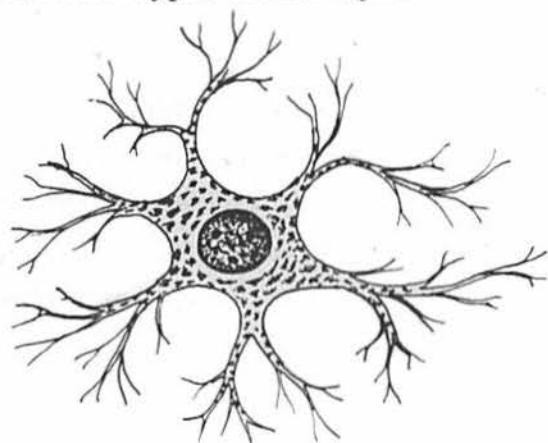
They are the largest type of neuroglia. There are 2 Types of Astrocytes:

(1) Protoplasmic Astrocytes.

(2) Fibrous astrocytes.

a) Protoplasmic Astrocytes:

- They are ectodermal in origin (arising from spongioblasts).
- They are present in the grey matter of the C. N. S.
- They are branched cells with multiple short thick processes.



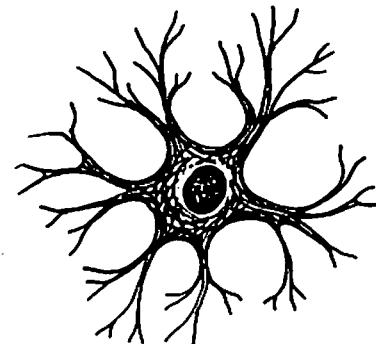
Protoplasmic Astrocyte

- Their cytoplasm as well as their processes are rich in cytoplasmic granules known as **gliosomes** which are considered as lysosomes.
- Astrocytes communicate with one another by gap junctions, therefore information can flow from one cell to another.
- Astrocytes influence the activity of neurones through the secretion of **opioid substance called Enkephalin**.
- Astrocytes contain centrosomes, so they **can divide**.
- They have neither axons nor Nissl's granules.
- They have large rounded darkly-stained nuclei.
- Their processes end on B.V. by foot-like expansions known as vascular end feet or sucker processes.

b) Fibrous Astrocytes:

They are similar to protoplasmic astrocytes but:

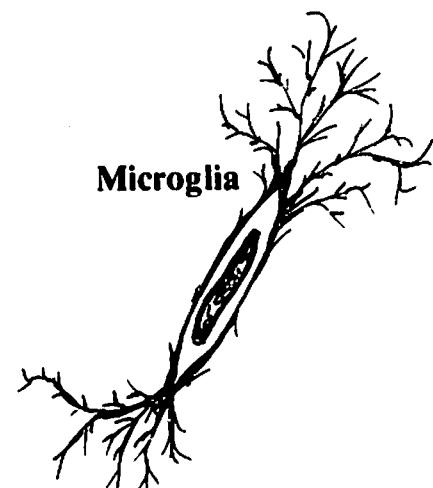
- They are present in the **white matter** of C. N.S.
- Their cytoplasm as well as their processes are rich in straight neuroglia fibres.
- Their cytoplasm is non-granular.
- They have long, slender, smooth processes that branch infrequently.



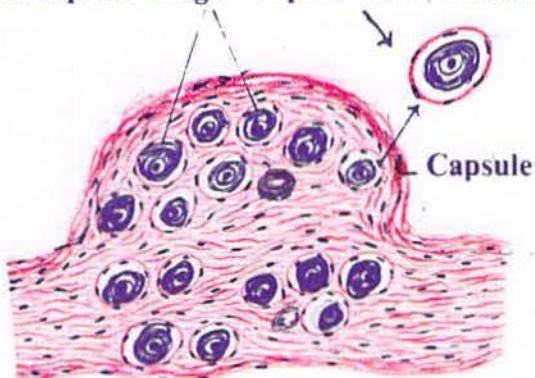
Fibrous Astrocyte

2- Microglia Or Mesoglia:

- They are **mesodermal** in origin=mesoglia.
- They are present in **grey and white matter**.
- They are small **spindle-shaped cells** with few short processes.
- They have neither centrosomes nor Nissl's granules.
- They have flat oval darkly-stained nuclei.
- They have an amoeboid movement and may change into macrophages.
- They are **phagocytic cells** during inflammation and during degeneration and regeneration of neurones. They eat foreign bodies, so they are called "**Police Man of The Brain**".
- They play a defensive role during AIDS disease.

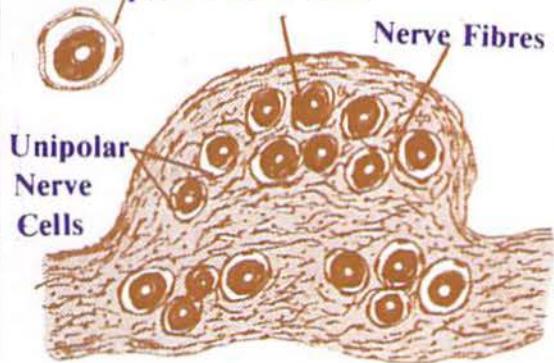


Group Of Large Unipolar Nerve Cells



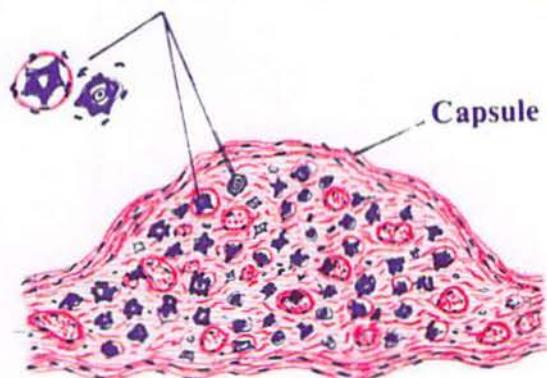
Spinal Ganglion (Hx & E)

Unipolar Nerve Cells



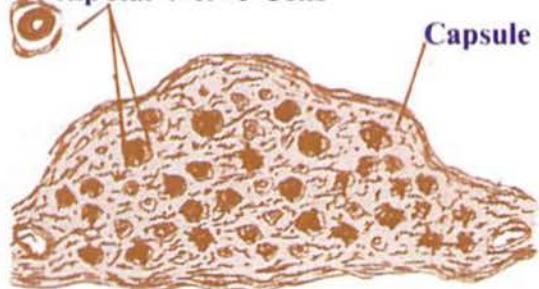
Spinal Ganglion (Silver Stain)

Scattered Small Multipolar Nerve Cells



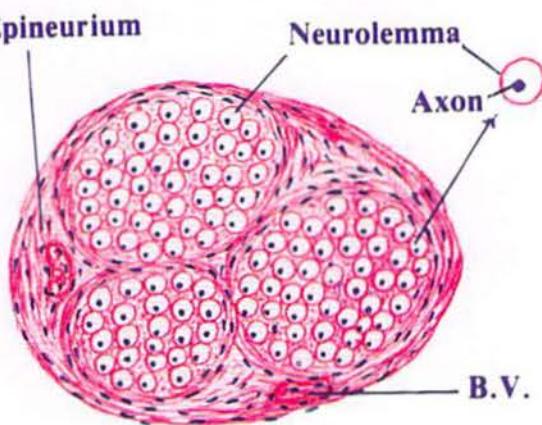
Sympathetic Ganglion (Hx & E)

Multipolar Nerve Cells



Sympathetic Ganglion (Silver Stain)

Epineurium



T.S In Nerve Trunk (Hx & E)

Muscle Fibre



Motor End Plate (Silver)

Zakaria

[Plate 9]

3. Oligodendroglia

- They are present in the grey **and white matter**.
- They are small branched cells with **large** deeply stained nuclei. They contain centrioles.
- Their processes are few, short and thick.
- They are ectodermal in origin.
- They form myelin sheaths around C. N. S. nerves.
- They are supportive, nutritive and insulators for brain neurones.



Oligodendroglia

Functions Of Neuroglia

1. They support the neurones. They form the blood brain barriers.
2. They **form the myelin sheath** around axons (as the oligodendroglia).
3. They act as insulator between neurones (separating the neurones).
4. They have a **nutritive** function for neurones (as macroglia and satellite cells).
5. They **defend** against inflammations of neurones (as microglia).
6. They help in **regeneration** of neurones (as oligodendroglia and microglia).
7. They secrete the C.S.F. (as the ependymal cells).
8. They secrete Enkephalin to influence neuronal activities.

Degeneration And Regeneration Of Neurones

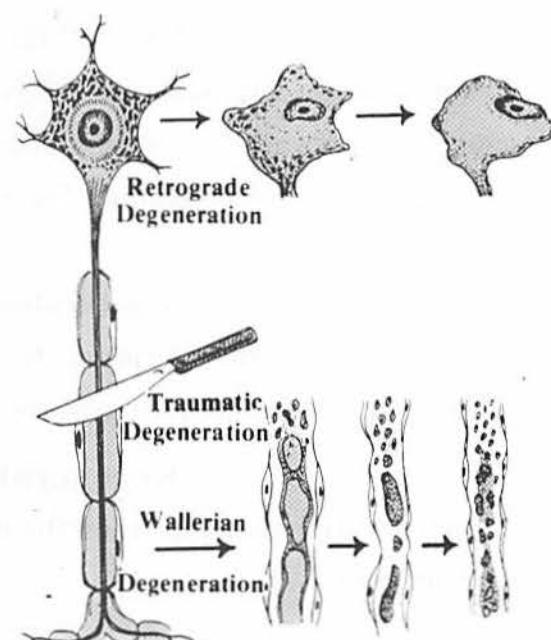
Cutting of an axon of a neuron by a knife, trauma or infection will result in:

1. Retrograde degeneration in its nerve cell.
2. Traumatic degeneration at the site of injury.
3. Wallerian degeneration at the peripheral part of the axon.

Retrograde Degeneration:

These are the changes which occur in the **nerve cell** as a result of **partial cutting** of its axon. The changes are in: the shape, size, nucleus, cell organoids and cell inclusions of the nerve cell.

Changes in nerve cell: It swells, loses its dendrites, becomes oval in shape and small in size, its cytoplasm becomes pale.



Types Of Neuronal Degenerations

The nucleus: It becomes **pyknotic**, eccentric in position and its nuclear membrane disappears. Degeneration of other nuclear components occur.

Chromatolysis: It is the process of degeneration and disappearance of **Nissl granules**.

Nissl granules: They are very sensitive to any toxin and to mild injuries. They break into small particles, they **disappear** completely from the nerve cells after 15 days. These changes in the Nissl granules can be observed by methylene blue or by hematoxylin stains.

Neurofibrils as well as Golgi apparatus degenerate gradually and finally disappear (they can be stained by silver). If the axon is completely cut, it will lead to complete death of the nerve cell especially if no regeneration takes place.

Wallerian Degeneration

These are the changes that occur in the **axon, myelin sheath and neurolemma** after partial cutting of the axon of one neuron.

1. **Changes in the axon:** The neurofibrils of the axon are swollen at interrupted areas giving the axon a **beaded appearance**. Later on, the axon begins to break into amall pieces of different lengths which can be stained by silver.
 2. **Changes in the myelin sheath:** The myelin sheath is segmeneted to form fermentation chambers. Finally, the normal shape of the myelin sheath is changed into **droplets of neutral fat and oleic acids**. The myelin can be stained by **osmic acid**. The nodes of Ranvier will become widen and the inter-nodal segments retract and become irregular in shape.
 3. **Changes in the neurolemma:** The neurolemmal cells increase in size and their nuclei divide by mitosis. Later on, the cells form a tubular cord around the myelin sheath helping in **regeneration** of the cut neurones.
- N. B.: Traumatic degeneration:** It is a rapid process of Wallerian degeneration occurring at the site of injury with the same previous changes.

Regeneration Of Neurones

Regeneration depends upon the degree of nerve injuries and upon these conditions:

- Whether the axon is partially or completely cut. It also dpends upon the distance between the two cut ends.
- Whether the wound is infected or not.
- Whether the neurolemma is intact or not.

If there is **no infection in a partially cut axon** and if the neurolemma is intact; **regeneration starts in the nerve cell** by resuming its normal shape and contents. The neurofibrils of the central stump **will grow** to be connected with the distal cut end of the nerve to complete nerve regeneration.

N. B. There are Other Types of Nerve Degenerations as:

- 1. Retrograde Transport Degeneration:** When nerve axons are infected with **Rabies or Herpes viruses**, Retrograde Transport of these viruses occur through the axons of certain neurones causing infections to these neurones. Therefore, **Retrograde Transport Degeneration** occurs to these infected neurones.
- 2. Transneuronal Degeneration:** The neurones are functionally connected with each other by the synapse. If we isolate any neuron by **cutting its dendrites**, So, it will be disconnected from the other neurones. Therefore, it **will receive no stimuli from the other neurones**. In this case, transneuronal degeneration will occur in its axon.

Nerve Endings

These are special nervous structures present in certain areas of the body and are classified according to their functions into: **Receptors and Effectors**.

The receptors

The receptors receive sensory impulses from outside the body or from the tissues in which they are present. **These Receptors Include:**

- 1. Receptors For Special Sense As:**
 - a) **Photoreceptors of vision** by the **retina of the eyes**.
 - b) **Audiorreceptors of hearing** by the **organ of Corti of the ear**.
 - c) **Chemoreceptors of smell** by the **olfactory epithelium of the nose**.
 - d) **Chemoreceptors of taste** by the **taste buds of the tongue**.
 - e) **Reception of changes** in the posture and different movements of head and body by the **crista ampularis and macula utriculi of the internal ear**.
- 2. Receptors For Cutaneous Sensibility (Exteroceptors):**
 - a) **Pain sensation** by **free nerve endings**.
 - b) **Temperature sensation** by **Krause bulb, Ruffini organ and free nerve endings**.
 - c) **Touch sensation** by **Merkel's disc, Meissner's corpuscle and free nerve endings**.
- 3. Receptors For Deep Pressure and Vibration Sense (proprioceptors):**
 - a) From skin, muscles and wall of organs by **Pacinian corpuscles**.
 - b) From muscles, tendons and joints by **muscle spindles and tendon spindles**.
- 4. Receptors from the wall of viscera (Visceroreceptors) to transmit autonomic sensation from the stomach, bladder.. etc. to the central nervous system.**

The Exteroceptors

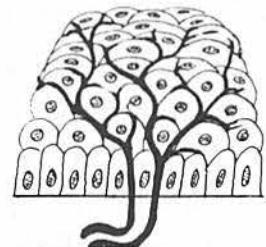
1. Receptors In The Epithelial Tissue

Non - Capsulated Receptors

a) Free or Bare - Nerve Endings

These endings are formed of **non myelinated sensory nerve fibres**. They branch inbetween the epithelial cells.

Sites: epidermis of skin, stratified squamous epithelium of the cornea, conjunctiva, oral cavity, dental pulp, present also in periosteum and perichondrium.

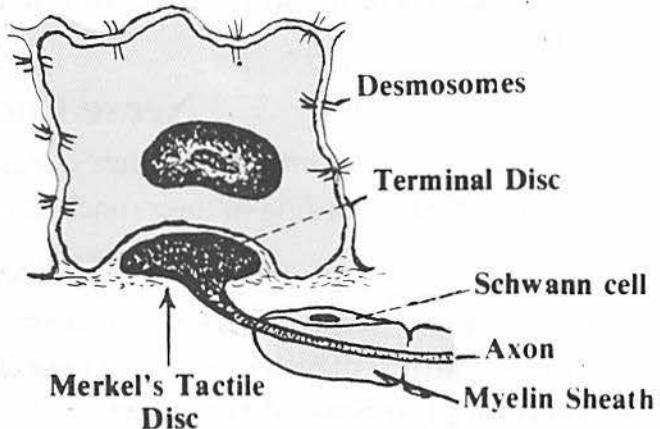


Free Nerve Endings

Function: They are receptors for pain, temperature, touch, pressure and itching.

b) Merkel's Discs

- They are present in the skin of palm, sole and lip.
- They are formed of non-myelinated nerve discs under certain specialized epithelial cells of the epidermis of the skin **called Merkel Cells**.
- **Merkel Cells:** They are polygonal epidermal modified cells. Their cell membranes are irregular with cytoplasmic granules.
- **Merkel Cells:** have many desmosomal junctions with the neighbouring epidermal cells. Their cytoplasm is rich in enzymatic vesicles. The sensory nerve, terminates by a disc - like structure under the bases of the Merkel's cells.



Functions: They respond to light and deep pressure.

c) Plexus Of Bounet Or Peritrichial Endings

They are formed of **non - myelinated nerve fibres** which form a plexus of nerve fibres **around the roots and shafts of the hair follicles**.

Sites and Functions: They are present around the hair follicles of the skin. They are responsible for the sensation of **hair movements and act as mechanoreceptors**.

d) Other Epithelial Receptors Around The Neuro-Epithelial Cells

These nerve endings are the sensory nerve fibres present around the **neuro-epithelial cells of the taste buds and around the epithelial receptors of the internal ear** (organ of Corti, crista ampularis and macula utriculi).

2 – Receptors In The Connective Tissue

Capsulated Receptors in the C.T. (e.g. in the C.T. dermis of the Skin):

a) Meissner's Corpuscles

Each Meissner's Corpuscle is an oval structure. It is covered by a capsule formed of fibroblasts and collagen fibres. Its central area contains flattened cells which are modified Schwann cells.

The non-myelinated sensory nerve, penetrates the capsule of Meissner's corpuscle. The nerve fibres branch repeatedly and its nerve endings are surrounded by Schwann cells and by collagenous fibres.

Sites: Meissner's Corpuscles are present in the dermal papillae of non-hairy skin of the palm, sole, fingers, toes, eyelid, nipples, glans penis and clitoris.

Functions: Reception of touch sensation. (tactile discrimination).

b) Krause's end bulb

– It is formed of a spherical corpuscle covered by a thin capsule. The sensory myelinated nerve fibre enters the corpuscle. The nerve loses its myelin sheath outside the corpuscle. Inside the corpuscle, the nerve fibre and its branches terminate by coiled expanded ends.

Sites: Krause's bulbs are present in the C.T.

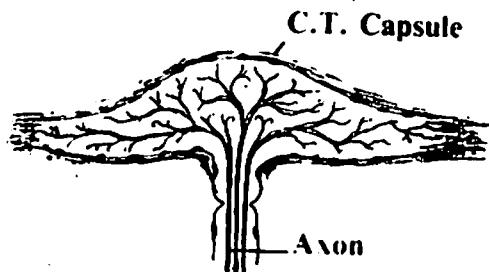
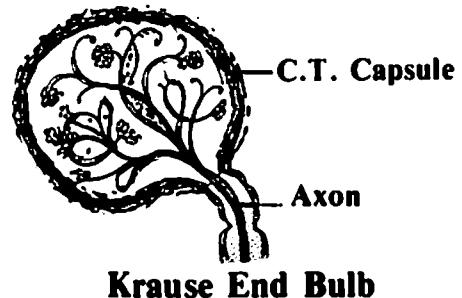
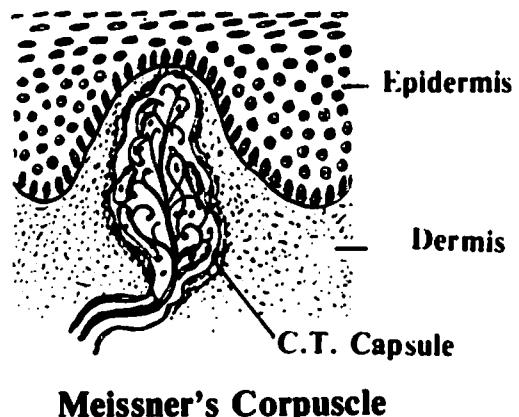
dermis of the external genitalia, in the lip, tongue and conjunctiva of the eye.

Functions: They are receptors for deep pressure and cold sensation.

C – The Ruffini End Organ

– It is formed of an elongated thin C.T. capsule. Inside the capsule there are bundles of elongated collagenous fibres separated by small amounts of fluid and fibroblasts

– As the myelinated nerve fibres penetrate the capsule, its Schwann cells and its myelin sheath are lost. The sensory nerve fibres branch to form a dense cluster of nerve endings.



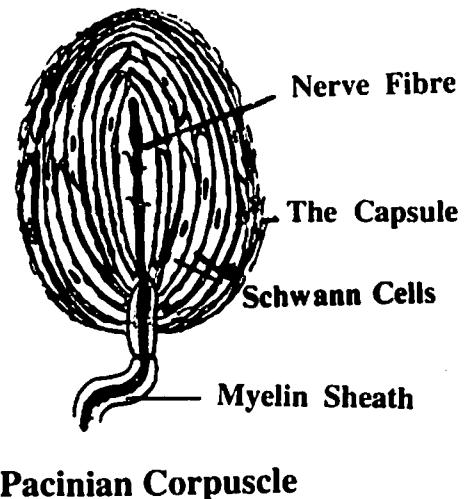
Ruffini's End Organ

Sites: They are present in the dermis and hypodermis of skin especially in the plantar surface of the feet.

Functions: They are mechanoreceptors for joint movements, for deep pressure and may receive hot sensation.

d– The Pacinian Corpuscle

- Each pacinian corpuscle is oval in shape. It is formed of numerous concentric lamellae. On section, the corpuscle resembles a sliced onion.
- The concentric layers are formed of modified Schwann cells which are joined together by desmosomes. The concentric layers are separated from one another by collagenous fibres and by spaces filled with fluid.
- A large myelinated nerve fibre enters one pole of the corpuscle. Inside the corpuscle, it loses its myelin sheath, then it loses its Schwann cells. The naked axon passes through its centre and terminates by an expansion.
- A thin C.T. capsule covers the outer surface of the pacinian corpuscle. The subcapsular space contains fluid, collagenous fibres and some macrophages.



Sites of Pacinian Corpuscles

- They are present in the dermis of skin especially in the palm and sole. In the nipples, tips of fingers, breast and external genitalia.
- Present in the striated muscles, tendons, joints, walls of large B.V. and wall of urinary bladder, stomach and rectum.
- In the C.T. of the Pancreas, mesentery and serous membranes.
- Present also in certain glands as the thymus.

Functions of Pacinian Corpuscles:

They respond to changes in position, vibration sense, tactile localization, discrimination and stereognosis (They act as proprioceptors).

Proprioceptors

They are special receptors which carry to the central nervous system the information concerning the state of muscles, the position of limbs and movements of joints. These informations allow the C.N.S. to control and to coordinate the manner of locomotion of the body. To meet this need, skeletal muscles contain Muscle Spindles and Golgi Tendon Spindle Organs.

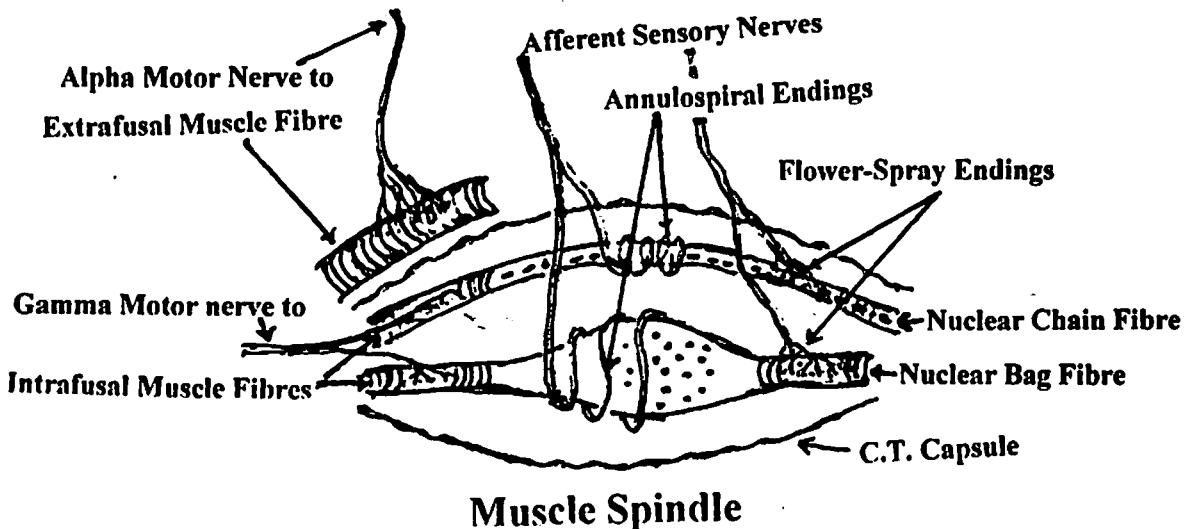
The Muscle Spindles or Neuromuscular Spindles

- They are modified fusiform structures. Each one is about 5-10 mm long and 200 microns in diameter. It is called also as Neuro-muscular Spindle.

Sites: They are found near the musclo-tendinous junction of skeletal muscles.

- They are found more in the antigravity muscles as: the flexor muscles of the upper limb, the extensor muscles of the lower limb and in muscles of the back. Present also in the small muscles of the hand, foot and the intercostal muscles.
- One end of the muscle spindle may be attached to the tendon of the muscle.

Structure: Each muscle spindle is covered with thick C.T. capsule. Under the capsule there are the subcapsular perilymphatic space containing areolar C.T., gelatinous substance and from 2 to 12 intrafusal muscle fibres.



- The intrafusal muscle fibres are of 2 types:

a) **Nuclear Bag Type:** They are long and large fibres. They are from 1 to 4 in number in each muscle spindle. Each one is expanded at its centre, having no striations but it is very rich in nuclei. (About 50 nuclei in each fibre).

The nuclear bag muscle fibres are of 2 types according to their histochemical reactions: **Dynamic and Static Nuclear Bag Muscle Fibres**.

b) **Nuclear Chain Type:** They are narrower and shorter fibres than the nuclear bag type. They are more numerous, from 1 to 10 in number in each muscle spindle. Each fibre is not expanded at its centre. The myofibrils of the nuclear chain fibres are non-striated. Each nuclear chain muscle fibre contains a chain of nuclei which are present in a single row.

N.B. The nuclear chain and the nuclear bag muscle fibres are composed of a non-contractile parts at their centres and contractile parts at their both ends.

Innervation Of Muscle Spindles

- The extra fusal skeletal muscle fibres which are present outside the capsule of muscle spindles are innervated by motor nerves which arise from the large **Alpha Motor Nerve Cells** which are present in the **anterior horns** of the spinal cord.
- The contractile parts of the intra fusal muscle fibres are innervated by **Gamma Motor nerves** which arise from small **Gamma motor nerve cells** of the anterior horns of the spinal cord.
- The sensory nerves carrying sensation from the intrafusal muscle fibres start as **annulospiral and flower spray** nerve endings. They carry sensory impulses from muscle spindles to the posterior horn cells of the spinal cord.

The Tendon Spindles Or Golgi Tendon Organs

They are similar to muscle spindles in their structures but the intrafusal fibres are **collagenous fibres**. They are present in tendons and joints. The sensory nerve fibres branch on these intra-fusal collagenous fibres of the tendon, they carry proprioceptive sensation from the tendons to posterior horn cells. There is no efferent (motor) supply to tendon spindles.

Functions: Muscle and tendon spindles are responsible for stretch reflex

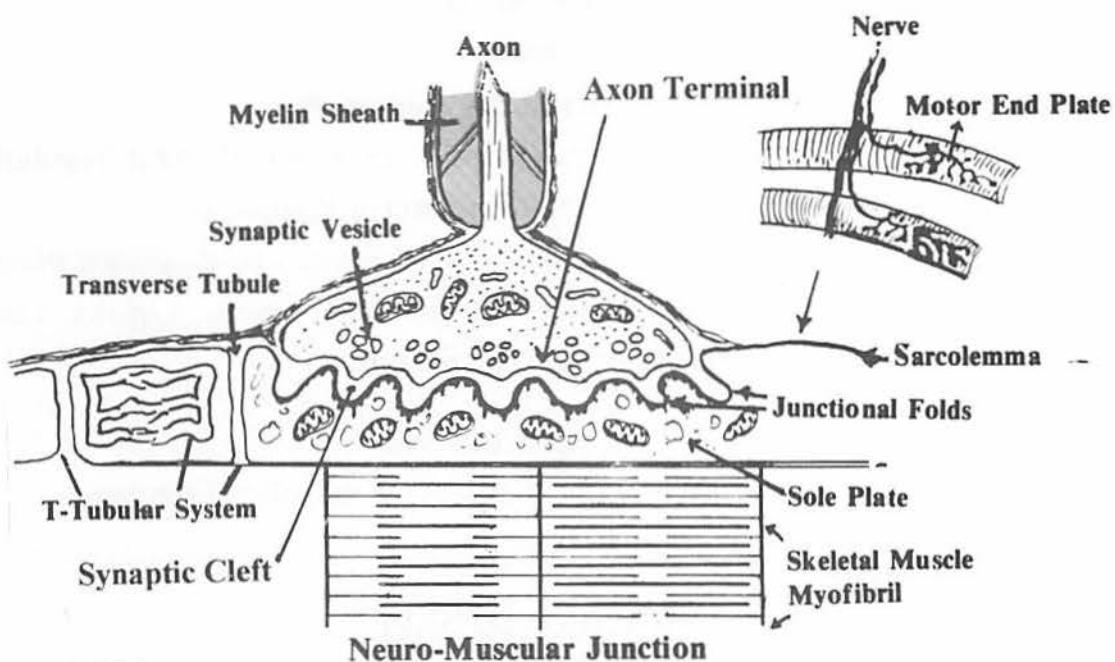
The Effector Nerve Endings

- Axons of motor neurones of the spinal cord innervate skeletal muscles.
- Axons of motor cranial nuclei innervate muscles, glands and organs.
- Axons of autonomic neurones in autonomic ganglia innervate smooth muscles, secretory glands and organs.

Motor Nerve Ending

Motor End Plates (Myoneural Junctions)

- These motor-end plates represent the terminations of motor nerve fibres into the skeletal muscles.
- As the motor nerve reaches the muscle, it branches into many terminal buttons which supply the muscle fibres.



Neuro-Muscular Junction

- When the nerve axon reaches the muscle fibre, it loses its myelin sheath.
- The neurolemma and Schwann cells which cover the nerve axon spread over the sarcolemma and then disappear.
- The naked axon when comes in contact with the muscle fibres, it pushes the sarcolemma (covering of the muscle) in front of it and the axolemma of the nerve becomes separated from the sarcolemma by a space called **synaptic cleft**. This termination is known as **epinefferal ending**.
- The expanded end of the terminal part of the axon is called **axon terminal**. It is very rich in mitochondria and synaptic vesicles which contain **acetyl choline**.
- The **synaptic cleft** is the space between the terminal end of the axon and the sarcolemma. It is very rich in **acetyl cholin esterase enzyme**.

The sarcolemma of the muscle and the layer of sarcoplasm just beneath the axon terminal is known as **Sole plate** which is characterized by:

1. **The sarcolemma at the sole plate** is corrugated forming the so called **junctional folds** which are rich in acetyl choline esterase enzyme.
2. **The sarcoplasm** of the muscle at the sole plate shows less striations but it has numerous nuclei and mitochondria.

N.B. Myasthenia Gravis Disease is characterized by muscular weakness caused by reduction in the number of acetyl choline receptors in the sarcolemma at the myoneural junction.

The Skin

The skin is the largest organ in the body.

It forms a protective layer to the **surface of the whole body**.

Functions: It is very important in the processes of: **excretion of sweat, regulation of heat, reception of stimuli and in the formation of Vitamin D.**

Many diseases reflect their signs on the skin and can be diagnosed through skin examination as: Anaemia, jaundice, smallpox, chickenpox, syphilis, scarlet fever, Vitamin deficiency and the specific skin diseases.

Types of skin

1. Thick Skin present in the palms of the hands and in the soles of the feet.
2. Thin Skin present in the other body areas.

Structure Of Skin

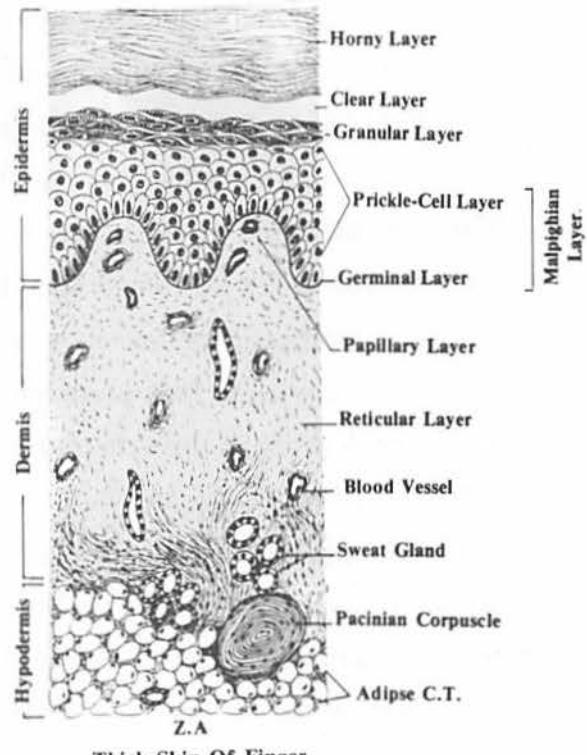
The skin is formed of **Two main layers:**

1. **Epidermis** which is formed by the covering **stratified squamous epithelium**.
2. **Dermis** which is formed by the underlying **C.T.**

The subcutaneous C.T. fascia under the dermis is called the **hypodermis**.

The Thick Skin

- **It is found in the palms and soles.**
- It is formed of epidermis, dermis and hypodermis.
- **The epidermis** is thick and is formed of **keratinized stratified squamous epithelium**.
- **The epidermis** is formed of four layers: Hornyl layer, clear layer, granular layer and Malpighian layer.
- **The dermis** is formed of C.T. which is differentiated into two layers: **papillary layer and reticular layer**.
- **The hypodermis** is formed of C.T. and is rich in fat cells.



The Epidermis of Thick Skin

- The epidermis is thicker in the skin of soles than that of the palms.
- There are four types of cells in the epidermis which are:
 1. **Keratinocytes:** They form about 85% of the cells and are responsible for regeneration of epidermal cells. They produce keratin.
 2. **Melanocytes:** They form the melanin pigments and are responsible for pigmentation of skin.
 3. **Langerhan's Cells:** They are the phagocytic macrophage cells of the epidermis.
 4. **Merkel's Cells:** They are the sensory receptor cells of the epidermis.

(1) Keratinocytes

The Keratinocytes of the Epidermis are Arranged in Four Layers Which Are:

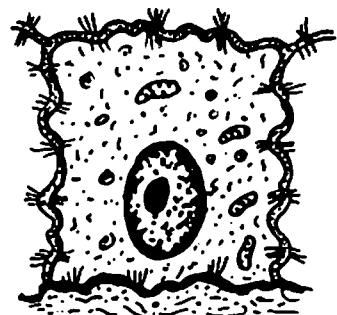
(1) Malpighian Layer (2) Granular Layer (3) Clear Layer and (4) Horny Layer.

1. The Malpighian Layer of the Epidermis.

It is formed mainly of keratinocytes which are arranged in two layers:

A) The Basal Cell Layer (Germinal Layer or Stratum Germinativum).

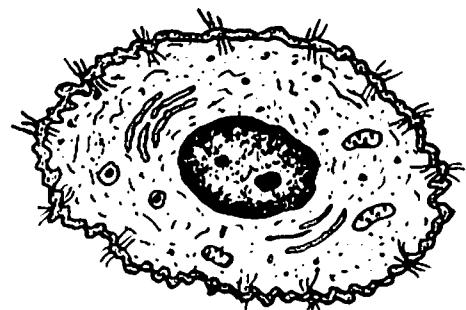
- It is formed of columnar cells with deeply-stained, oval, basal nuclei. The columnar cells rest on a clear basement membrane and are anchored and fixed to it by hemidesmosomes.
- The columnar cells show junctional complexes between their cell boundaries.
- The cytoplasm of the cells is deeply basophilic, because it is rich in ribosomes.
- The cytoplasm contains filaments of cytokeratin or Tonofilaments.
- The columnar cells show mitotic figures. Their repeated mitosis is responsible for regeneration of the epidermal cells (hence the name germinativum).



A Basal Cell

B) The Prickle cell Layer (Spinous Layer or Stratum Spinosum).

- This layer is formed of 4-8 layers of polyhedral cells (Keratinocytes) with rounded central nuclei.
- The cells are large near the basal layer, Their cytoplasm contain tonofilaments and melanin granules.



A Prickle Cell

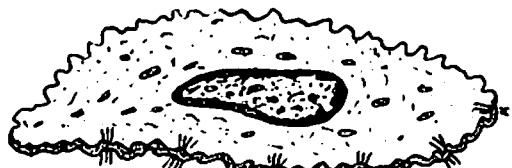
- The deep cell layers show **mitotic figures**. (signs of cell division)
- The cells of this layer have **cytoplasmic processes** which are joined to those of the neighbouring cells by **desmosomes**.
- The flat cells of this layer near the top accumulate **keratohyaline granules** in their cytoplasm.

2. The Granular Cell Layer

Skin Barrier Layer or Stratum Granulosum

- This layer consists of 2-4 layers of flat **basophilic cells** with **flat nuclei**.
- Their cytoplasm contains:
 1. Keratohyaline basophilic granules.
 2. Coated granules covered by membranes.

These granules contain mucopolysaccharides and phospholipids. These granules act as **skin barrier**, they prevent foreign materials from penetrating the skin.



A Granular Cell

3. The Clear Layer (Stratum Lucidum)

- This layer appears as thin clear, homogeneous line between the granular layer and the horny layer.

This **Clear Layer** is formed of non-nucleated flat cells which are rich in:

1. Keratin filaments.
2. Eleidin granules which are protein in nature.

4. The Horny Layer (Stratum Cornium)

- This layer consists of several layers of **acidophilic horny scales** called **squames**.
- These horny scales (squames) are firmly adherent to one another by the remnants of the **desmosomes**.
- These scales contain no nuclei and no cell organoids because they have disappeared from these cells by the lysosomal activity of the cytoplasm.



Horny Layer

These scales are rich in **keratin filaments** and **Eleidin granules**.

- These scales (squames) are continually shed off from the surface and are continually replaced by new ones from the deeper cells.

N.B: Renewal of the epidermis occurs every three weeks.

2. Melanocytes

- They are large branched cells derived from the ectoderm.
- They are present inbetween the cells of the basal cell layer of the epidermis.
- Their cytoplasm contains **tyrosinase enzyme** which converts tyrosine to melanin.

The formed melanin is injected by a process of **cytocrine secretion** to the epidermal cells resulting in their pigmentation.

Melanocytes are DOPA Positive Cells.



Melanocyte

3. Langerhan's Cells

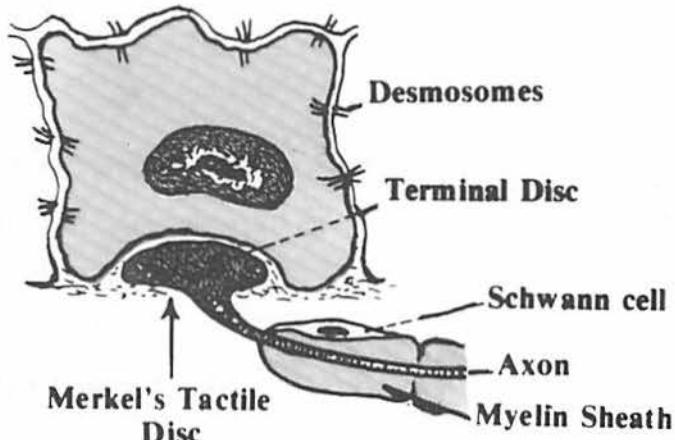
- They are the **phagocytic** macrophage cells of the epidermis of skin.
- They are **branched cells** with many cytoplasmic processes.
- They have **no keratin, no** melanin and not connected to epidermal cells.
- Their cytoplasm is rich in specific **Langerhan granules**.
- They are more common in the skin after skin injuries.
- They are present between the cells of the prickle cell layer.
- They **act as antigen presenting cells** in allergic dermatitis.



Langerhan's Cell

4. Merkel's Cells

- These are **mechano receptor cells** in the epidermis of palm and sole.
- They are present in the **basal cell layer** of the epidermis.
- They are large cells. They are attached to basal cells by desmosomes.
- Merkel's Cells receive **pressure sensation**, which is carried to spinal cord along sensory nerves. These sensory nerve fibres start as Merkel's disc under the Merkel's cell.



Receptors In The Epidermis Of Skin Are:

1. **Free Nerve Endings** for pain and temperature sensation.
2. **Merkel's Nerve Disc** for pressure sensation.
3. **Plexus of Bounet** around hair follicles which act as mechanoreceptors.

The Dermis Of The Skin

It is the C.T. layer which is present under the epidermis. It varies in thickness in the different areas of the body, but it is thicker than the epidermis.

The Dermis Consists of two Layers: Papillary and Reticular Layers:

1. The Papillary Layer of the Dermis:

- It forms the dermal papillae under the concavities of the basement membrane of the stratified squamous epithelium of the epidermis.

- It is formed of a loose **vascular connective tissue**. It contains type III fine collagenous fibres, with some reticular and elastic fibres.
- **It is very rich in:** fibrocytes, fibroblasts, macrophages and mast cells.
- It is rich in blood capillary loops.
- It contains **Meissner's tactile corpuscles** which are **touch receptors**.

2. The Reticular Layer of the Dermis:

- It is formed of a network of reticular fibres and some collagenous fibres.
- It contains sweat and sebaceous glands and hair follicles.
- It is less vascular than the papillary layer and it has few C.T. cells.
- **It contains these sensory nerve endings:**
Ruffini corpuscles, Krause end bulbs and Pacinian corpuscles.

N.B.: The epidermis is fixed to the dermis by:

1. **The basement membrane** fixes the basal cells to the dermis.
2. The dermal papillae fit into the concavities under the surface of the epidermis.
3. **Hemi-desmosomes** are present in the basal columnar cell layer of the epidermis in order to fix these cells to the basement membrane and to the underlying C.T.

Subcutaneous Tissue

This layer is known as **hypodermis**. It is formed of loose C.T. rich in fat cells. The adipose C.T. in the hypodermis varies according to the different body areas and according to the nutritional status of the individuals.

The Sweat Glands

- Sweat glands are present deep in the dermis all over the body except the **glans penis, clitoris, the nail beds and the red margin of the lip**.
- They are **simple coiled** tubular glands.
- **There are two types of sweat glands: Merocrine and Apocrine glands.**

1. The Merocrine (Eccrine) Sweat Glands

Sites: They are present in the dermis of 90% of the skin.

The Merocrine Sweat Glands are formed of: **Secretory Acini and Excretory Ducts.**

- **The Secretory Acini** are lined with the following **Two Types of Cells:**
 - a) **Clear or Pale Cells:** They form the majority of the acinar cells. They are cuboidal or columnar cells with **pale cytoplasm** rich in glycogen.

Intercellular conalliculi are present between these pale cells to conduct sweat secretion to the lumen. **Each cell has a wide base and a narrow apex.**

- b) **Dark Cells** which are less common than the clear cells. Each cell has a **narrow base and a wide apex**. They have dark cytoplasm rich in granules.
- Both types of cells are surrounded by **contractile myoepithelial cells**.

The Excretory Ducts Of Sweat Glands:

- The excretory ducts collect the sweat secretion from the secretory acini.
- They run in spiral manner in dermis and epidermis of the skin.
- The sweat duct is lined with 2 or 3 layers of **stratified cuboidal cells**.
- Sweat glands secrete sweat secretion which is rich in: water, sodium chloride, urea and ammonia.

2. The Apocrine Sweat Glands

Sites: They are present in the **axilla, pubic and perineal regions** and in the skin of the breast around the nipple.

- **Each gland is formed of secretory acini and excretory ducts.**
- **The secretory acini** are lined by single layer of columnar cells. The acini are surrounded by myoepithelial cells.
- **The excretory ducts** are lined with 2 layers of **stratified cuboidal cells**, They open into the upper part of the hair follicles.
- **The apocrine sweat glands** start to secrete after **puberty**. Their secretion is milky, rich in protein, it gives a very bad odour if it is contaminated with bacteria.

The Thin Skin

Thin skin covers all the body **except** the palms of the hands and the soles of the feet. The skin covering the eyelid is **the thinnest skin in the body**.

Thin skin is similar in its structure to thick skin, But:

Characteristics of Thin Skin:

- The epidermis is **thinner** than that of the thick skin.
- **The prickle cell and the granular cell layers** are reduced in thickness.
- **The lucidum layer** is absent or very thin.
- **The horny layer** is much thinner than that of the thick skin.
- **The dermal papillae** are irregular.
- **Thin Skin Contains:** hairs, sebaceous and sweat glands.

Hairs

- Hair follicles develop during the third month of the intrauterine life of the embryo.
- Hairs are found all over the skin Except: Palm, Sole, lip, glans penis and clitoris.
- **Colour, nature and distribution of hairs** vary according to race, sex and body regions.
- Growth of hair varies according to body regions, race and to hormonal factors.
- **Short Villus Hair** are present on body surface and **Terminal Long Hairs** are present on scalp and axilla.

Each hair is formed of:

- a) **Shaft** projecting above the surface of the skin.
- b) **Root** embedded in the skin.
- c) **Hair follicle** which is an epidermal invagination. It terminates by a dilatation called **hair bulb**.

a) The Shaft of The Hair

The shaft of the hair is formed of 3 layers: inner medulla, middle cortex and an outer cuticle.

The Medulla: It is formed of keratinized cuboidal cells separated by air spaces.

The keratin is of the soft type.

The Cortex: It is formed of cornified cells rich in pigments. These pigments are responsible for the colour of the hair.

The Cuticle: It consists of thin, flat, scale-like cells which have a special arrangement preventing hairs from being pulled out easily.

The cortex and cuticle of hair contain Hard Keratin

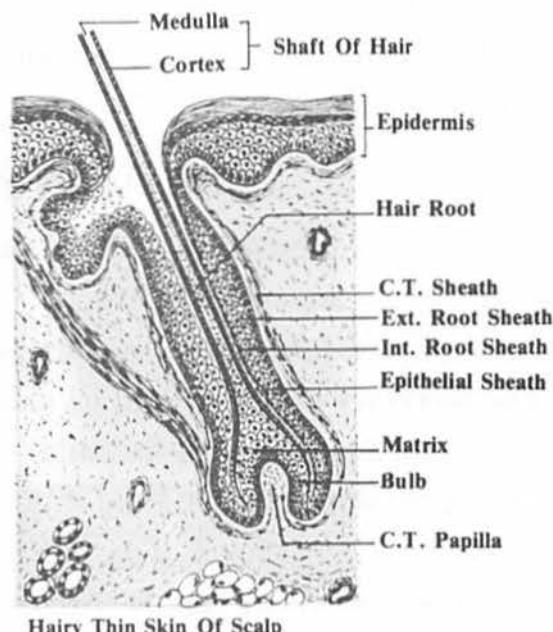
b) The Root of The Hair

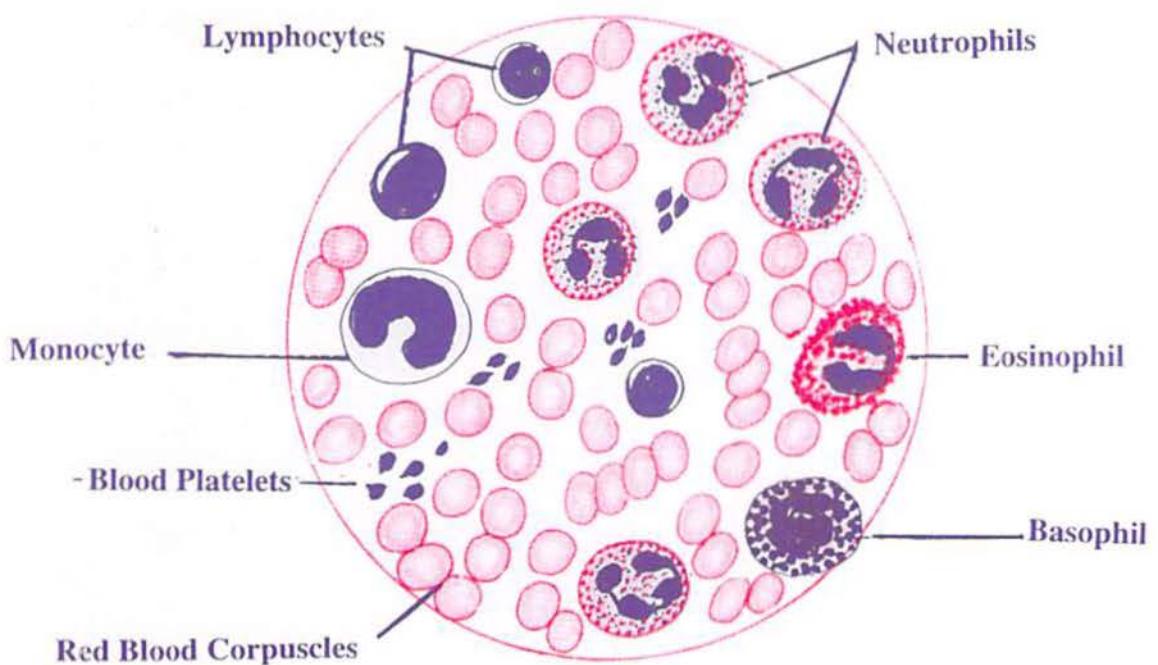
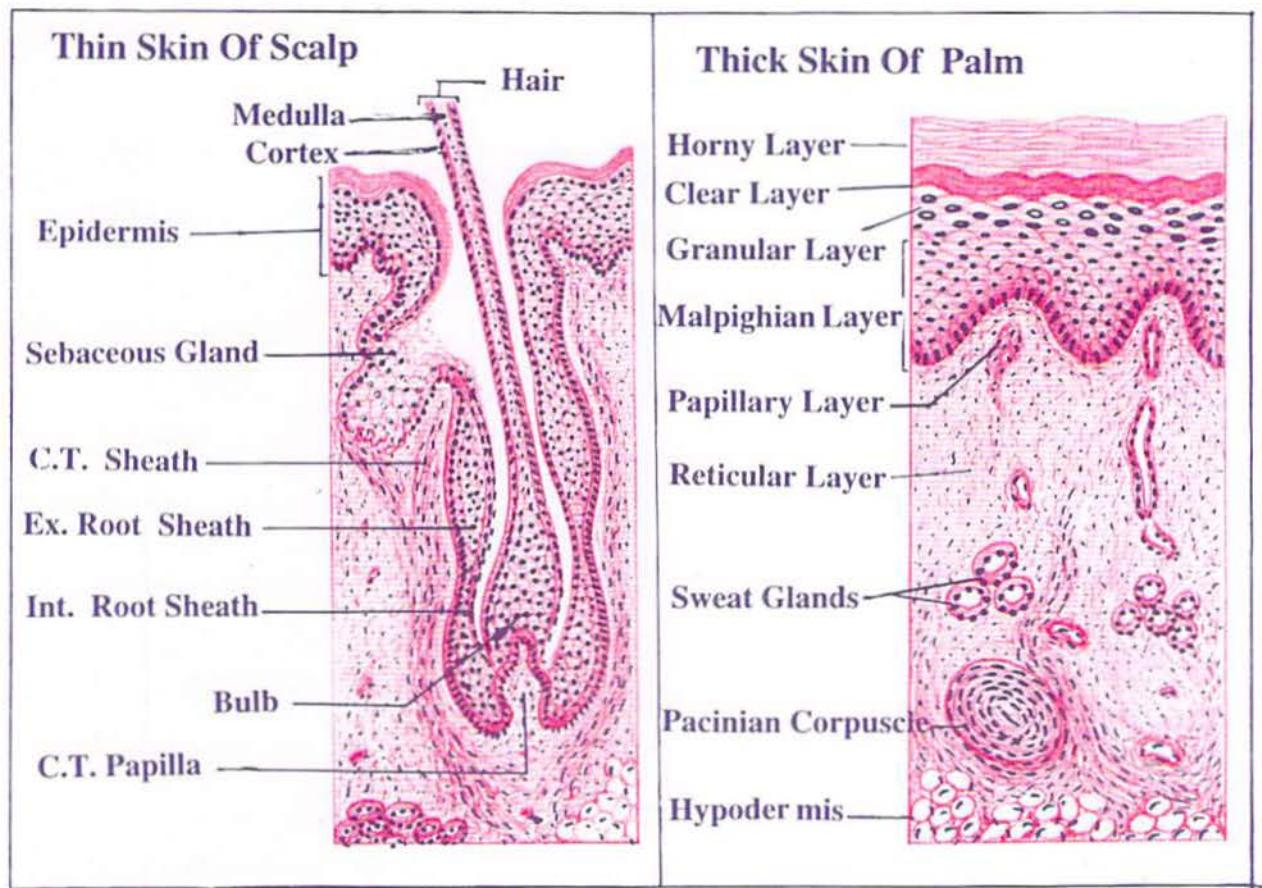
It is the embedded part of the shaft of the hair. It is surrounded by the **inner and outer root sheaths of the hair follicle**.

c) The Hair Follicle: It is formed of epidermal and dermal cells:

The **epidermal cells form** the inner and outer root sheaths of the hair follicle.

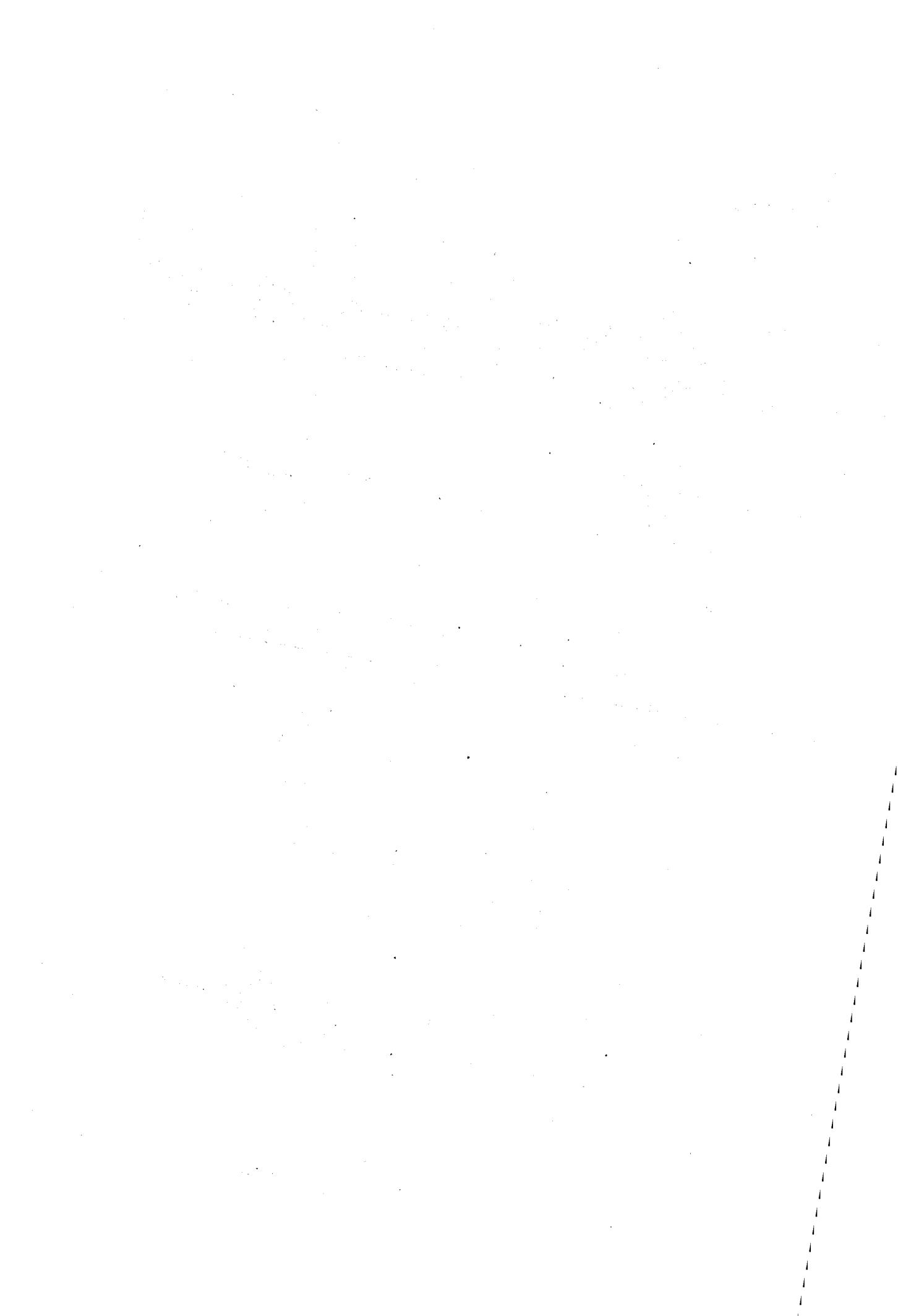
1. The Inner Root Sheath Of The Hair Follicle Is Formed Of:





**Blood Film
(Microscopic Field)**

[Plate 10]



- a) **Inner cuticular** layer formed of scales rich in soft keratin.
- b) **Huxley** layer formed of transparent cells rich in hyaline granules.
- c) **Henle's** layer formed of elongated cells rich in hyaline granules.

2. The Outer Root Sheath of the hair follicle:

It is formed only of the germinal **Malpighian layer** of the epidermis.

3. The C.T. sheath of the hair follicle is formed of the C.T. of the dermis.

The Hair Bulb: It is the terminal part of the hair. It is present over a vascular portion of the dermis called **hair papilla**.

Colour and Pigmentation of Hair

Melanocytes are present among the basal cells of the hair follicle. They form melanin pigments which are then distributed in the cortex of the hair.

Grey Hair: As people become older, their hair turns grey. This is, due to the inability of melanocyte cells to form tyrosinase enzyme and melanin pigments.

Yellow Hair: It is under the control of genes, it contains pheomelanin pigments.

Baldness: It is not common in women, it is controlled by genetic factors and by male sex hormones.

The Arrector Pili Muscles Of Hair:

These are **smooth muscles** extending between the C.T. sheath of the hair follicles and the papillary layer of the dermis. Contraction of these muscles erects the hairs. These muscles are innervated by the autonomic nervous system.

The Sebaceous Glands

- They are simple or compound branched acinar glands.
- They are commonly associated with hairs.
- They are present also in non-hairy skin of the prepuce of the penis, labia minora, lip and in the areolae of the nipples.
- **They are formed of secretory parts and excretory ducts:**

a) **The Secretory Parts of Sebaceous Glands** are formed of acini lined with peripheral basal flat germinal cells and central polyhedral vaculated cells. They secrete **sebum** which is formed of lipid and cellular debris.

Sebaceous glands are holocrine gland, they secrete all their products.

b) **The excretory Ducts of Sebaceous Glands** open in the upper parts of the hair follicles. They are lined with stratified squamous epithelium.

Function of the Sebum: It acts as a cream preventing evaporation and protecting the skin from cracking. It has some antibacterial and antifungal actions.

The Nail

- It is formed of a translucent hard keratin layer.
- Each nail consists of a **free edge, a body and a root** resting on the nailbed.
- **The nail bed:** It is present under the body of the nail. It is formed of the Malpighian layer of the epidermis and by the C.T. dermis of skin. It is rich in B.V. There is no dermal papillae in the nail bed.
- Nails protect the tips of fingers, they are also used as tools.

Pigmentation Of Skin

The Colour Of The Skin Depends Upon These Factors:

1. Contents of **melanin and carotene pigments** in the skin.
2. Degree of **skin vascularity** by blood vessels.
3. Colour index of the **circulating blood** in the B.V.
4. Concentration of **melanin pigments** in melanin forming and melanin carrying cells. **These cells are the following:**
 1. **Melanocytes** which form melanin from the protein (tyrosin).
 2. **Melanophores** which carry and store melanin in their cytoplasm.
 3. **Keratinocytes;** are the epidermal cells which carry melanin.

1. Melanocytes

- They are branched cells with multiple processes. They form melanin pigments.
- They are present between the basal cell layer of the epidermis.
- Melanocytes are derived from embryonic cells called melanoblasts.
- **Melanocytes synthesize melanin which is injected by their processes to the keratinocytes of the epidermis and to melanophore cells in the dermis by a process called Cytochrome Secretion.**
- Melanocytes are rich in tyrosinase enzyme, they give **Positive Dopa Reaction.**

2. Melanophore Cells

Melanophores are C.T. cells and are **mesodermal** in origin. They do not form melanin, but they receive melanin pigments from melanocytes. They give **negative Dopa Reaction.**

3. The Pigmented Keratinocytes

Pigmented Keratinocytes are the deep pigmented cell layer of the epidermis. They receive melanin pigments from melanocytes.

N.B. The Blood Supply of Skin is through cutaneous and papillary arterioles. Arterio venous anastomoses are also present to regulate blood pressure and body temperature.

The following table shows the differences between melanocyte and melanophore

Melanocyte	Melanophore
<ol style="list-style-type: none"> 1. It is ectodermal in origin. 2. It is present between the basal cells of the epidermis and the basal parts of the hair follicles. 3. It forms melanin pigments. 4. It contains tyrosinase enzyme. 5. It gives positive DOPA reaction. 6. Its melanin pigments are fine and regular. 7. It gives its melanin pigments to the epidermal cells and to melanophores. 	<ol style="list-style-type: none"> 1. It is mesodermal in origin. 2. It is present in the C.T. of the dermis. 3. It Carries melanin pigments. 4. It has no tyrosinase enzyme. 5. It gives negative DOPA reaction. 6. Its melanin pigments are much larger and more irregular. 7. It does not elaborate easily its melanin pigments.

The following table shows the differences between the thick or non-hairy skin (skin of the palm and sole) and the thin or hairy skin (skin of the scalp and of other body surfaces).

Thick or non hairy skin	Thin or hairy skin
<ol style="list-style-type: none"> 1. Present in the palms, soles, lateral surfaces and the tips of fingers, toes, nipple, glans penis and clitoris. 2. The epidermis is thick and is formed of: <ol style="list-style-type: none"> a) Thick Malpighian layer. b) Thick granular layer. c) Presence of Lucidum layer. d) Very thick horny layer. 3. No hair follicles. 4. No sebaceous glands. 5. No arrector pili muscles. 6. Presence of ridges and furrows on the surface. 7. Regular dermal papillae. 	<ol style="list-style-type: none"> 1. Present in the other body areas. 2. The epidermis is thin and is formed of: <ol style="list-style-type: none"> a) Thin Malpighian layer. b) Very thin granular layer. c) No lucidum layer. d) Very thin horny layer. 3. Presence of hair follicles. 4. Presence of sebaceous glands. 5. Presence of arrector pili muscles. 6. Presence of less ridges and furrows on the surface. 7. Irregular dermal papillae.

The Blood Vascular System

There are 3 types of blood vessels:

Arteries, veins and connecting vessels between arteries and veins.

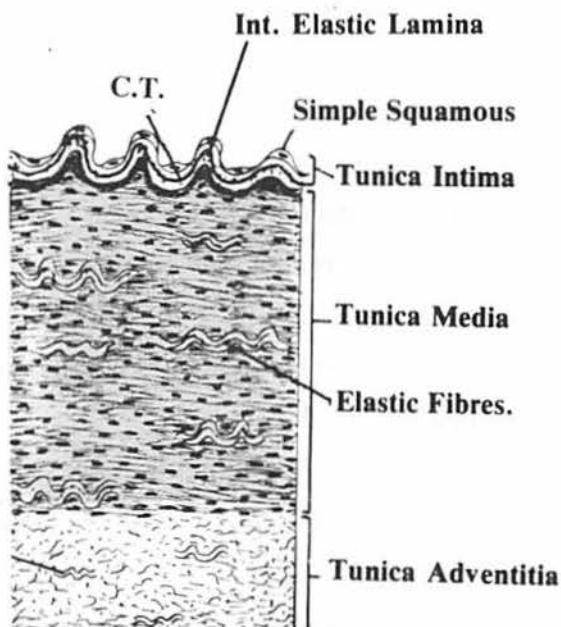
Any medium-sized artery is made up of 3 layers or coats from inside outwards, these layers are:

1. **Tunica Intima:** It is the innermost layer and is formed of 3 elements:
 - a) Simple squamous endothelium.
 - b) Subendothelial layer of C.T.
 - c) Internal elastic lamina.
2. **Tunica Media:** It is the middle layer and is formed of 3 elements:
 - a) Circular smooth muscle fibres.
 - b) Few scattered elastic fibres.
 - c) Fine collagenous fibres.
3. **Tunica Adventitia:** It is the outermost layer and is formed of 3 elements:
 - a) Mostly collagenous fibres.
 - b) Some elastic fibres.
 - c) Some C.T. cells.

The Medium-sized Vein: It is formed also of the 3 tunicae or layers.

The following table shows the differences between a medium-sized artery and a medium-sized Vein (See Plate 11)

Medium- Sized Artery	Medium - Sized Vein
<ol style="list-style-type: none">1. The lumen appears rounded.2. The lumen contains no blood after death.3. It has a thick wall but narrow lumen.4. There are no valves.5. The intima is thick, folded and has a well-developed internal elastic lamina.6. The media is thick and contains elastic fibres.7. External elastic lamina may be present between the media and adventitia.8. The adventitia is thin and contains some elastic fibres.9. No lymphatic capillaries in its wall.10. It has a rapid flow of arterial blood.	<ol style="list-style-type: none">1. The lumen appears collapsed.2. Its lumen usually contains blood.3. It has a thin wall but wide lumen.4. They often have valves.5. The intima is thin, not folded and has no elastic lamina6. The media is thin with very few elastic fibres.7. No external elastic lamina.8. The adventitia is thick and is very rich in collagenous fibres.9. Lymphatic capillaries may be present in its adventitia.10. It has a slow flow of venous blood.



A Medium-Sized Artery

The Arterioles

The arterioles are the small branches of the arteries. They supply the tissues and organs with arterial blood. They control the blood pressure.

The arterioles are characterized by:

1. They have **narrow lumens** not more than 0.1 mm. in diameter.
2. The **intima** is made up of endothelium and thin elastic lamina.
3. The **media** is formed of one or two layers of smooth muscles.
4. The **adventitia** is formed of C.T.

The Metarterioles, are the terminal parts of the arterioles before their connections with the blood capillaries. They have sphincters at their terminals.

Large Elastic Arteries

The large elastic arteries in the body are: the aorta, the pulmonary, the subclavian and the innominate. Their walls, maintain the blood pressure during ventricular relaxation. They have **thick walls**, very wide lumens and their media are very rich in **elastic fibres**. Their structures are more or less the same as the Aorta.

The Aorta (see plate 11)

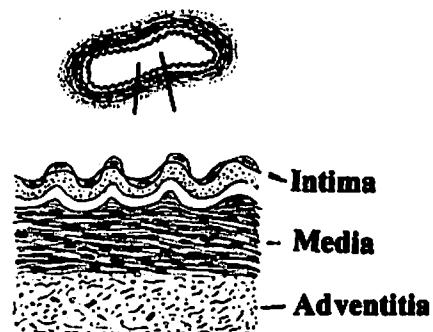
Characteristics of the Aorta:

- It has a very thick wall and a very wide lumen.
- Its **intima** is thick and is rich in elastic fibres.
- The **media** is very thick and is made up of fenestrated elastic membranes enclosing between them smooth muscles, collagenous and reticular fibres.
- The **adventitia** is thin. It contains collagenous and elastic fibres. It also contains **nerves and small blood vessels (vasa vasorum)**. These vasa vasorum supply the outer part of the tunica media and tunica adventitia with blood and nutrients.

The Basilar Artery

Characteristics of basilar or cerebral arteries:

1. They supply the brain.
2. They have thin walls.
3. Their **internal elastic lamina** are thick.
4. Their media and adventitia are thin.
5. They have wide lumens.



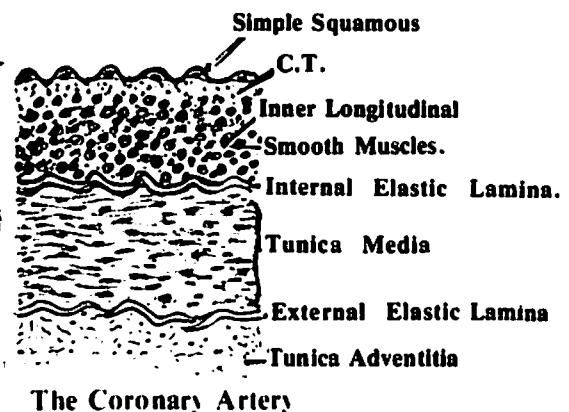
Basilar Artery

Coronary Arteries

They supply the heart with blood.

They are characterized by:

1. Thick Intima Which is Formed of:
 - a) Simple squamous endothelium.
 - b) Subendothelial layer of C.T.
 - c) Longitudinal smooth muscle fibres.
2. The media is thin, it is formed of circular smooth muscle fibres, internal and external elastic laminae.
3. The adventita is formed of areolar C.T. with collagenous and elastic fibres.



Umbilical Artery

The Umbilical Artery is characterized by:

1. It is present in the umbilical cord and it carries venous blood.
2. It has no elastic laminae.
3. The smooth muscles of its media are arranged as an inner longitudinal and an outer circular.
4. Its adventitia is formed of mucoid C.T.

Functions of the Different Types of Arteries:

1. The Aorta allows a constant flow of blood by its elastic recoil.
2. The medium-sized arteries distribute the blood to the whole body.
3. The arterioles control the blood pressure.

Veins

Veins carry venous blood from the tissues. They start as post-capillary venules which are collected to form muscular venules, then form large Veins.

The Post Capillary Venules Are Characterized By:

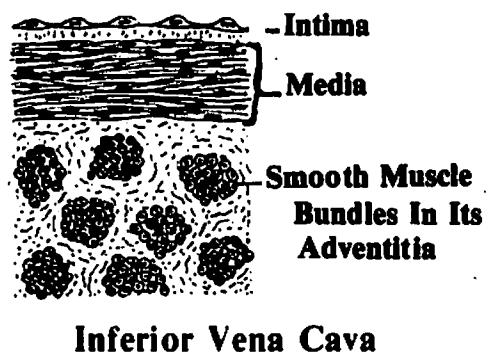
1. They are lined by simple squamous cells rich in actin filaments.
2. A basement membrane enclosing some Pericyte cells.
3. Capillary venules can retract to allow leucocytes to pass to enter the tissues.

Large Muscular Venules Are Characterized by:

1. They are lined by simple squamous endothelium rich in actin filaments.
2. Presence of a basement membrane outside the endothelial lining.
3. Thin media formed of smooth muscles.
4. Thin adventitia formed of areolar C.T.

The Inferior Vena Cava

- Characteristics of large Veins e.g. Inferior Vena Cava:
 - They have wide lumens with many valves.
 - The valves are folds of their intima.
 - They have thin media with no elastic lamina.
 - The adventitia is thick and contains longitudinal smooth muscle bundles (see plate 11).



Connections Between Arterioles And Venules

Arterioles are connected with venules by:

1. Blood capillaries.
2. Sinusoids.
3. Arteriovenous anastomosis.

1. The Blood Capillaries

1. They are present all over the body. They branch to form capillary beds.
2. They have rounded regular and complete lumens about **8 microns** in diameter.

Functions of Blood Capillaries:

1. Selective exchange of materials between blood and tissues.
2. Secrete prostaglandin which prevent formation of thrombus.
3. Convert angiotensin I into angiotensin II.

Each capillary is formed of:

1. Simple squamous endothelium.
2. Basement membrane surrounding the endothelium. This basement membrane may split to enclose small cells called pericytes. These pericytes are undifferentiated cells, they can differentiate to form smooth muscle cells, or endothelial cells or fibroblast cells.

Types of Blood Capillaries

1. Non Fenestrated Capillaries which have the following characters:
 - They have **no pores** in their walls.
 - Lined with endothelial cells joined together by tight junctions.
 - Surrounded by **continuous layer** of basal lamina.
 - Brain capillaries are more surrounded by neuroglia.
 - **They are present in:** Brain, bone, lungs, exocrine glands and skin.
2. Fenestrated Blood Capillaries which have the following characters:
 - They have **pores** in their walls.
 - Lined with **fenestrated endothelium** separated by pores which are covered by **diaphragms** except kidney capillaries.
 - They are present in: kidney, intestine and endocrine glands.
3. Sinusoidal Capillaries or Blood Sinusoids: in liver, spleen and bone marrow:

2– The Blood Sinusoids

1. They have irregular, wide lumens from 5-30 microns in diameter.
2. They are lined with simple squamous endothelial cells. The sinusoids are surrounded by a thin layer of reticular C.T.
3. **Macrophages** are present outside the sinusoidal wall, they extend their pseudo-podia into the sinusoids in order to phagocytose foreign bodies which may be present in the blood stream.
4. Their walls contain pores not covered by diaphragms.

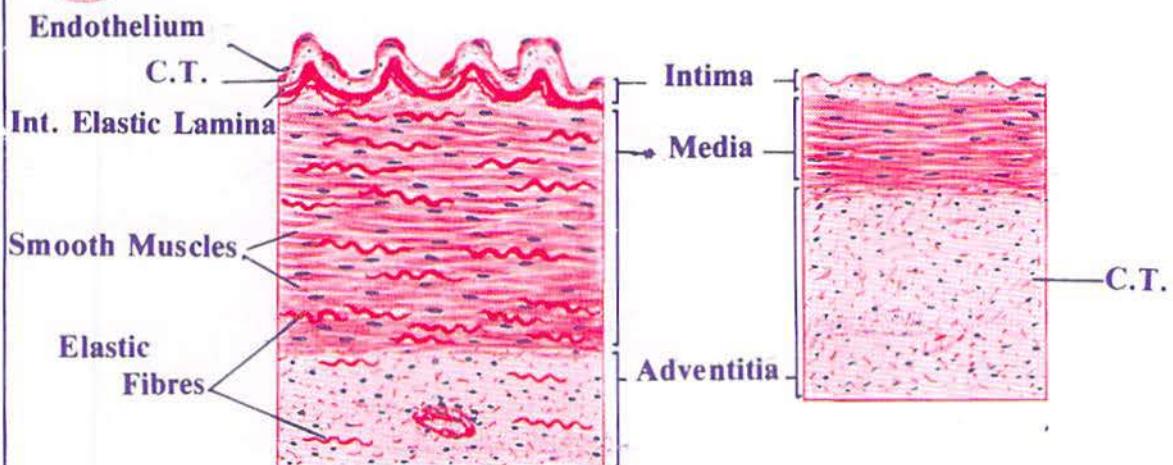
Sites and Functions of Blood Sinusoids:

- a) **Present in the bone marrow to carry the formed blood cells.** The slow circulation in the sinusoids causes a **low oxygen tension** which is essential in stimulating the process of formation of red blood cells in the bone marrow.
- b) **Present in the spleen to store blood.** The phagocytic cells present in the sinusoidal wall can clean the blood from any foreign bodies.
- c) **Present in the liver to allow liver cells to be in direct contact with the blood.**
- d) **Present in the endocrine glands to carry the secreted hormones** and to increase the blood supply to the endocrine secretory cells.

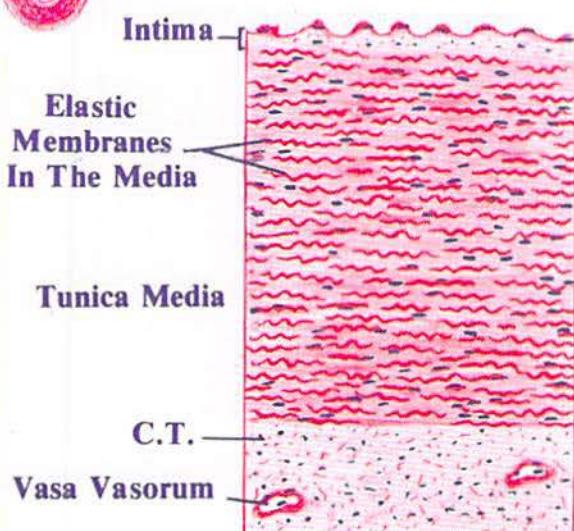
Differences Between Capillaries And Sinusoids

Capillaries	Sinusoids
1. Present all over the body.	1. Present in liver, spleen, bone marrow.
2. Having narrow regular lumens.	2. Having wider irregular lumens.
3. Their walls are formed of simple squamous cells and are surrounded by continuous basement membrane.	3. Their walls are lined by fenestrated cells and are surrounded by reticular C.T.
4. Their walls have no pores except in Kidney and endocrine glands.	4. Their walls contain Pores.
5. Undifferentiated pericyte cells are present in their walls.	5. Phagocytic macrophage littoral cells. are present outside their walls.

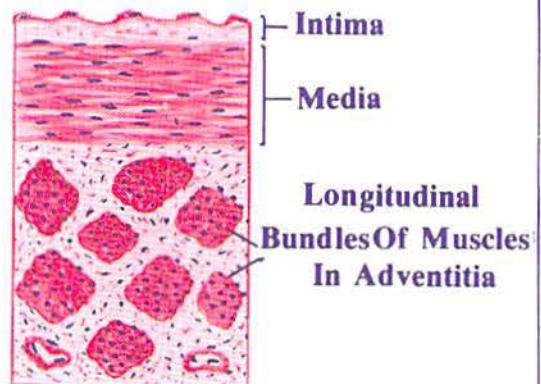
Medium - Sized Artery and Vein



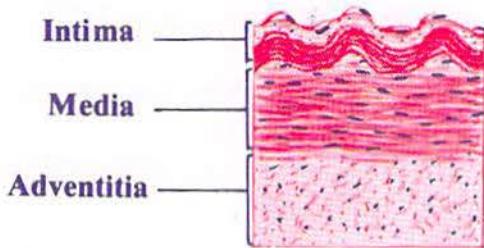
Aorta



Inferior Vena Cava



Basilar Artery



Blood Capillary

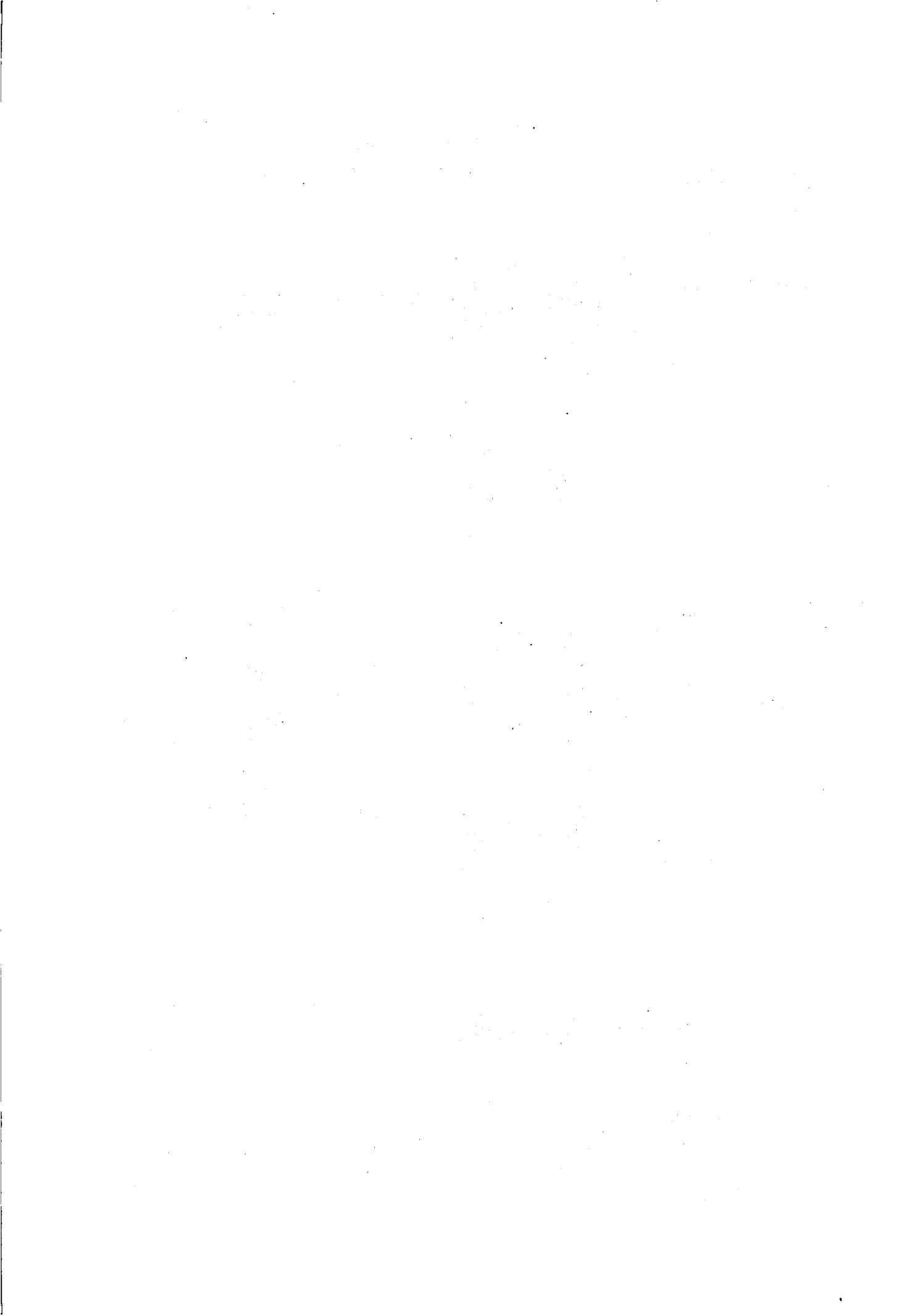


Blood Sinusoid



Zakaria

[Plate 11]

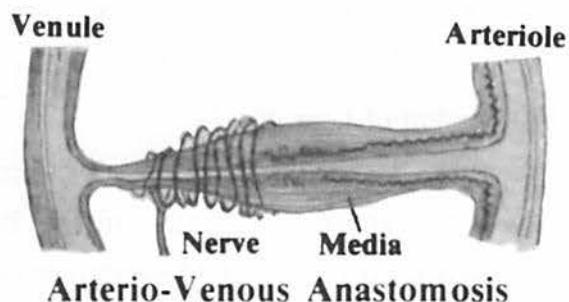


3- Arterio- Venous Anastomoses

Arterio-venous anastomoses arise as side branches from arterioles to venules without passing through the capillaries. They allow a short and rapid circulation of blood to certain areas or organs of the body.

Arterio-venous Anastomoses are of two types:

1. **Direct connection** between an arteriole and a venule by a side branch. This is found in skin, intestine and uterus.
2. **Glomus or complicated side branch** which is a tortuous shunt present in genital organs, nailbed and ear.



Structure of Arterio-venous Anastomosis

The wall of the connecting segment between an arteriole and a venule has the structural characteristics of a vein at the venous side, while their wall at the arterial side has the characters of an arteriole.

The intermediate segment of the A.V. anastomosis is characterized by:

1. The lumen of these side branches decreases gradually towards the venous side.
2. The internal elastic lamina disappears gradually towards the venous side.
3. The media is well-developed at the venous side and is very rich in longitudinal smooth muscles.
4. Myoepithelial cells are present also in the thick media at the venous side. These cells are richly supplied by autonomic nerves and they act as sphincters.
5. The adventitia becomes thicker at the venous side.

Sites of Arterio Venous Anastomoses:

They are present in the exposed parts of the body as in the tips of fingers and toes, in the external ear, in the nose, in the lip and tongue.

Present also in the internal organs as stomach, intestine, liver, endocrine glands, uterus, thyroid gland, placenta and sympathetic ganglia.

Functions of Arterio- Venous Anastomoses:

1. They conserve the body temperature; they dilate in cold weather, while in hot weather they constrict.
2. They regulate the venous return.
3. They regulate the blood flow to genital organs during erection.
4. They regulate the uterine blood flow during menstrual cycles and pregnancy.

The Lymphatic System

The Lymphatic System Includes:

1. The lymphatic tissues which are:

- a) Lymph nodes
- b) Spleen
- c) Scattered lymphatic nodules in certain organs of the body
- d) Tonsils
- e) Thymus

2. The Lymphatic vessels: They are the lymphatic capillaries and the lymph vessels. They carry the lymph.

Formation of Lymph:

The tissue fluid which is filtered from the tissues and from the blood capillaries around the cells of the body is drained by blind-ended lymphatic capillaries. This tissue fluid when it enters the lymphatic vessels it is called lymph.

The lymph may contain some harmful substances, so it is filtered in lymph nodes and nodules. Lymph flows in one direction inside the lymphatic capillaries and lymphatic vessels. The filtered lymph goes again to the blood stream through a large lymphatic vessel called Thoracic duct.

The following table shows the differences between blood capillaries and lymphatic capillaries:

Blood Capillaries	Lymphatic Capillaries
<ul style="list-style-type: none">1. Present superficial in position under the skin and mucous membranes.2. They are the branching vessels of arterioles and are connected with the venules at the other side.3. They have uniform diameters.4. The endothelium is fenestrated.5. They are surrounded with basement membranes and pericytes.6. The lumen is usually patent.7. No anchoring collagenous fibres outside their wall8. They carry blood.	<ul style="list-style-type: none">1. Present more deep in position than blood capillaries.2. They start as blind-ended channels and are connected to lymph vessels at one side only.3. Their diameters are irregular.4. Non-fenestrated endothelium.5. They have no basement membrane and no pericytes.6. The lumen may be collapsed.7. Anchoring collagenous fibres connect their wall to surrounding C.T.8. They carry lymph

Large LymphVessels are formed of intima, media and adventitia similar to veins, they also have valves.

Lymph Nodes

Shape and Functions of Lymph Nodes:

Lymph nodes are bean or kidney-shaped organs present along the course of lymphatic vessels in order to **filter the lymph** from any organisms or foreign bodies. They contain lymphocytes, macrophages, **Killer cells and plasma cells**.

Sites of Lymph Nodes: They are present in groups in the axilla, groin, in the neck, in the thorax, in the abdomen and in popliteal and cubital areas.

Size: They range in size from a small seed to the size of a large almond.

Afferent Lymph Vessels bring lymph to lymph nodes.

Efferent Lymph Vessels carry lymph away from lymph nodes.

Structure of Lymph Node

Each lymph node is formed of a C.T. stroma and a Parenchyma of Certain cells:

The Stroma Of Lymph Node

It is the C.T. framework of the lymph node; It Includes The Following:

(1) **C.T. capsule,** (2) **C.T. trabeculae** (3) **Reticular C.T. network**

The Capsule: It is formed of collagenous and elastic C.T. fibres separated by C.T. cells. Smooth muscles are present at the hilum of lymph node.

The Trabeculae, formed of C.T. cells and fibres, they descend from the capsule to divide the cortex of lymph node into compartments.

The Reticular Network: It is a fine network of reticular C.T. formed of **Dendritic reticular cells and reticular fibres**. It is condensed more in the cortex than in the medulla. It can be stained brown with silver.

Cells of the Stroma of the Lymph Node

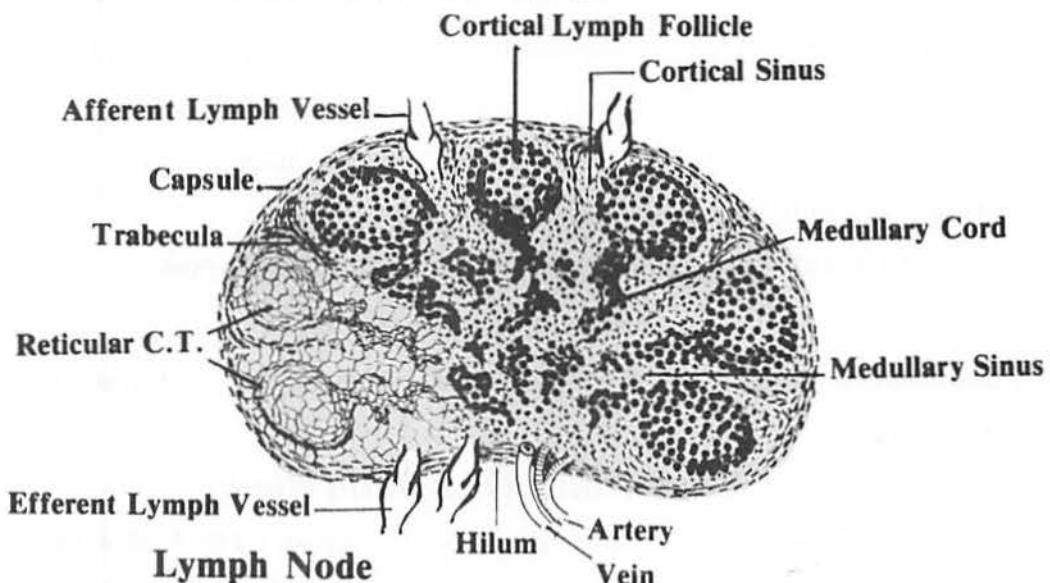
A. Dendritic Reticular Cells: They are branched cells with multiple cytoplasmic processes. They are **non-phagocytic cells** but they can attract and bind antigens on their surfaces. They are joined with each other by desmosomes. They are present in large numbers near B-lymphocytes.

B. Macrophage Cells: They are branched cells with large nuclei. They phagocytose foreign bodies, they are antigen-presenting cells. They secrete **Interleukin I** which regulates proliferation of lymphocytes.

C. Fibroblast Cells: They are present mainly around blood and lymph vessels.

The Parenchyma Of Lymph Node

The parenchyma are the functioning cells of the lymph node. These cells are arranged in condensed masses under the capsule forming the **cortex of the lymph node**. The centre of the lymph node contains irregular condensation of lymph node cells and is known as the **medulla of the lymph node**.



The Cortex Of Lymph Node

The Cortex of the Lymph Node Contains:

1. Cortical Lymphatic Nodules.
2. Cortical Lymphatic Sinuses.

1. The Cortical Lymphatic Nodules are of two types:

- a) Primary lymphatic nodules.
- b) Secondary lymphatic nodules.

a) Primary Lymphatic Nodules or Follicles

(Aggregation of lymphocytes without germinal centres)

- They are rounded, oval or pyramidal in shape.
- They are present under the capsule of lymph node.
- They are formed of aggregations of small lymphocytes without a germinal centre.

When these primary lymphatic nodules are exposed to infections or to any antigens, the small lymphocytes develop into **activated medium-sized lymphocytes**. These newly-formed activated lymphocytes aggregate in the centre of the primary lymphatic nodules to form its germinal centre and now the primary lymphatic nodule is changed into **Secondary Lymphatic Nodule**.

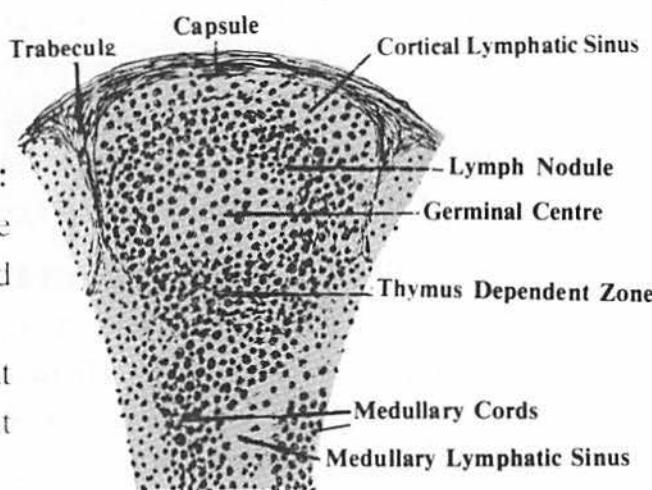
b) The secondary Lymphatic Nodules (Aggregation of lymphocytes with germinal centres)

The Secondary Lymphatic Nodules Are Formed of The Following Cells:

- a) Activated B and T Lymphocytes.
- b) Plasmablast and plasma cells.
- c) Macrophages.
- d) Dendritic reticular cells.

The Cortical Lymphatic Sinuses:

- These are the spaces which are present between the capsule and the cortical follicles.
- They are lined with fenestrated flat endothelial cells without basement membranes.
- **They contain:** B-lymphocytes Part Of Cortex And Medulla Of Lymph Node macrophages and plasma cells.



The Thymus Dependent Zones or The Para-cortical Zones

- These zones are present in the deep parts of lymph nodes.
- They are rich in T-lymphocytes which have migrated from the thymus.
- They contain the **post-capillary venules** which are lined with simple cubical cells. Through these post-capillary venules, the programmed T-Lymphocytes can migrate from blood to be settled here **in the thymus-dependent zones** in the lymph nodes to perform their multiple functions.

The Medulla Of Lymph Node

The Medulla of the Lymph Node is formed of:

1. Medullary Lymphatic Cords:

- These are collections of B-lymphocytes, plasma cells and macrophages.
- They may be continuous with the cortical follicles.
- They are separated from each other by medullary lymphatic sinuses.

2. Medullary Lymphatic Sinuses:

- They are irregular wide spaces between the medullary cords.
- They are lined with fenestrated flat endothelial cells.
- They contain free lymphocytes, macrophages and some plasma cells.

Circulation of Lymph Inside The Lymph Node

Lymph enters the lymph node by afferent lymph vessels through its cortex. The lymph is filtered through the cortical and medullary sinuses, then the lymph leaves the node through **efferent lymph vessels** at its hilum.

Blood supply of a Lymph Node

The arteries enter the lymph node at its hilum, their branches pass to the cortex where they branch to form arterial capillaries.

The venous capillaries descend from the cortex to form **Post-Capillary Venules** which are lined by simple cubical cells. These venules are collected to form veins which leave the lymph node at its hilum.

Cells Present in the Lymph Node

1. **B-Lymphocytes:** They are the most common cells in both cortex and medulla.
2. **T-lymphocytes:** Present in the Thymus Dependent Zones.
3. **Macrophages:** Present in both cortex and medulla.
4. **Dendritic Reticular cells:** Present in the whole stroma of lymph node.
5. **Plasmablasts:** present in the germinal centres of the cortical follicles.
6. **Activated B-Lymphocytes:** Present in the germinal centres of the follicles.
7. **Plasma Cells:** Present in cortex and medulla of lymph node.
8. **Endothelial Cells:** Lining the cortical and medullary lymphatic sinuses.

Functions of Lymph Nodes

1. **Filtration of lymph** from bacteria by their macrophages.
2. **Formation of lymphocytes.**
3. **Formation of immunoglobulins** by their plasma cells.
4. **Cell Mediated Immunity** by their T-Lymphocytes which are killer cells.

The Non Capsulated Lymphoid Tissue

The Non Capsulated Lymphoid Tissues are present in the digestive, respiratory and uro-genital systems. These **Lymphoid Tissues** are formed of reticular network, lymphocytes, plasma cells and macrophages. These lymphoid tissues are covered by **epithelial membranes** which contain **M-Cells**.

The M-cells: They are present mainly in the covering membranes of the non-capsulated lymphoid tissue of the digestive tract. They are dome-shaped cells with basal concavities. These concavities are rich in lymphocytes and macrophages.

These **M cells** transport the antigens present in the different body systems to the underlying lymphoid tissue.

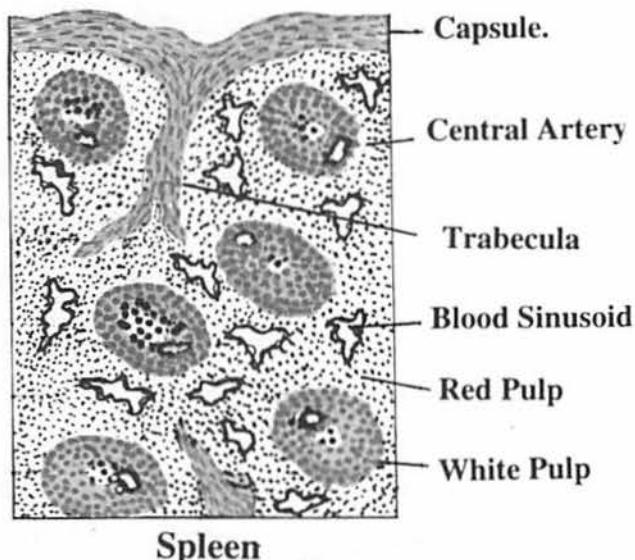
The Spleen

- The spleen is a single intra-abdominal haemolymphatic organ.
- Unlike the lymph node, the spleen acts as a general filter for the circulating blood.
- Unlike the lymph node, the spleen has no afferent lymph vessels, it has only efferent lymph vessels.

Structure of Spleen:

The spleen is formed of a C.T.

Stroma and a Parenchyma of lymphoid tissue in the form of white and red pulps.



The Stroma of Spleen

It is the C.T. framework which includes: **capsule, trabeculae and reticular C.T.**

1. The Capsule:

- It is covered with peritoneum.
- It is formed of collagenous and elastic C.T. fibres and fibroblast cells.
 - The capsule is thin in human spleen but thick in animal spleen.
 - The capsule is rich in smooth muscles.

2. The Trabeculae:

- They are formed of C.T. cells and fibres.
- The trabeculae are **long, thick and rich in smooth muscles**.
 - They radiate mainly from the hilum of the spleen. They contain B.V.

3. The Reticular Network:

- It is made up of reticular fibres and cells.
- It forms the background for the white and the red pulps of the spleen.
 - It can be stained brown with silver.

The reticular network is more condensed in the white pulp than in the red pulp.

The Parenchyma of Spleen

- It is the soft tissue which fills the C.T. framework of the spleen.
- It includes **the white and the red pulps**.

The White pulps or Malpighian Corpuscles

- They are rounded or elongated lymphatic nodules.
- They appear white or grey in fresh section of the spleen.

- Each white pulp is formed of reticular C.T. upon which **T-lymphocytes**, plasma cells and **macrophages** are present at its periphery and **B-lymphocytes**, plasma cells and macrophages are present at its pale **germinal centre**.
- Each pulp contains a small artery at one side known as **central arteriole**.
- The central arteriole is surrounded with **periarterial lymphatic sheath**.

The Differnt Zones Of The White Pulp

The white pulp can be divided into 4 zones from inside outwards.

1. **Thymus-Dependent Zone:** It surrounds the central artery. It is rich in **T-Lymphocytes**.
2. **The Germinal Centre Zone:** It surrounds the thymus-dependent Zone. It is rich in **B-Lymphocytes**, plasma cells and macrophages.
3. **The Follicular Zone** which is formed mainly of **B-Lymphocytes**. It surrounds the germinal zone.
4. **The Marginal Zone:** It forms the periphery of the white Pulp. It is formed of **B and T-Lymphocytes, plasma cells, macrophages and dendritic cells**.

The Blood Sinusoids and Billroth Cords

The areas between the white pulps of the spleen appear red in fresh sections due to the presence of two structures: (blood sinusoids and Billroth Cords).

The Blood Sinusoids

- They are wide blood channels lined with fenestrated flat endothelial cells.
- They are surrounded by non-continuous basement membranes.
- Macrophage cells are present in the wall of sinusoids and are called **Littoral cells**.

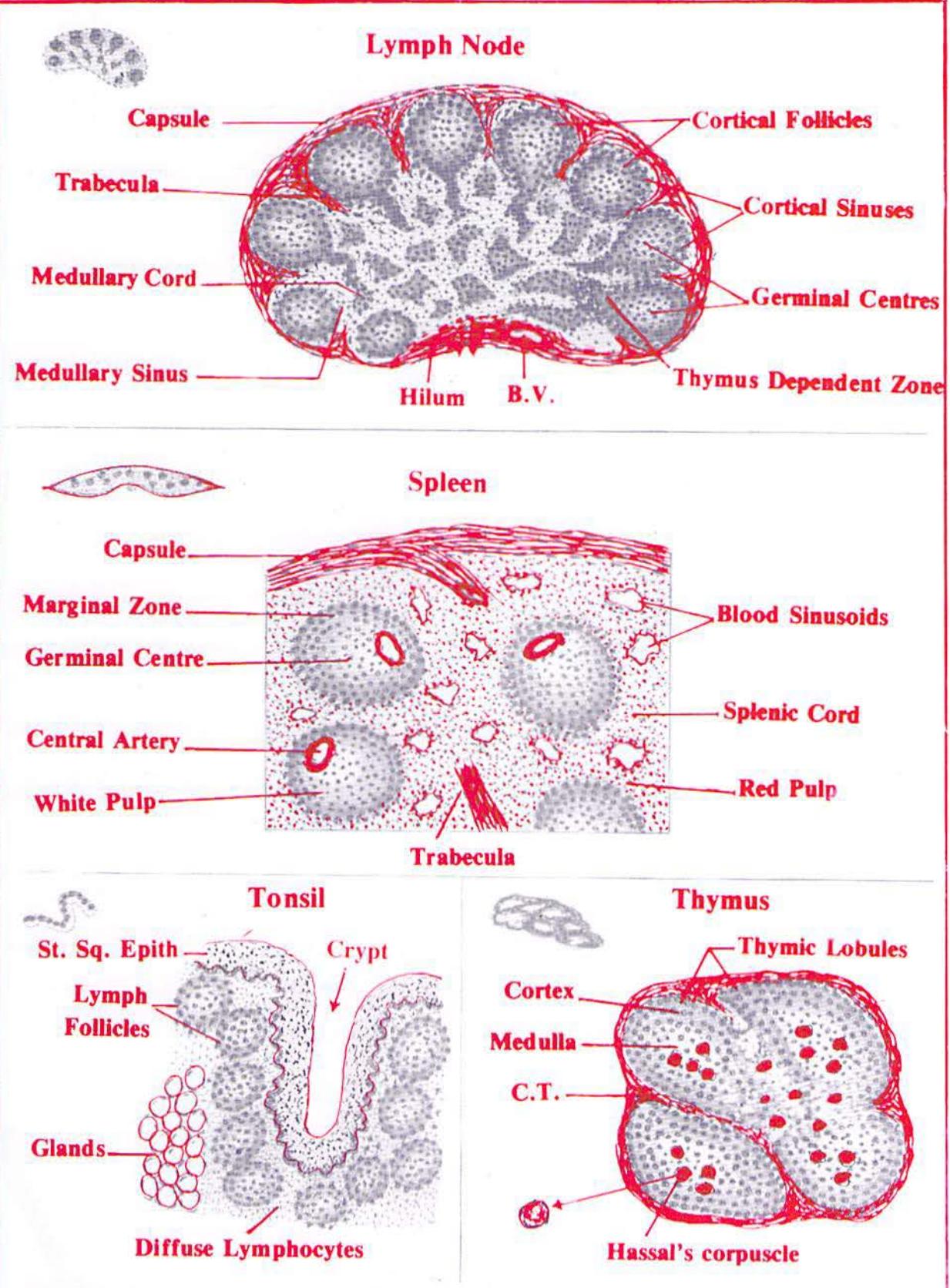
The Red Pulp Or Billroth Cord

- It is the soft tissue, present between the white pulps and the blood sinusoids.
- It is formed of: Lymphocytes, Erythrocytes, Leucocytes and Plasma cells.
- It is rich in phagocytic cells as: Histiocytes, Monocytes and Fixed Macrophages.

Blood Circulation In The Spleen

The **splenic artery**, arise from the coeliac artery, it enters the spleen at its hilum. It divides into **trabecular arteries**, then into smaller arteries. These small arteries enter the white pulps where they form the **central arterioles** of the white pulp. It supplies the white pulp with fine capillaries.

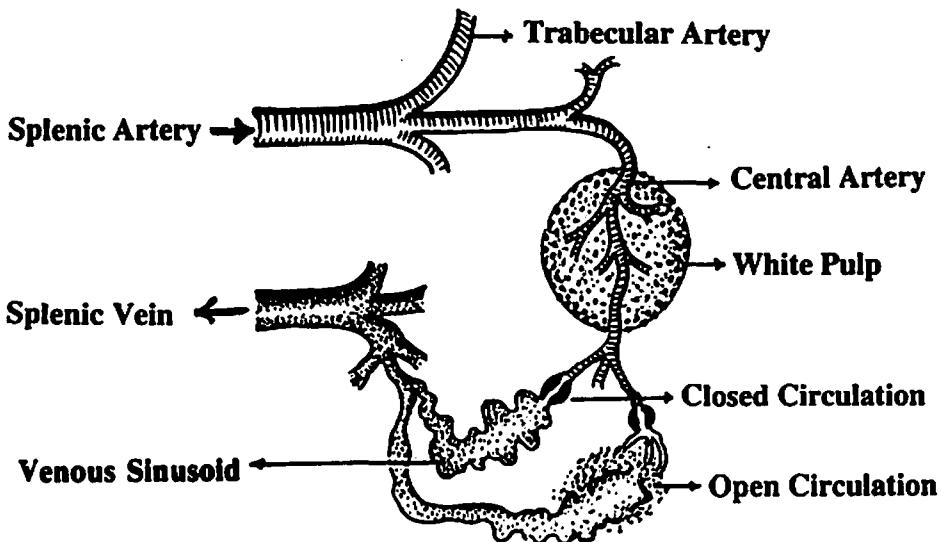
These central arterioles then leave the white pulps to enter the red pulp. In the



Zakarisa

[Plate 12]

red pulp each artery subdivides into small straight branches called **Penicillar Arterioles** of the spleen (The penicillar arterioles diverge like a fan or a brush). These **Penicillar arterioles** open in the tissue of the red pulp by 2 or 3 sheathed capillaries called **Ellipsoids**. These ellipsoids contain very thin holes through which blood can escape to the red pulp.



Blood Circulation In The Spleen

Theories of Blood Circulation Through The Red Pulp:

1. Open Circulation Theory:

This theory assumes that the arterial blood from the capillary **ellipsoids** is delivered directly into the red pulp. The blood then enters the sinusoids through small opening in the sinusoidal wall.

2. Closed Circulation Theory:

This theory assumes that the walls of the capillary ellipsoids are directly connected with the walls of blood sinusoids.

3. The Open and Closed Circulation Theory:

This theory assumes that the blood circulation in the red pulp is closed when the spleen is contracted and the circulation is opened when the spleen is relaxed.

4. Knisely Theory: Knisely assumed that, blood circulation in the human spleen is regulated by the presence of many arterio-venous anastomosis between splenic arterioles and venules.

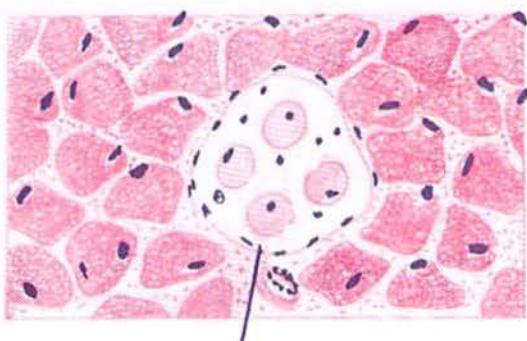
The Venous Blood from the spleen is drained by the red pulp veins which join each other to form trabecular veins then they join each other to form splenic veins.

Functions of The Spleen

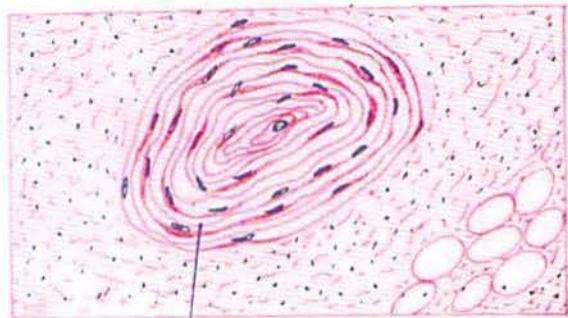
1. During foetal life certain blood cells are formed in the spleen.
2. In adults, it stores blood cells and blood platelets.
3. During haemorrhage, it contracts to pour blood to the circulation.
4. Splenic macrophages filter the blood from bacteria and foreign bodies.
5. Splenic macrophages phagocytose the destructed blood cells.
6. Splenic macrophages can store iron.
7. The spleen has humoral and cell mediated immunological functions.

Differences Between Lymph Nodes And Spleen

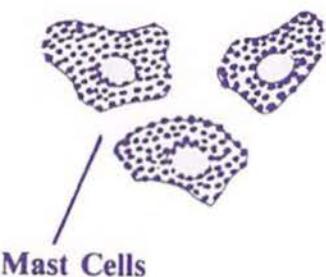
Lymph Nodes	Spleen
<ol style="list-style-type: none">1. Lymph nodes are multiple, present in groups all over the body.2. They filter the lymph.3. They have many afferent and efferent lymph vessels.4. Covered with fascia.5. Capsule is thin, and not adherent.6. Trabeculae are thin, short and arise from the capsule.7. Lymphatic nodules are arranged into cortex and medulla.8. In the cortex there are the lymphatic nodules with apparent germinal centres but with no central arterioles.9. Presence of cortical and medullary lymphatic sinuses.10. Presence of medullary lymphatic cords.11. Cells: are mainly lymphocytes, plasma cells and macrophages.12. Functions: Humoral and cell-mediated immunological functions.	<ol style="list-style-type: none">1. The spleen is a single organ present in the abdomen.2. It filters the blood.3. It has few lymph vessels in the capsule and trabeculae.4. Covered with peritoneum.5. Capsule is partially thick, adherent and rich in smooth muscles.6. Trabeculae are thick, long and arise from the hilum and from capsule.7. Lymphatic tissues are the white and the red pulps (not arranged in cortex and medulla).8. The white pulps are scattered in the spleen. They contain central arterioles but their germinal centres are not apparent.9. Presence of blood sinusoids all over the spleen.10. Presence of Billroth cords or red pulps.11. Cells: are mainly RBCs, Leucocytes, plasma cells and macrophages.12. Functions: Blood storage and immunological functions.



T.S. In Muscle Spindle



Pacinian Corpuscle



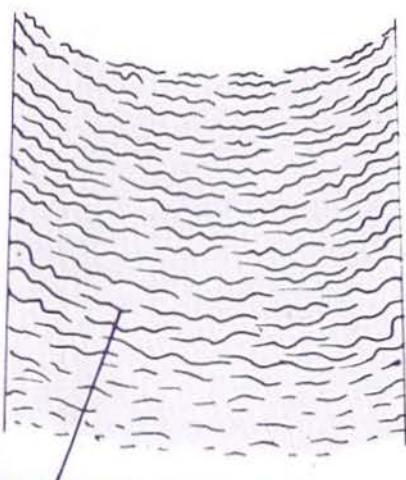
Mast Cells

Toluidine Blue Stain



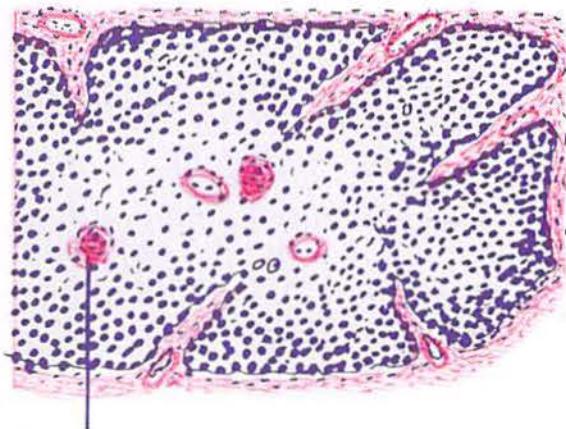
Megakaryocyte

In Bone Marrow



Elastic Fibres In Aorta

Verhoff Stain



Hassal's Corpuscle
of Thymus





The Tonsils

1. The Palatine Tonsils (see plate 12)

These are two ovoid masses of lymphatic tissue which are embedded in the C.T. under the mucous membrane of the oral part of the pharynx.

Each tonsil is covered with non-keratinized stratified squamous epithelium which dips into the underlying lymphatic tissue to form primary and secondary crypts.

The lymphatic tissue of the tonsils consists of the following:

1. Lymphatic nodules with or without germinal centers.
2. Diffuse lymphatic tissue formed of lymphocytes, plasma cells and macrophages.
3. Mucous glands are present in the C.T. of the tonsils but their ducts do not open into their crypts. Therefore, the tonsillar crypts are inflamed easily because they are not continuously washed by the saliva.

2. The Pharyngeal Tonsil or the Adenoid

This consists of a single mass or diffuse lymphatic tissue present in the nasopharynx. Its structure is similar to palatine tonsil.

It is covered by pseudo-stratified columnar ciliated epithelium.

A child who has an enlarged pharyngeal tonsil is said to have Adenoid,

3. The Lingual Tonsil

- It is a collection of lymphatic nodules in the C.T. under the tongue.
- Its lymphatic nodules have germinal centers and are separated by diffuse lymphatic tissue rich in lymphocytes, plasma cells and macrophages.
- Their covering stratified squamous epithelium extends down into their crypts. The mucous secretion of their glands wash bacteria and debris thoroughly. Therefore, infection is not common in the lingual tonsil.

4. The Tubal Tonsils

- These are 2 masses of lymphoid tissue present in the nasopharynx around the Eustachian opening of the Eustachian tubes. Some of their inflammatory cells may migrate to the middle ear causing otitis media.

Functions of Tonsils:

They are present at the beginnings of the digestive and respiratory tracts to guard against infections. They also form antibodies and lymphocytes.

The Thymus

- The thymus gland acts as the site of development and differentiation of **T-Lymphocytes**. It has also an **endocrine function**.
- It is a single gland formed of two lobes.
- It is present behind the sternum and extends upwards into the neck.
- The size of the thymus varies greatly in relation to age. It continues to increase in size from the second year of life until the age of puberty. After puberty, It begins to decrease in size due to the effect of Sex Hormones.
- It has only efferent lymph vessels but no afferent lymphatic vessels.

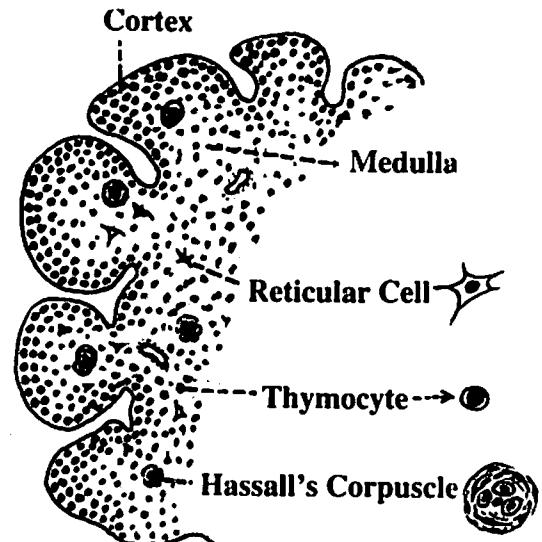
Structure Of The Thymus

- The Thymus gland is formed of **C.T. Stroma and parenchyma of cells**.
- **The C.T. Stroma** Consists of Capsule and Trabeculae.
- **The Capsule:** It is formed of C.T fibres and C.T cells rich in B.V.
- **The Trabeculae** are thin septa of C.T. fibres descending from the capsule dividing the thymus into two lobes and many lobules.
- **The Reticular Network** is absent and is replaced by reticular cells.

The Parenchyma of the Thymus:

- **Each thymic lobule** is formed of an outer cortex and a central medulla.
- **The medullae** of several lobules may be continuous with each other.
- **The Cortex and Medulla of the thymic lobules contains these cells:**
- **Epithelial Rrticular Cells, T-Lymphoblast, T-Lymphocytes and Macrophages.** Hassall's Corpuscles are present only in the medulla. The Thymus has no B-Lymphocytes and no plasma cells.

1. **The Epithelial Reticular Cells:** They are branched cells with oval nuclei and basophilic cytoplasm. They secrete Thymic factors and thymic Hormones.
2. **The T-Lymphoblasts (thymoblasts):** They are the immature cells of T-Lymphocytes. They have basophilic cytoplasm and larg rounded nuclei.
3. **The T-Lymphocytes (Thymocytes):** They are mature cells. They leave the thymus to be settled in the thymus dependent zones of the other lymphatic tissues as lymph nodes and spleen.



One Lobule Of A Thymus

4. **Hassal's Corpuscles:** They are present in the medulla of the thymic lobules only. Their number increase with the progress of age. **Each Hassall's corpuscle** is formed of a central acidophilic mass of degenerated reticular cells surrounded by concentric layers of epithelial reticular cells.
5. **The Thymic-Macrophages:** They are branched large cells. They engulf (eat) the degenerating thymocytes and foreign bodies.

Blood supply Of Thymus: Multiple arteries pierce the capsule and branch into small arterioles and capillaries to supply the cortex and medulla of the thymic lobules. The antigens in the blood of these capillaries are separated from the cells of thymus by the **Blood Thymic Barriers**. The thymic capillaries drain into the Post Capillary Venules which are lined by **simple cubical cells**.

Thymic Barrier

Definition: It is a wall of cells and tissues which protect the developing T-Lymphocytes from the circulating blood antigens. Thymic Barrier is present only in the Cortex of Thymus.

The Thymic Barrier is formed of the following layers:

1. The endothelial cells of the blood capillaries of the thymus.
2. The basement membrane of these blood capillaries.
3. Macrophage cells outside the blood capillaries: these cells remove the antigens which may escape outside the blood capillaries.
4. Epithelial reticular cells which form a sheath outside the blood capillaries and around the macrophages.

Functions of the Thymic Barrier

The Thymic barrier form a protecting layer between the circulating blood antigens and the cells of the thymus. Thus, the thymic barrier protects the newly formed thymic T-lymphocytes from being exposed to any circulating antigens.

N.B.: The absence of afferent lymph vessels in the thymus protect it also from the circulating antigens.

Functions of The Thymus

1. It is essential for the normal development of lymphoid tissue in early life.
2. Important for the development of immunological response in adult.
3. The Thymic Epithelial Reticular Cells secrete different Thymic Factors and Thymic Hormones as: Thymosin, Thymopoietin and Thymulin which regulate the development and differentiation of T-Lymphocytes.

The Immune System Of The Body

Definition: It consists of several Immuno-Competent Cells which have the capacity to react with foreign substances (Antigens) entering to the body. They can induce immune response (cellular, humoral or both) against the entered foreign substances in order to inactivate or destroy these foreign antigens.

The Immune System Includes: Lymph Nodes, Spleen, Thymus, Tonsils And The Following Free cells:

1. **B-Lymphocytes:** Concerned with humoral immunity.
2. **T-Lymphocytes Which are:** T-Helper cells, T-Suppressor cells, T-Memory cells and T-killer cells. They secrete lymphokines which include: Interleukin, Interferon, and Chemotactic Stimulating Factors.
3. **Null Cells:** which are Natural Killer cells.
4. **The Macrophage Cells** which act as antigen-presenting cells.
5. **Langerhan's Cells of the Skin** act as antigen presenting cells.
6. **M-Cells In the Digestive Tract** act as antigen presenting cells.
7. **Blood Monocytes** which can differentiate to Macrophages.
8. **Von-Kupffer Cells** of the liver have immunological functions in liver.
9. **Microglia In Brain Tissues** have immunolgical functions in brain.
10. **Plasma Cells** secrete immunoglobulins IgG. Mast cells and Basophil Leucocytes carry IGE. Lymphocytes carry IGA. (immunoglobulin A).
11. Some body fluid secretions as tear, saliva and bile contain IGA.

The Macrophage System

OR The Mononuclear Phagocytic Cells

OR The Reticulo Endothelial System

Definition: This system is formed of groups of phagocytic cells which are present in different tissues and organs of the body to destroy foreign elements.

How can we study the sites and distribution of these cells?

This is done by injecting vital non-toxic stains as trypan blue or India ink into living animals. The dye will be phagocytosed by these cells.

Sites Of The Mononuclear Phagocytic Cells In The Body

1. **Bone marrow:** The bone marrow is rich in phagocytic cells as:
 - a) **Monocyte Cells.**
 - b) **Macrophage histiocyte cells** in the C.T. stroma.

- c) **Macrophage Littoral cells:** present outside the wall of blood sinusoids.
- 2. **Brain:** In the C.N.S. there are the **microglia cells**. These cells are mesodermal in origin, with multiple dendrites but with no axons and no Nissl granules. They can move and phagocytose foreign bodies.
- 3. **Blood:** Blood monocytes change into macrophage cells when they migrate to the surrounding tissues.
- 4. **Bone Osteoclast Cells:** It is a multinucleated giant phagocytic cell.
- 5. **Connective tissue:** C.T. **histiocytes or clasmatocytes.** They are highly phagocytic cells. C.T. Macrophages are of 2 types; Fixed and Free Macrophages.
- 6. **Lung:** The lung alveoli contain these free phagocytic cells:
 - a) **Dust cells** which engulf dust particles.
 - b) **Heart-failure cells** which can engulf blood cells in case of heart failure.
- 7. **Liver:** It is rich in these phagocytic cells:
 - a) **Von Kupffer's cells:** Which are branched fixed cells with basophilic cytoplasm. They are present outside the blood sinusoids of the liver.
 - b) **Histiocytes:** They are present in the C.T. stroma of the liver.
 - c) **Monocytes:** They migrate from the blood to C.T. of liver.
- 8. **Lymph Node:** Macrophages are present in the cortical and medullary lymphatic sinuses.
- 9. **Spleen:** The spleen contains Histiocytes and Macrophage phagocytic cells.
- 10. Skin Epidermis contain Langerhan's cells.

Histological Characteristics of the Mononuclear Phagocytic Cells

- They originate from the circulating blood monocytes.
- Their cell membranes are rich in receptors.
- Their cytoplasm usually contains foreign residual bodies.
- They have many lysosomes and ribosomes.
- They have well-developed Golgi complex and rough endoplasmic reticulum.
- Their nuclei are oval or kidney-shaped.
- They can live for several months in the tissues.
- They may fuse together to form Multinuclear Giant Cells.

Functions Of The Mononuclear Phagocytic Cells

- 1. They phagocytose bacteria and foreign bodies.
- 2. They remove the dead cells and foreign bodies from the tissues.
- 3. They store the iron of the worn-out RBCs.
- 4. They have an important role in immunological function.
- 5. They help in healing of tissues after injuries or inflammations.

The Respiratory System

The respiratory System includes:

1. The nose and the nasal air sinuses.
2. The naso-pharynx, the larynx and the trachea.
3. The lungs.

The Nose

The lining epithelium of the nasal cavity is divided into three areas:

1. The vestibular area.
 2. The respiratory area.
 3. The olfactory area (olfactory mucosa).
1. **The Vestibule:** Its anterior cartilagenous part is lined with **keratinizing stratified squamous epithelium** with hair follicles, sweat and sebaceous glands.
The hairs prevent the entrance of particles into the nose. The posterior part of the vestibule is lined with **non-keratinizing stratified squamous epithelium**.
 2. **The Respiratory Area:** It is present in the posterior part of the nasal cavity.
 - It is covered by **pseudo-stratified columnar ciliated epithelium with goblet cells**
 - There are 5 types of cells in this epithelium: **Columnar ciliated cells, Brush cells** covered by microvilli, **Basal stem cells, Goblet cells, and Neuroendocrine cells** which secrete serotonin substance.
 - **The corium of C.T. under the epithelium contains:** mucous and serous glands, lymphatics, plasma cells, macrophages, leucocytes and an erectile tissue which is formed of many venules, muscles, collagenous and elastic fibres.

3. The Olfactory Mucosa

- There are **2 olfactory areas**, one in each side of the roof of the nasal cavities.
- They are concerned with the sense of smelling of **different odours**.
- The mucous membrane of the olfactory area is thick and yellow in colour due to presence of pigments in its covering epithelium.

Types Of Cells In The Olfactory Mucosa

1. **Olfactory Bipolar Nerve Cells (Receptor cells).**
2. **Tall Columnar supporting cells (Sustentacular cells).**
3. **Short Basal Cells.**

1. **The Olfactory Bipolar Nerve Cells:** The axons of these cells pass into the C.T. under the epithelium to form the **olfactory nerve**. The dendrites of these cells extend towards the surface where they form the **olfactory hair vesicles**. These vesicles are rich in smooth endoplasmic reticulum, microtubules, mitochondria and

contain the basal bodies of the cilia. From these basal bodies, about 6 to 12 cilia project into the surface.

The olfactory cilia are non-motile, they lie parallel to the surface of the mucosa. These cilia cover the microvilli of the supporting cells.

The cytoplasm of the olfactory nerve cells contains small Golgi body, many ribosomes and an oval nucleus in the widest part of the cell.

2. The Supporting or Sustentacular Columnar Cells:

- They are tall columnar cells, each with wide apex and narrow base.
- Their free surfaces are covered with microvilli.
- Their cytoplasm is rich in yellowish pigments.
- They have pale oval nuclei.
- The sustentacular cells are secretory and supportive in function.

3. The Basal Cells:

- They are short triangular cells present near the basement membrane.
- Their nuclei are rounded and are darkly stained.
- The basal cells may act as stem cells from which new sustentacular cells can arise.

Lamina Propria of C. T.:

Under the olfactory epithelium there is a layer of erectile C. T. rich in veins, elastic fibres and **Bowman's glands**.

The Bowman's Glands are tubulo-alveolar **serous glands** which secrete serous secretion which acts as solvent to facilitate the process of smelling.

The Nasal Air Sinuses

These are paranasal air spaces present in the bones of skull. They are lined with **pseudo-stratified columnar ciliated epithelium with goblet cells**. The C. T. under the epithelium is rich in mucous glands, lymphocytes and lymph follicles.

Functions: Humidification of the nasal cavity and **production of clear voice**.

The Naso-Pharynx

It communicates the nasal cavity with the larynx. Its surface is lined with **pseudo stratified columnar ciliated epithelium with goblet cells**.

The C.T. corium under the epithelium of nasopharynx contains mucous glands, B.V. and the pharyngeal tonsil (adenoid).

The Oropharynx is covered with **stratified squamous** epithelium.

The Larynx

The larynx connects the pharynx with the trachea. It has 2 functions:

1. Prevention of food and fluid from entering to the respiratory passages.
2. Production of voice.

The larynx is kept opened by the laryngeal cartilages which are:

- The thyroid and cricoid cartilages which are formed of **hyaline cartilage**.
- The epiglottis, corniculate, cuniform cartilages are **elastic fibro-cartilage**.
- The larynx is lined with **pseudo-stratified columnar ciliated epithelium** with **goblet cells** except the **vocal cords** and the anterior surface of the epiglottis which are covered with **stratified squamous epithelium**.

The Vocal Cords

It includes two folds: **Vocal folds** for phonation and **Vestibular folds** which protect the larynx from the entrance of foreign particles into its lumen.

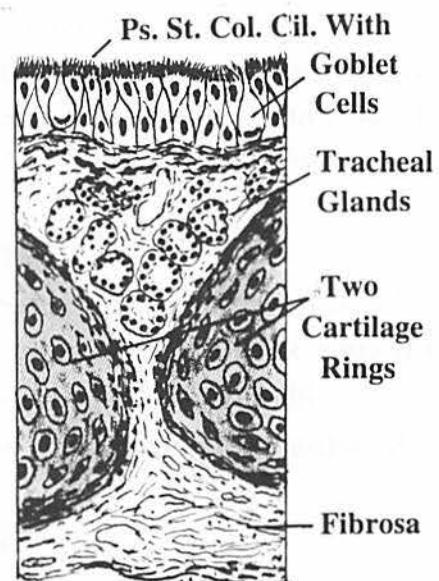
- **The Vocal Folds** are formed of C.T. rich in muscle and elastic fibres.
- **The vestibular folds** are formed of C.T. and mucous glands.
- Both folds are covered with **non-keratinizing stratified squamous epithelium**.
- **The larynx** below vocal cords is lined with Ps. St. Col. Cil + Goblet Cell.

The Trachea

- It is formed of a tube about 10 cm long. It is connected upwards with the larynx and divides below into **2 primary bronchi**.
- It is kept patent all the time, due to the presence of about 20 C-shaped or incomplete rings of hyaline cartilage in its wall.
- The trachea is concerned with conduction and conditioning of air.
- The wall of the trachea is formed of four layers.

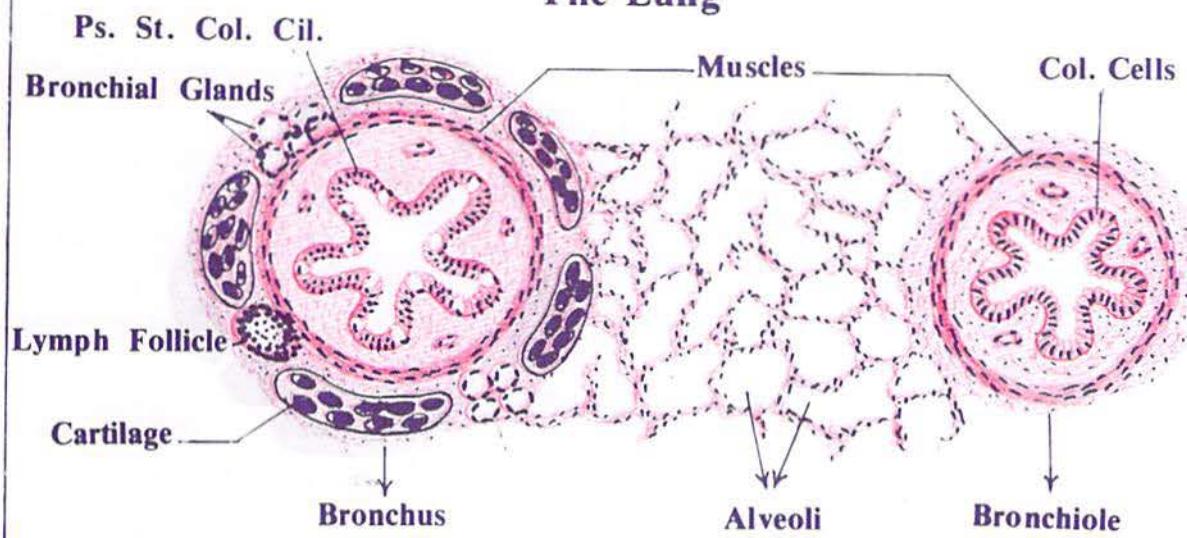
From inside outwards these layers are:
Mucosa, Submucosa, Cartilagenous coat
and Fibrosa.

1. The Mucosa of Trachea is formed of:
 - a) Epithelium.

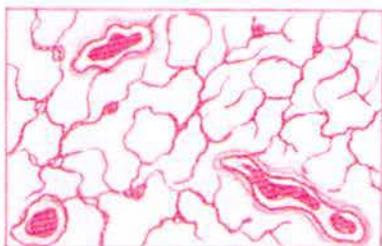


Longitudinal Section In Trachea

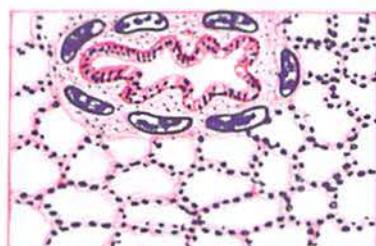
The Lung



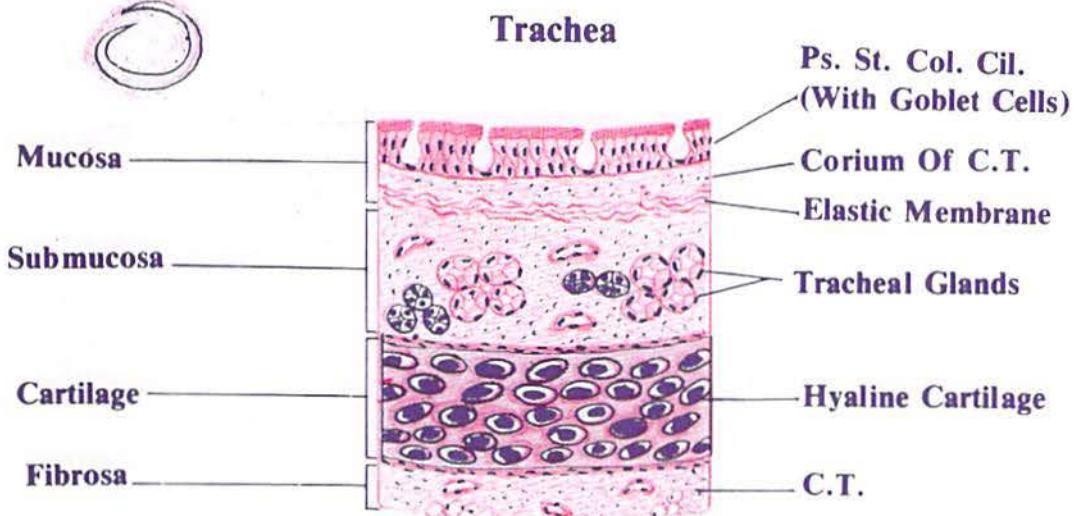
**Lung Injected
(By Gelatin Carmine)**



Foetal Lung



Trachea



Zakaria

[Plate 14]



- b) **Lamina Propria of Connective Tissue.**
 - c) **Elastic membrane.**
 - a) **Epithelium Of Trachea:** It is a Pseudo-stratified columnar ciliated epithelium with goblet cells.
 - **The Lining Epithelium of the Trachea and Bronchi. Includes The Following 7 Types Of Cells:**
 - 1. **Columnar ciliated cells.** Each cell has about 300 cilia.
 - 2. **Goblet cells which secrete mucus.**
 - 3. **Brush Cells** with microvilli on their surfaces. They are sensory receptor cells.
 - 4. **Basal Cells** which act as stem cells. They differentiate into tracheal cells.
 - 5. **Neuro-endocrine Cells of the APUD System which are of 3 types:**
 - a) Serotonin secretory cells.
 - b) Calcitonin secretory cells.
 - c) Cells secreting a hormone which produces cell proliferations and tumours.
 - 6. **Migrating lymphocytes.**
 - 7. **Migrating mast cells.**
 - b) **Lamina Propria of C. T.** Present under the tracheal epithelium. It is rich in elastic fibres, B. V., nerves and lymphatics.
 - c) **Clear Elastic Membrane** formed of dense elastic fibres.
- II. Submucosa of Trachea:** It is formed of areolar C. T. containing B. V., nerves, lymphoid follicles and tracheal glands.
- III. Fibrocartilagenous coat of the Trachea:** It is formed of multiple C-shaped hyaline cartilage rings embedded in a dense C. T. layer. The two ends of each cartilage ring are completed posteriorly by the trachialis smooth muscles.
- IV - Fibrosa of the trachea or the adventitia is formed of areolar C. T.**

The Lungs

- There are 2 lungs, each one is present at one side in the thoracic cavity.
- The right lung has 3 lobes, while the left lung has only 2 lobes.
- Each lung is subdivided by C. T. septa into lung lobes and lobules.
- Each lung is formed of bronchial tree, alveolar ducts, alveoli, blood vessels and is covered with the pleura.
- The continuous branching of the bronchi results in the formation of the different types of bronchioles.

The Bronchial Tree

- The trachea divides into **extra-pulmonary bronchi**, these enter the lung to divide into **intra pulmonary bronchi**, these divide in the lung into **terminal** and then into **respiratory bronchioles**. The alveoli, alveolar sacs and the alveolar ducts open in these **respiratory bronchioles**.

Extra-pulmonary bronchus	Intra-pulmonary bronchus
<ol style="list-style-type: none">1. It has a wide lumen.2. Its mucosa is less folded.3. Epithelium is pseudo-stratified columnar ciliated with many goblet cells.4. It has a definite submucosa.5. Presence of C-shaped cartilagenous rings in its wall.6. Smooth muscles are present posterior only at the ends of C-shaped cartilage.7. Presence of an elastic membrane in the C. T. of the lamina propria.8. Mucous glands are present in the submucosa	<ol style="list-style-type: none">1. It has a narrow lumen.2. Its mucosa is highly folded.3. Epithelium is pseudo-stratified columnar ciliated with few goblet cells.4. It has no submucosa.5. Presence of multiple plates of cartilage in its wall.6. Smooth muscles are arranged spirally and encircling the whole lumen.7. Elastic fibres are distributed between cartilage plates and in the adventitia.8. Mucous glands and lymphatic nodules are present between cartilage plates and in the adventitia.

The Bronchioles

- Continuous branching of the bronchi form different types of bronchioles.
- The bronchioles are small tubes, each with a diameter less than 1 mm.
- The wall of each bronchiole consists of: mucosa, musculosa and C. T. fibrosa.

The mucosa of each bronchiole is formed of: Epithelium and C. T.

The Epithelium Of Bronchioles Includes The Following Three Types Of Cells:

- a) Large bronchioles are lined with **Simple columnar ciliated cells** alternating with **Clara cells**. Small bronchioles are lined with simple cuboidal non-ciliated cells alternating with **Clara Cells**.
- b) **Clara cells:** They are tall dome-shaped cells. They have well-developed smooth endoplasmic reticulum, mitochondria, RNA, Golgi body, and secretory granules. They secrete a serous fluid rich in protein to protect the epithelium.
- c) **Neuro-epithelial Cells:** They are a group of cells rich in nerve receptors. They act as chemoreceptors to hormones and drugs which regulate bronchial dilatation and constriction.

2. **Lamina propria** of C. T. under the epithelium very rich in elastic fibres.
3. **Smooth muscle layer** which are spirally arranged and are ensheathed by elastic fibres.
4. **Outer C. T. layer** with **no glands, no cartilage** and **no lymph nodules**.

The following table shows the differences between a Bronchus and a Bronchiole

Bronchus	Bronchiole
<ol style="list-style-type: none"> 1. It is long, wide and its lumen is usually patent (not collapsed). 2. Its mucosa is folded and is lined with pseudo stratified columnar epithelium which is formed of seven types of cells similar to the trachea. 3. Presence of few neuro-epithelial cells (Chemo-Receptors). 4. Presence of goblet cells. 5. The C. T. adventitia is rich in elastic fibres and lymphoid follicles. 6. Presence of muco-serous glands. 7. Presence of plates of cartilage in a layer of fibrous tissue. 	<ol style="list-style-type: none"> 1. It is short, narrow and its lumen may be collapsed as in bronchial asthma. 2. Its mucosa is highly folded and is lined with ciliated or non-ciliated columnar cells, clara cells and receptor cells. 3. Presence of many neuro-epithelial cells (Chemo-Receptors). 4. No goblet cells. 5. The C. T. corium has No lymphoid follicles. 6. No glands. 7. No cartilage because they have no tendency to collapse on inspiration.

Different Types Of Lung Bronchioles

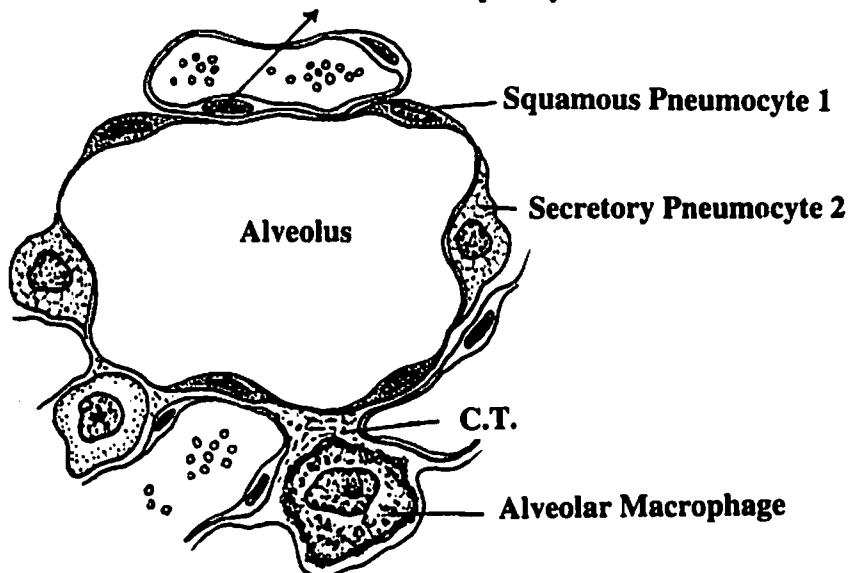
The bronchioles divide into smaller branches to form the following bronchioles:

1. **The preterminal bronchioles** which are lined with simple columnar ciliated cells alternating with Clara cells and neuroepithelial cells.
2. **The terminal bronchioles** are lined with simple columnar partially ciliated epithelium.
3. **The respiratory bronchioles:** Each one has a diameter about 0.5 mm. Its wall is lined with simple cuboidal epithelium. Under the epithelium, there is a layer of C. T. rich in elastic fibres. Outside the C. T. there are some circular smooth muscle fibres, some alveoli open in the walls of respiratory bronchioles. Gaseous exchange occurs in these alveoli so they are called respiratory bronchioles.
4. **The alveolar ducts:**
 - These are the free terminations of the respiratory bronchioles.
 - Alveolar ducts are lined with simple cubical epithelium.
 - Outside the epithelium, there is a layer of C. T. containing some elastic and smooth muscle fibres.
 - Alveolar sacs and alveoli open into the wall of these alveolar ducts.

Alveoli And Alveolar Sacs

- The alveoli are the structural and functional units of respiratory gas exchange.
- They are small air spaces in the lung which are in contact with blood capillaries.
- Air and blood are separated only by thin layers of tissues formed by the alveolar and capillary walls through which diffusion of gases occurs.
- Lung alveoli open directly into the alveolar sacs, or into the alveolar ducts or into the respiratory bronchioles.
- Between the alveolar walls there are alveolar pores through which air can pass from one alveolus to another.
- The alveolar sacs are groups of pulmonary alveoli which open into common central spaces that exist in the lung.
- The alveoli are lined with the alveolar cells (alveolar epithelium) and are separated from one another by the interalveolar septa.

Endothelium Of Blood Capillary



Types Of Cells In Alveolar Wall

The Alveolar Cells

- The alveolar epithelium consists of 2 types of cells.
 1. Type One Pneumocytes.
 2. Type Two Pneumocytes.

A) Type I Pneumocytes (Squamous Cells)

- They are the most numerous cells in the alveolar wall (97%)
- They are flat squamous cells with small amounts of cytoplasm.
- They are very poor in rough endoplasmic reticulum.
- They have short microvilli at their alveolar surfaces.
- They have thin basement membranes which fuse with the basement membranes of the nearby blood capillaries.
- They are connected together by tight junctions to prevent leakage of fluid into the alveolar air spaces.
- They provide a very thin membrane through which gaseous exchange occurs.
- They are differentiated cells, they cannot divide.

B) Type II Pneumocytes (Secretory Cells)

- They are less numerous than type I pneumocytes (3%).
- They are rounded cells with vaculated cytoplasm.
- They have the capacity to divide and act as progenitor cells for type one and type two pneumocytes.
- They are rich in mitochondria, ribosomes, rough endoplasmic reticulum and Golgi bodies which secrete phospholipid substance called **surfactant**.
- They have microvilli on their cell membranes.
- Pneumocyte II are secretory cells. They secrete phospholipid substances known as **pulmonary surfactant**.
- The surfactant is a thin layer of fluid which is phospholipid in nature. It lines the inner aspects of the alveoli in order to reduce the surface tension of the alveoli, thus preventing them from being collapsed especially in newborn infants. Surfactant has also an **antibacterial** function.

Blood Air Barrier

- It is the wall which separates the alveolar air present inside the alveoli from the circulating blood which is present in the blood capillaries of the lung.
- It is the wall through which exchange of gases takes place and is composed of :
 1. The film of pulmonary surfactant on the alveolar surfaces.
 2. The cytoplasm of the type 1 pneumocytes.
 3. The fused basement membranes of pneumocyte 1 and that of pulmonary blood capillaries.
 4. The cytoplasm of the endothelial cells of the blood capillaries.

The Inter-Alveolar Septum

– It is the partition which is present between two adjacent alveoli.

The Inter-alveolar Septum is Formed of:

1. The alveolar epithelium on either side of the alveolar septum.
2. The basement membranes of the lining alveolar epithelium.
3. Network of reticular and elastic C. T. containing leucocytes and phagocytic cells.
4. Basement membranes of the cells which line the blood capillaries.
5. The cytoplasm of the endothelial cells that line blood capillaries.

The Alveolar Phagocytes

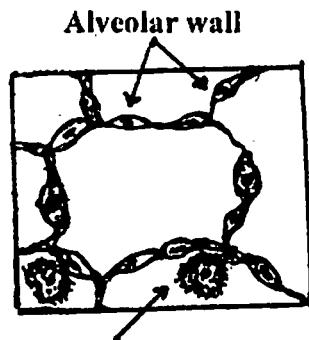
- They are macrophage phagocytic cells, present in or around the alveoli.
- They have an important role in the defence mechanism of the respiratory system.
- There are 2 types of phagocytic cells in the lung; dust cells and heart failure cells.

1. Dust Cells

- They are mononuclear phagocytic cells.
- They are present around lung alveoli.
- They can engulf (eat) any foreign particles like dust or carbon.
- They can be stained with vital stains.

Origin of these dust cells:

1. From blood monocytes which can phagocytose (eat) dust or carbon particles.
2. From the C. T. histiocytes present outside the alveoli.



Dust Cell in Alveoli

Fate of dust cells: (their future)

1. They may be coughed with the sputum.
2. They may pass through the lymph vessels to the regional lymph nodes.
3. They may die in or around the alveoli.

2. Heart Failure Cells

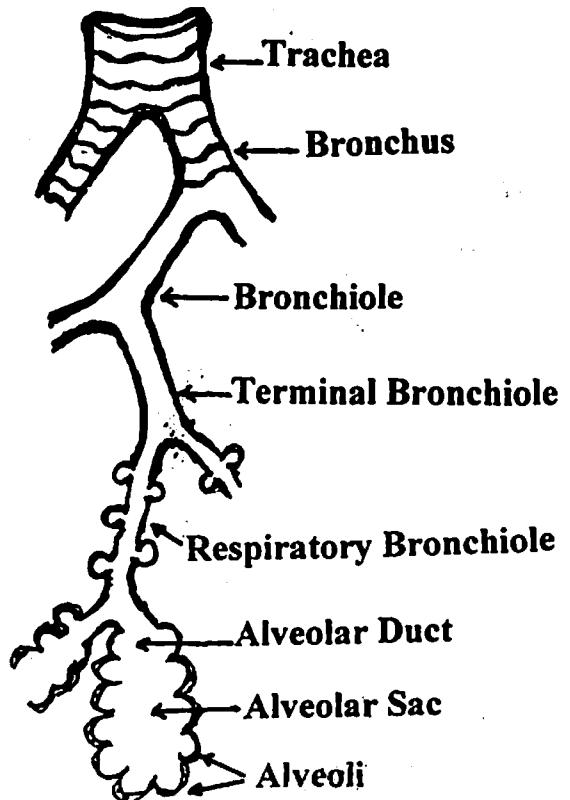
In certain heart diseases, failure may occur to the heart, so it can't distribute all the blood coming to it from the lung. Congestion will occur in the capillaries around the alveoli and they may rupture leading to appearance of blood cells in the alveoli. The previous phagocytic cells of the lung (Monocytes) will engulf the remnants of blood cells and are transformed into heart failure cells. So the heart failure cells are similar to dust cells in their origin and in their fate.

The Non-Respiratory Secretory Functions Of The Lungs:

1. Secretion of Immunoglobulin A = IgA.
2. The endothelium of the lung blood capillaries secrete enzymes that convert angiotensin I into angiotensin II which is a vasoconstrictor substance.
3. Pneumocyte II of lung secrete pulmonary surfactant.

The Bronchial Tree And Their Lining Epithelium

- Trache + Extra and Intrapulmonary bronchi are lined with Pseudo Stratified Columnar ciliated + goblet cells.
- Terminal Bronchioles lined with simple Columnar ciliated + Clara cells.
- Respiratory Bronchioles lined with simple Cubical cells and Clara cells.
- Alveolar Ducts with simple Cubical cells.
- Alveolar Sac and Alveoli lined with pneumocytes 1 and 2.



The Pleura

It covers the lung and is formed of two layers: an outer or Parietal layer and an inner or Visceral layer: Both layers are separated by a thin film of fluid to lubricate their sliding movements. Each layer is a fibroelastic membrane rich in elastic and collagenous fibres. Few fibroblasts and macrophages are also present. The pleura is covered with a layer of simple squamous mesothelium which secretes pleural fluid. The pleura contains lymph capillaries and nerve fibres.

Foetal Lungs

- The Lung has no function in the foetus, it is thus collapsed in the intra-uterine life.
The foetal lung is characterized by:
 - Its lobes and lobules are well-demarcated due to presence of thick C. T. septa.
 - The foetal lung is similar to a gland formed of acini and ducts.
 - Its alveoli are collapsed and are lined by simple cubical epithelium.
 - Its bronchi and bronchioles are partially collapsed. Cartilage plates are present around the bronchi, this differentiates foetal lung from glands.
 - Its pulmonary B. V. are full of blood (congested).
 - The whole lung sinks in water (this is of medico-legal importance).

Other Published Books For The Same Author

1. Part II Of This Book “**Histology For Medical Students**”.
2. Part I Of A “**Review and Atlas of Histology**” with Coloured Photographs From The Original Practical Histology Slides.
3. Part II Of A “**Review and Atlas of Histology**” With Coloured Photographs From The Original Practical Histology Slides.

Other Book By the Same Author is Coming Soon “In Shaa Allah”

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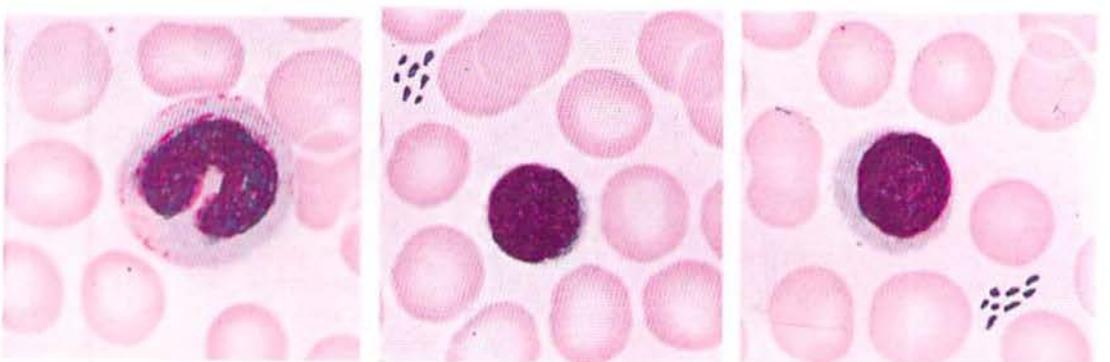




Neutrophils

Eosinophil

Basophil



Monocyte

Lymphocytes and Blood Platelets