CHAPTER I

CELL

The living substance of plants and animals is described by the general term, **protoplasm,** which is bounded by a delicate membrane and contains various microscopic and submicroscopic structures. The smallest unit of protoplasm, capable of carrying out independent existence, is the **cell** (Fig. 1). The word *cell* (L. *cella*=a storeroom, a chamber) was first introduced in the biology by Robert Hooke (1635–1703). ***The* cell is the structural and functional unit of the living matter** and **is capable of carrying on the processes of life independently.** The *tissues* which form the body consist entirely of cells and of extracellular materials elaborated by cells. Furthermore, growth, reproduction and continued responsiveness to stimuli are the characteristics of cells and not of their parts. In unicellular organism like *Amoeba*, a single cell can perform all these physiological functions, but in multicellular organism different cells have got various activities and accordingly these structures have been changed according to its functions. These functional differentiations are inevitable in a multicellular organism and for this reason different kinds of cells become dependent upon one another. These functional differentiations of the cells in multicellular organism are mostly dependent upon the specific properties of the protoplasm with which a particular cell is constituted. In the unicellular organism, the protoplasm of the single cell has got the basic properties like *irritability*, *conductivity*, *contractility*, *absorption*, *assimilation*, *excretion*, *secretion*, *growth* and *reproduction*. Thus in the unicellular organism, a single cell is capable of multiple functions. But in the multicellular organism, all these properties of protoplasm have divided and delegated to specific cells and their protoplasms as well. So, for the particular functions of a cell, certain physical equipment capable of expressing their functions must be present in the protoplasm of those cells.

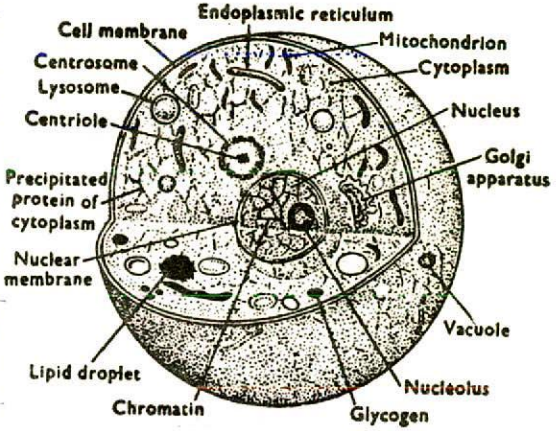


Fig. 1. Composite structure of a cell based on what is seen under light microscopes (diagrammatic).

The protoplasm which bears the specific physical equipments of a particular cell unit, can be divided into two major organisations: (*i*) *nucleus*, composed of *nucleoplasm* (karyoplasm), which controls the activities of a cell and (*ii*) *cytoplasm* (Gr. *kytos*=hollow (cell)+*plasma*=thing formed) surrounding the protoplasmic nucleus, which carries out such activities.

In 1833 Brown recognised a conspicuous spherical body, *nucleus*, in

the interior of plant cell and subsequently it was also found in all animal cells. The nucleus contains chromosomes which harbour the genetic materials and typically one or more **nucleoli,** which are concerned with the synthesis of proteins.

Nucleus and cytoplasm contain a number of components of characteristic form and staining properties. These components belong to *organelles* (organoids) and *inclusions* (paraplasm). The **organelles** are small internal organs of the cells, which are concerned as organised units of living substance possessing important specific functions in cell metabolism. The nature and number of organelles determine the volume and function of the cytoplasm. The **inclusions** are lifeless (non-protoplasmic) accumulations of metabolites, e.g., protein, lipoids (fatty, phospholipid and steroidal compounds) and carbohydrate, crystals, pigments, secreting droplets, etc. In addition, the nucleus and cytoplasm contain an apparently amorphous protoplasm which serves as a ground or *matrix* where organelles lie.

At some places, the cell membrane is incomplete and the protoplasm of the adjoining cells runs together, such as in liver, umbilical cord (Wharton's jelly), etc. Such a mass of undifferentiated protoplasm with scattered nuclei is called **syncytium** or **plasmodium.**

THE STRUCTURE OF A CELL

In multicellular organs, the cells are not of same size and shape only due to the presence of differentiation of functions. But there are certain structural characteristic features which are common to them all. Each cell can be broadly divided into two principal units—(*i*) cytoplasm and (*ii*) nucleus (FIG. 2).

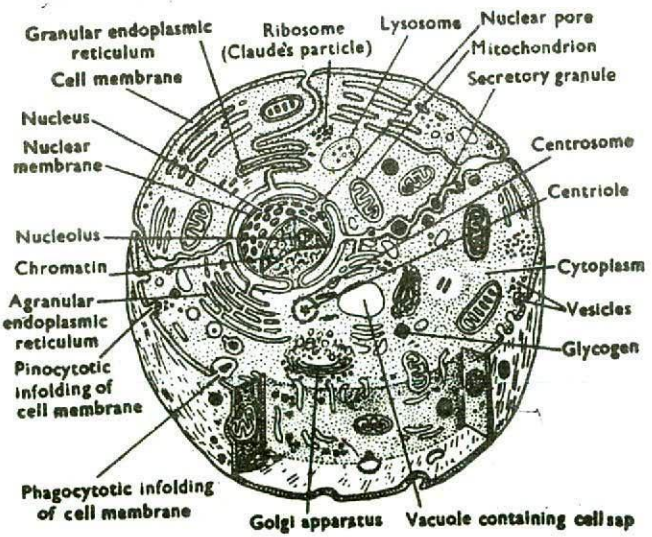


FIG. 2. A diagrammatic view of a typical animal cell as it might be seen under the electron microscope. *No single electron micrograph reveals all the structures and patterns shown above. The above representation is a composite view of many such electron micrographs.*

A. Cytoplasm

The cytoplasm is the protoplasm which surrounds the nucleus and is bounded peripherally by the cell membrane. It may be homogeneous, vacuolated, granular, reticular or fibrillar. The ground substance of the protoplasm, **hyaloplasm,** contains a number of bodies and structures, vacuoles, and so on and also a number of very tiny particles which undergo active movement—**Brownian movement.** The cytoplasm is capable of performing different kinds of work directed by the nucleus. Specialisation of the cytoplasm for special functions, the appearance as well as the protoplasmic constituents are also changed from cell to cell. Hence certain groups of cells will be identified by their nuclei and also by the appearance and the amount of cytoplasm. In the light microscope the cytoplasm can be classified into two groups: (*i*) cytoplasmic inclusions, (*ii*) cytoplasmic organelles.

CYTOPLASMIC INCLUSIONS. These are not the living metabolic machineries of the body but certain structures present in the cytoplasm of the cell. These are: (*a*) *stored foods* (carbohydrate, lipoids and protein), (*b*) *secretion granules*, (*c*) *pigments*—(*i*) endogenous (haemoglobin and melanin) and (*ii*) exogenous (due to carotene from vegetable, dusts like carbon and minerals like lead and silver), (*d*) *crystals* (proteinacious crystalline materials of the Sertoli and interstitial cells of the testis).

CYTOPLASMIC ORGANELLES. Under the electron microscopic studies, certain organelles have got membranous structure. These can be classified as follows:

1. Membranous organelles—(*a*) plasma membrane, (*b*) endoplasmic reticulum (E.R.), (*c*) Golgi apparatus, (*d*) mitochondria, (*e*) lysosomes.
2. Cytoplasmic ribonucleic acid (RNA)—ribosomes.
3. Centrosomes.
4. Various fibrils, filaments and tubules.

1. Membranous organelles

(*a*) **Plasma membrane.** The plasma membrane or *plasmalemma* or *cell membrane* is the outer covering of the cell and is a flexible, responsive and dynamic structure. This membrane isolates the individual cell from its neighbours and takes part in the maintenance of the internal environment by active transport of ions and nutrients. Under the light microscope, the membrane is thin and invisible, and sometimes the limits of a cell may be distinguished because the cell membrane is folded to form a cuticular or brush border or because mucoprotein or other cellular secretion is present to coat the membrane. By the electron microscope it is claimed to be about 80Å (or 80A.U.)* thick and shows the membrane to be a *trilaminar* (triple-layered) structure. This basic trilaminar structure of all cell membrane, is generally described as **unit membrane.** At high magnification with electron microscope, the cell membrane consists of double (bimolecular) layer of lipid molecules (light-stained), which are sandwitched within the two densely stained protein layers. It is also suggested

*Equivalent measurements:

1 m (metre)	=	100 cm (centimetres)	= app. 39·37 inches.
1 centimetre	=	10 mm (millimetres)	= app. 0·3937 inch.
1 millimetre	=	1000 μ (microns)	= app. 1/25 of an inch.
1 micron	=	1000 mμ (millimicrons)	= app. 1/25,000 of an inch.
1 millimicron	=	1000 $\mu\mu$ (micromicrons)	
	=	10 Å (angstrom units or A.U.)	= app. 1/25,000,000 of an inch.

that the thickness of lipid layer is about 30Å and that of the *each* protein layer is about 25Å. Total thickness of the cell membrane then becomes 80Å. Lipid layer is mostly **phospholipid** of which the head end contains the water-soluble and positively charged phosphate group (**polar** or **hydrophilic**) while the tail end contains the water-insoluble and negatively charged lipid group (**non-polar** or **hydrophobic**). Phospholipid molecules of the lipid layer are arranged in two rows where the hydrophobic ends line up side by side in same row but abutting on the hydrophobic ends of the other row (FIG. 3). Thus the *non-polar groups* of lipid molecules face each other but the protein molecules that form the inner and outer layers of the unit membrane are adsorbed on the *polar groups*. **Functions**—The main function of the plasma membrane is the transport of materials across it. The process may be *direct*, possibly controlled by enzymes, as in the case of sodium or potassium. Small vesicles, by a process of **pinocytosis** (drinking by cells), encircle and carry fluid within it across the membrane. By the pinocytic process fluid of *smaller molecules* (0·01–2·0 μ) can be gulfed in (FIG. 4). The **inducer** can increase greatly the process of pinocytosis. **Reverse pinocytosis** or **emeiocytosis** (vomiting by cell) is a process under which the granule or vacuole surface membrane fuses with the cell membrane and the fused portion then ruptures out within the pericapiliary space leaving the cell membrane intact. **Rhopheocytosis** is the process by which *larger molecules* of fluid are taken in. **Cytopemphis** or **podocytosis** is the process by which the molecules are engulfed into the cell but the vacuole containing them moves across the cell and discharges its contents onto another surface of the same cell. This process is commonly seen in kidney tubular cells and intestinal epithelial cells. The **phagocytosis** (eating by cells) is similar to engulfing of solid materials by the amoeba. When various end products of digestion diffuse out of the vacuole into the cytoplasm, the indigestible residue is eliminated by **reverse phagocytosis.** In addition to transport, the cell membrane (*a*) helps in the protection of cell, (*b*) receives stimuli from the outside, (*c*) takes in food and (*d*) excretes waste products. When broken, it is quickly regenerated from the cytoplasm possibly with the help of surface tension.

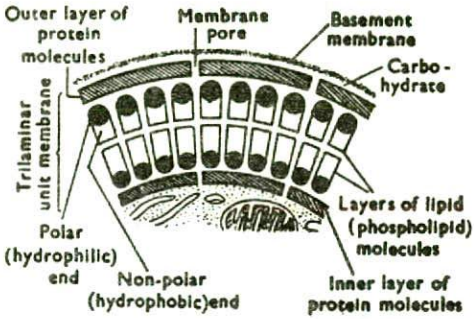


FIG. 3. Diagrammatic representation of the structure of cell membrane that is seen under electron microscope (E.M.).

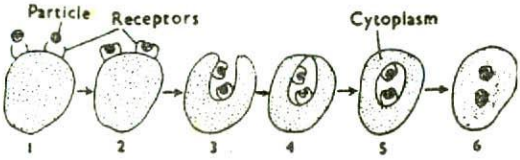


FIG. 4. Different phases of pinocytosis showing the particle in solution to approach the cell surface (1, 2) and gradually drunk (3, 4, 5, 6).

(*b*) **Endoplasmic reticulum (Ergastoplasm).** These consist of

network of canals (tubules) and vesicles (cisteranae). These are three-dimensional and bounded by membrane of about 80Å in thickness. The elements of the endoplasmic reticulum may connect intermittently with the plasma membrane at one hand and on the other hand with the outer nuclear membrane. Two types of endoplasmic reticulum have been recognised—(*a*) rough-surfaced (α-cytomembranous or granular) reticulum and (*b*) smooth-surfaced (β-cytomembranous or agranular) reticulum. (*a*) **Rough-surfaced endoplasmic reticulum**—This reticulum is studded with osmeophilic granules—the ribosomes lying in rows in contact with the membranes of the endoplasmic reticulum (Fig. 5). The roughness of the membrane is due to the presence of these granules—**Palade granules.** (*b*) **Smooth-surfaced endoplasmic reticulum**—This type of endoplasmic reticulum does not possess osmeophilic granules—the ribosomes at the outer border of the membrane. This is why it is smooth. **Functions**—As the smooth-surfaced endoplasmic reticulum is very abundant in the interstitial(Leydig) cells of the testis and in cells of the corpus luteum, this reticulum is concerned with the synthesis of steroid hormones. This type of reticulum in the parietal cells of the gastric mucosa is concerned with secretion of hydrochloric acid. In the skeletal muscle it (sarcoplasmic reticulum) is concerned in some way with binding of the Ca^{++} ions and also plays in conducting impulses in the substances of muscle cells. In the liver cells both types of reticula are concerned with the synthesis of protein and carbohydrate.

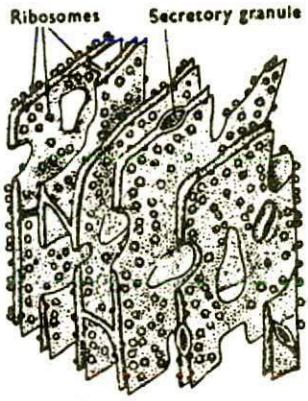


Fig. 5. Three-dimensional structural representation of endoplasmic reticulum(rough), showing embedded ribosomes and secretory granules on the wall (diagrammatic).

Microsome and microsomal fractions. Different fractions of cells can be obtained by *centrifugation*. After removing the nuclei and mitochondria, one such cell fraction obtained by centrifugation at about 20,000 to 100,000 g* was known as microsomal fractions and was erroneously known to be a separate type of cell organelle. But in electron microscopic studies of this microsomal fractions reveal that this is nothing but a chief composition of rough-surfaced and smooth-surfaced membranous vesicles of the endoplasmic reticulum. In the intact fractions the ribosomes are adherent to the rough-surfaced vesicles. Smooth-surfaced vesicles are also present in some portions of microsomal fractions. So there is nothing to believe that the microsome or microsomal fractions have got a discrete and independent structure in the cytoplasm.

(*c*) **Golgi Apparatus** (Golgi Complex). The structure (Fig. 6) looks like a network of fine threads (Golgi network) or irregular granular material. It is usually located near the nucleus, and in the gland cells found between the nucleus and apex of the cell. Three main structures can be observed in Golgi apparatus under electron microscope. These are: (*i*) *flattened vesicles*, (*ii*) *secretory vesicles* and (*iii*) *microvesicles*. (*i*) **Flattened (distended) vesicles.**—These are the most prominent vesicles in the

*g=981 cm per sec. per sec. (=981 cm $sec.^{-2}$).

Golgi apparatus. In a longitudinal section it looks like tubules arranged in stack. The peripheral portion of each vesicle becomes distended with its content and then the distended portion becomes separated from the vesicle to constitute the *ovoid-to-round-shaped* secretory vesicles. (*ii*) **Secretory vesicles**—Under electron microscope the secretory vesicles are not normally visible until these are budded off from the distended peripheral end of flattened vesicles. These vesicles become electron dense only after being distended with their contents—the protein material. Recently it is known that protein material after being synthesised in the rough surface (granular) of the endoplasmic reticulum (*vide* Ribosomes) is stored in the flattened vesicle and the secretory vesicle as well. The contents of the secretory vesicles are ultimately discharged at its cell surface as **zymogen granules.** Protein materials, being synthesised in the ribosome of the endoplasmic reticulum, are not transferred to the flattened vesicles directly but through a *via* medium—the microvesicles of the Golgi apparatus. (*iii*) **Microvesicles**—These are small in size and their diameters are about 40 mμ. Microvesicles have been considered to be the **carrier systems** of the protein molecules synthesised in the rough surface of the endoplasmic reticulum to the flattened vesicles. From autoradiographic studies Caro and Palade have described that protein molecules, after being synthesised, first appear in the microvesicles and then in the flattened vesicles or the secretory vesicles. In certain cells these are numerous in between the region of the rough-surfaced endoplasmic reticulum and the flattened vesicle. **Functions**—It is probably concerned with synthetic process of the cell, specially—secretions. The secretory substance, being synthesised by the endoplasmic reticulum, passes to the Golgi apparatus which possibly modifies the products of synthesis by concentrating and chemically altering it to some extent. In addition, Golgi apparatus independently synthesises polysaccharide part of glucoprotein secretion.

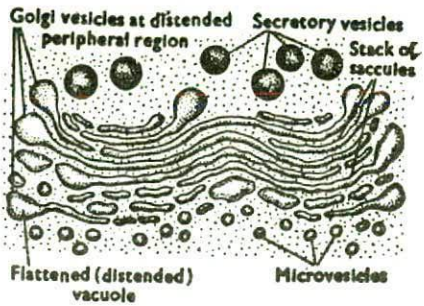


FIG. 6. Diagrammatic representation of the structure of Golgi apparatus.

(*d*) **Mitochondria.** These are relatively solid bodies, granular, rod-shaped or filamentous in form and remain scattered throughout the cytoplasm (dimensions varying from 0·5 to 5·0 microns). They are surrounded by a trilaminar double membrane, the inner one of which remains folded and forms a number of partitions, the *cristae mitochondriales*. These cristae may be *complete*, *septate* or *incomplete*. In the living cell they are found to move about. They are more numerous and longer in the young and active cells. The sites where Krebs cycle enzymes (*cyclophorase system*) are present in high concentration, like liver, kidney (FIG. 7) and heart, possess mitochondria in a larger amount. They are comparatively few in skeletal muscle fibres where the enzymes are also less. Numerous projecting particles known as *elementary particles* are present on the inner mitochondrial membrane and cristae, the fluid of the intramitochondrial space is called *matrix*. The matrix may contain small dense granules. It has been postu-



FIG. 7. Electron micrographic representation of the basal portion of the renal tubular epithelium (rat) embedded on basement lamina showing part of the nucleus (N), Golgi apparatus (G), numerous mitochondria (M).

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lated that most of the enzymes of the mitochondria are present on the elementary particles, the coenzymes in the matrix, and inorganic ions like calcium and magnesium in the granules (FIG. 8). The number and size of mitochondria give an indication of the energy requirements of a particular cell. Mitochondria are comparatively rare in cancer cells which derive their energy from *anaerobic glycolysis*. For light microscopy, mitochondria can be stained supravitally with Janus Green B. Sometimes they remain grouped together at one pole of the cell. *Chemically* they contain about 40 per cent. of fat (neutral fat, phospholipids

and cholesterol) and two different kinds of proteins. Ribonucleic acid (RNA) remains in combination with protein as *ribonucleoprotein* (RNP).

Functions—All the enzymes of the citric acid cycle with the exceptions of certain dehydrogenase are present in the fluid content of the mitochondria. The acetic acid—the breakdown products of pyruvic acids, fatty acids and also of amino acids are fed into the mill of Krebs cycle enzymes of the mitochondria. In presence of oxygen the Krebs cycle runs within the mitochondria with the catalysing help of another set of enzymes—**respiratory enzymes.** These are *flavoprotein* enzymes and *cytochrome*, and present in the inner membrane of the mitochondria. These respiratory enzymes use certain products of Krebs cycle as substrate. These enzymes present in the mitochondria help in oxidative phosphorylation and are the site for formation of adenosine triphosphate (ATP) which is the high energy-producing substance in the cell. The mitochondria supply 95 per cent. of cell's energy and are called *power-house* or *power-plant* of the cell. Recently it has been studied that the mitochondria also possess some amount of deoxyribonucleic (desoxyribonucleic) acid (DNA). There is also some indication that RNA is also synthesised in association with DNA and this RNA helps in synthesising certain amount of protein in the mitochondria.

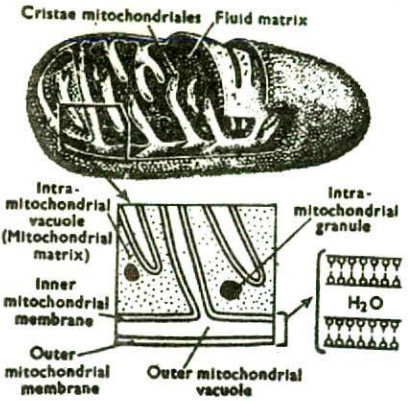


FIG. 8. Diagrammatic representation of mitochondrion showing the different internal structures including the outer mitochondrial vacuole containing H_2O seen under E.M.

(*e*) **Lysosomes.** The lysosome has been discorvered and recognised as a separate cytoplasmic organelle. Its size varies from 0·25μ to 0·50μ. These are membranous vesicles having a spherical and bag-like structure and are filled with hydrolytic enzymes capable of demolishing large molecules (protein, carbohydrate, lipids and nucleic acids) into fragments which may then be oxidised by the mitochondria. The lysozymes are present in all animal cells *except* in the *erythrocytes*. Certain leucocytes contain a specific type of granules which are considered to be lysosomes. The enzymes of lysosomes are potent enough to digest its own cellular contents in which it inhabits but in ordinary conditions it is not so happened. Under certain conditions it may digest its own cellular content and for this reason it is sometimes described dramatically as **suicide bag.** Lysosomal enzymes, like other proteins, are synthesised by the ribosomes of granular endoplasmic reticulum of the same cell and are transported to the Golgi apparatus in the form of microvesicles for storage. The stored enzymes are ultimately budded off from the stack of **Golgi saccules** and developed into primary or inactive lysosomes. Primary lysosome develops into active or secondary lysosome (autolysosome) only during intracellular digestion. The **fusion of primary lysosome** with the particle brought into the

*In 1955 Chrestian de Duve and his associates first postulated this existence.

surface of the cell (**phagosome**) or the intracellular material gives rise to **secondary** or **active lysosome.** Lysosomes that digest the degenerated mitochondria or other intracellular structures are specifically described as **cytolysosome. Functions**—(*i*) The general function of the lysosome is in the intracellular digestion and for this reason it is sometimes described as **digestive apparatus** of the cell (Fig. 9). When a particulate or food substance comes in contact with cell surface, the substance is engulfed by the cell membrane forming a membranous vesicle with engulfed particle. The lysosome thus meets with the particle and is fused. **Hydrolysing enzymes** of the lysosome thus digest the food particle. However this is happened in some kinds of cells, because in such cells the particulate is not utilised by the cell without the help of lysosomes. (*ii*) Another function is *cell necrosis* or *autolysis*. When the cell is damaged, the lysosomal digestive enzymes are released and digest off cellular elements. In case of degeneration of its own cellular organelles, such as mitochondria and ribosomes during acute anoxia, the lysosomes then digest them only to maintain the energy requirement of the cell. (*iii*) *Phagocytosis* is also a remarkable function of lysosome. Leucocytes contain lysosome-like granules which destroy the ingested bacteria. During this process, the blood cells themselves are destroyed along with the bacteria. For this phagocytic (phagocytotic) functions, certain cells contain (macrophages and polymorpho-nuclear leucocytes) recognisable lysosomes. In damaged cells the number of lysosomes are increased greatly. Thus it is clear that lysosome stores safely a quite good number of destructive enzymes within the cells only to remove the foreign material through phagocytosis. (*iv*) It has been postulated that the lysosome brings about death of cells only to make space for the new cells. Systemic growth of cells are made through the planned death of cells through the lysosomal activity. (*v*) The rupture of lysosome is the stimulus for cell division and alteration of the behaviour of lysosome may be one of the causes of cancerous growth. (*vi*) Furthermore *acrosome of the spermatozoa appears to be a large lysosome.*

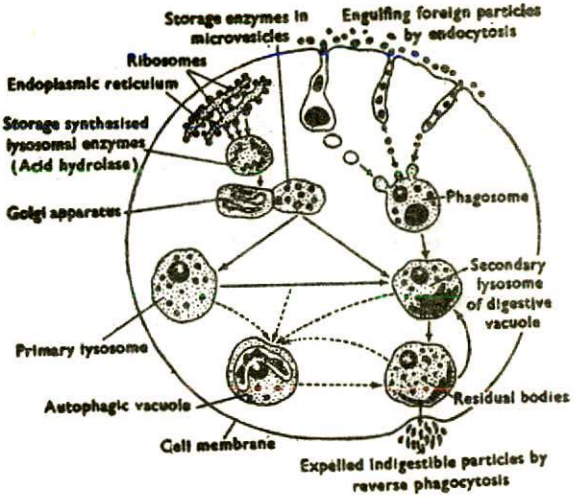


Fig. 9. Diagrammatic representation of the digestive function of lysosomes.

2. **Ribosomes** or **Claude's particles** are ribonucleoprotein in nature and are found scattered throughout the cytoplasm either singly or in groups (*polyribosomes* or *polysomes*) and range in size from 100 to 150 Å in

diameter. They are so rich in RNA that they may contain as much as 60% of total RNA in the entire cell. These ribonucleoproteins are concerned with protein synthesis and their presence gives the membrane a strong basophilia. Cells responsible for the secretion of proteins have an abundance of granular reticulum. **Functions**—Being attached to the rough-surfaced endoplasmic reticulum ribosomes (FIG. 5) synthesise protein and canals of the reticulum work as passageways through which proteins move on way to Golgi apparatus. So ribosomes are **protein factories.**

3. **Centrosome** (*Cytocentrum* or *cell centre*). It consists of another specialised part of clear cytoplasm, the *centrosphere*, containing in its interior two or more deeply staining particles—the **centrioles** (generally arranged in pairs, i.e., *diplosome*) lying close to the nucleus in the resting cell. Electron microscopy has revealed the centriole to be an empty cylinder which is 3 to 5 μ long, the compact walls of which are made of thin parallel nine tubular structures longitudinally arranged. Each tubule consists, in turn, of three subunits or triplets. The **pericentriolar bodies** or **satellites** which are round in shape, are attached to centriolar tubules by a filament of chromatid (FIG. 10). *Centriole is closely related to spindle formation during mitosis* (*normal cell division*) and also in sustaining other fibrillar structure like cilia and flagella. At the beginning of cell division, the centriole and centrosome divide. A system of radiating lines, made up of microtubules, then grows out from each of the two newly formed centrioles and the whole structure, due to its star-like shape, is called **aster.** The two asters grow in size and repel each other till they occupy the opposite poles of the elongated cell. The diverging fibres from the two asters meet at the equator of the cell and form the **achromatic spindle.** Along the fibres of this spindle half the number of *chromosomes*—formed by the breaking up of the nucleus in the mean time—are drawn towards each aster and then the cell divides. Each daughter cell thus carries one aster and half the number of chromosomes. After division the radiating lines (microtubules) of the astral system disappear leaving the centrioles and the centrosome only. *Nerve cells have got no centrioles and are incapable of reproduction.* **Functions**—Centrioles control polarisation of spindle fibres and play some part in their formation.

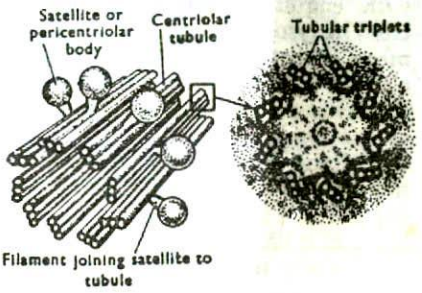


FIG. 10. Diagrams show the arrangement of centriolar tubules, *nine* in number, each tubule consisting of *three* centriolar subunits in right-sided inset.

4. (*a*) **Plasmosin.** It is a constant and characteristic constituent of cytoplasm. It consists of elongated protein particles rich in deoxyribonucleoprotein. They join up lengthwise and form the so-called intracellular fibrils, e.g., *tonofibrils* in the epithelial cells, *myofibrils* in the muscles, and *neurofibrils* in the nerves. (*b*) **Vacuoles.** They are demonstrated by placing living cells in a dilute neutral red dye solution. Some amount of lipid material are often found around the vacuoles. (*c*) **Nissl Bodies. (Granules)** are found in nerve cells.

B. Nucleus

The nucleus (FIG. 11) is generally a round body occupying the centre of the cell. Its shape, size, position and number vary. The nucleus may contain many lobes. Usually most mature cells possess a nucleus, but there are certain larger cells in the body which may contain more than one nucleus. If the nucleus is removed, the cell dies. The nuclear material differs from the cytoplasm in several respects. *First*, it is more opaque to the ultra-violet rays. *Secondly*, it shows many selective staining reactions but usually takes basic stain, while cytoplasm may take neutral, basic or acid stain. *Thirdly*, the nucleus is very rich in deoxyribonucleic acid (DNA), while cytoplasm is rich in ribonucleic acid (RNA). The nuclear membrane is also a unit membrane. Surrounding the nucleus,

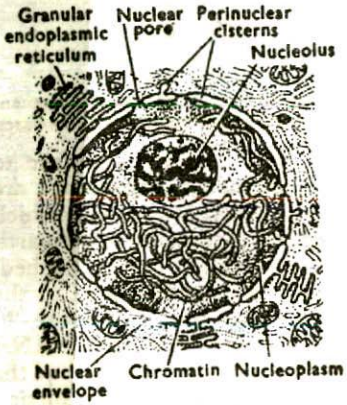


FIG. 11. Electron microscopic structure of nucleus (diagrammatic).

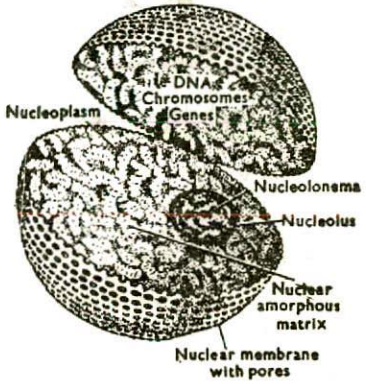


FIG. 12. Diagram shows chromosomes extending through the amorphous matrix and innermost limit of cytoplasm and porous nuclear membrane.

there is a **lipoprotein nuclear envelope.** This envelope is double-layered and the spaces between two folds are known as **perinuclear cisterns.** In the apparently quite permeable membrane of the nucleus, pores (areas of discontinuity) of about 6 mμ in diameter are closed by a thin homogeneous membrane which permits passage of molecules from the nucleus to the cytoplasm (FIG. 12). This indicates connecting link between the genes and ribosomes, the site of cytoplasmic protein synthesis. (*a*) **Nucleolus**—Inside a nucleus there is usually single or may be from two to five smaller bodies known as **nucleolus** or **nucleoli** which lie among nuclear sap (*karyoplasm*) and among the pale-staining karyoplasm *chromatin granules* lie. The nucleolus comprises the irregular network or rows of fine granules, **nucleolonema** as seen in E.M. The nucleolus loses its identity during cell division. (*b*) The nucleolus contains still smaller nucleus known as **nucleololus** or **nucleolinus** or **nucleolonucleus.**

The nucleus is responsible for the synthesis of **messenger RNA** (mRNA) which carries the genetic information in code through the pores in the nucleus. Recently it has been studied that mRNA is formed in the strands of DNA within the nucleus and actually the strands of DNA (FIG. 13) direct the synthesis of specific mRNA. The mRNA thus formed

in the nucleus comes out of the nucleus for carrying the DNA-message to the protein-synthesising centre (ribosome) of the cytoplasm. Here it is

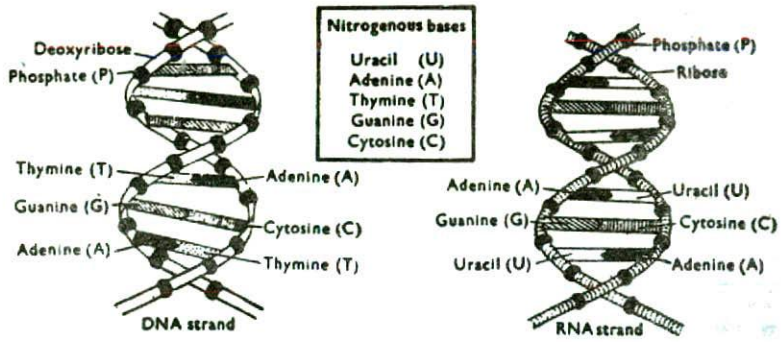


FIG. 13. Diagrammatic representation of the structural difference of helical arrangement of DNA strand and RNA strand having joints with their corresponding nitrogenous bases.

attached to the ribosome and stretched out (FIG. 14) on its surface to direct the protein synthesis. The amino acid sequences in the protein are determined by the **transfer** or **soluble RNA** (tRNA or sRNA) which recognises the code for the amino acids the tRNA is carrying to the particular spot of the ribosomal surface where the mRNA is already attached. Main **functions of tRNA** is to transfer the specific amino acid to the template of mRNA for correct amino acid sequence. There are 20 specific tRNA for 20 specific amino acid. With the help of these tRNA the protein is synthesised with proper sequences at the template of the mRNA and are stretched on the surface of the ribosome. After completion of protein synthesis, the protein molecules become detached from ribosomal particles and pass into the canal of the endoplasmic reticulum. From here it passes into the Golgi complex.

According to staining reactions, two types of nucleoli are found. Those taking *basic stain* are called **karyosome,** and those taking *acid stain*, **plasmosome.** The body of the nucleus is made up of a fine network of a particular substance, called **linin.** The meshes of this network are filled up with clear protoplasm—the **nucleoplasm** (karyoplasm, karyolymph or nuclear sap). In unstained specimens nothing more can be seen. But in stained specimen, numerous particles of blue-staining materials of irregular shape but smaller than nucleoli are found in the nucleus. This material is generally described as **chromatin.** It was believed for many years that chromatin was the breakdown products of chromosome during the interval between successive cell division (resting stage or more correctly the interphase stage) and chromosome is the recollection of chromatin into visible rod-like structure during cell division, but very recent observations hold just the opposite views. Because if chromatins contain different **genes** which determine the heredity of the cell and again the reassembly of different chromatins to form chromosome then it would invite different accidents. Because in such case the genes belong to one chromosome would have been incorporated into another chromosome. Recent observations thus claim that chromatins seen in interphase nucleus are nothing

but densely stained certain scattered portions of chromosomes which are visible in the microscope. This visibility of the chromosome mainly depending upon the **coiling** and **uncoiling of the chromosomes.** During cell

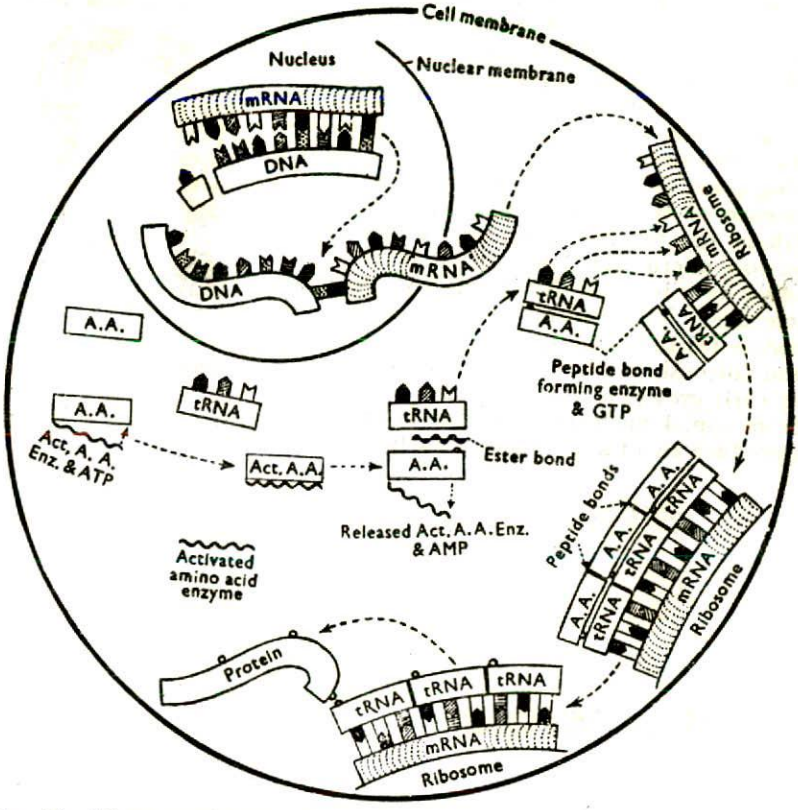


FIG. 14. Diagrammatic representation of the functions of DNA, mRNA and tRNA in protein synthesis. A. A.=amino acid; Act. A. A. Enz.=activated amino acid enzyme; Act. A. A.=activated amino acid; ATP=adenosine triphosphate, AMP=adenosine monophosphate; GTP=guanosine triphosphate.

division the chromosomes become tightly coiled and this coiled chromosomes or the coiling portions of the chromosomes are stained deeply. But following cell division or in interphase stage the coiled chromosomes become uncoiled all over its length but some portions still remain coiled. These tightly coiled portions become visible as granules or granular mass in the interphase nuclei. Chromatin can thus be described as **heteropyknotic,** because of having one or two densities. On the basis of density in staining, the chromatin can be grouped into two types. The coiled portions of the chromosomes are called the **positively heteropyknotic** and the uncoiled (expanded) portion is called the **negatively heteropyknotic.** But on the genetic basis, there is another terminology for chromatin. The extended portion of the chromosome is genetically active and

is called **euchromatin** and the coiled portion (positively heteropyknotic) is genetically inactive and is termed **heterochromatin** (FIG. 15). The euchromatin is actively engaged in the synthesis of specific messenger RNA (mRNA). It is believed that the *heterochromatic portion* is concentrated with DNA and RNA while the *euchromatic region* contains DNA and histone.

It has recently been possible by Miller and Beatty (1969) to study under electron microscope the structure and function of isolated living genes in the amphibian egg cells. The presence of extrachromosomal nucleoli in amphibian oöcytes has permitted isolation and electron microscopic observation of the genes coding for ribosomal RNA (rRNA) precursor molecules. Visualisation of these genes was possible because many precursor molecules are simultaneously synthesised on each gene. During early growth of the amphibian oöcyte, the chromosomal nucleolus organiser is multiplied to produce about a thousand extrachromosomal

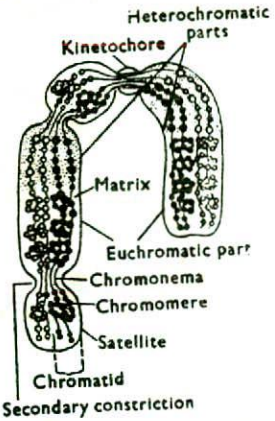


FIG. 15. Electron microscopic structure of chromosome (diagrammatic).

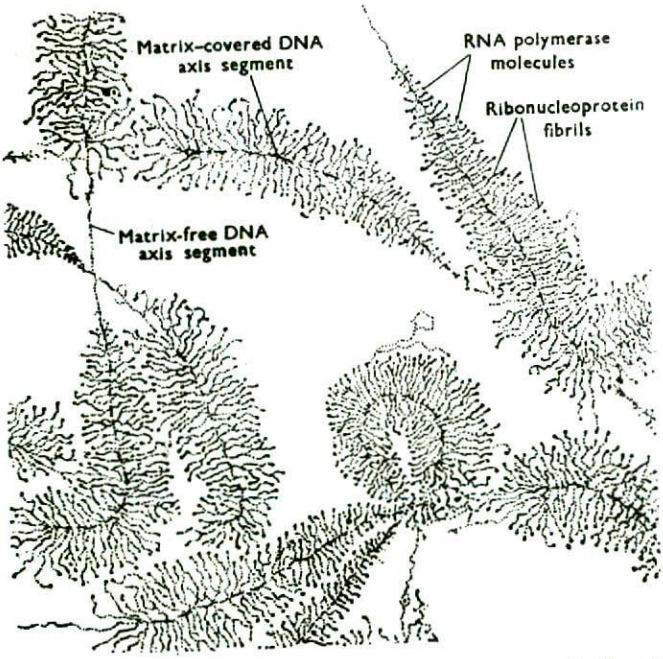


FIG. 16. Electron microscopic structure of isolated living genes in the amphibian egg cells. From 'SCIENCE—*Visualization of Nucleolar Genes*' (Volume 164, May 1969) reproduced with kind permission of authors O. L. Miller and Barbara R. Beatty, Oak Ridge National Laboratory, Tennessee.

nucleoli within each nucleus. These extrachromosomal nucleoli have been claimed to function similarly to chromosomal nucleoli in the synthesis of rRNA precursor molecules. The figure shows the nuclear genes from an amphibian oöcyte (Fig. 16). Extrachromosomal molecules are composed of a compact, fibrous core and a granular cortex. Each fibrous core consists of an axial fibre or core axis that is covered with matrix material. Each matrix unit is composed of 80–100 fibrils. The core axis is DNA coated with protein and the fibrils of matrices are ribonucleoprotein (RNP). It has been shown that RNA synthesis occurs within matrix units. It is believed that each matrix-covered DNA axis is a gene coding for rRNA precursor molecules. Each matrix segment along an axis is separated from its neighbour by a matrix-free axis segment. These genes which code for ribosomal RNA, repeat along the DNA axis and are visualised because approximately 100 enzymes are simultaneously transcribing each gene. The gradient of fibrils that extend from each gene contains rRNA precursor molecules in progressive stages of completion.

Chromosomes. Thus from the preceding section it can be emphasised that the chromosome is present as individual bodies in the interphase as well as in the mitosis. The predominant component in the chromosome is DNA molecule. The genes are located in chromosome of the nucleus and can be called as the discrete unit of transmission of hereditary character, because it is the specific locus or spot on a chromosome carrying the genetic material or information for a specific character. The gene is a part of the DNA molecule. Each chromosome consists of one to four coiled threads called **chromonema** and also contains juxtaposed minute particles known as **chromomeres** (Fig. 15) which are rich in DNA. Most of the chromosomes possess usually two constrictions—*primary* (**kinetochore**) and *secondary*. Chromosomes having terminal or almost terminal kinetochore are called **acrocentric chromosomes.** While chromosomes having unequal arms and almost centrally situated kinetochore are known as **metacentric chromosomes.** Chromosomes possessing secondary constriction in addition to primary one are called **submetacentric chromosomes** (Fig. 17).

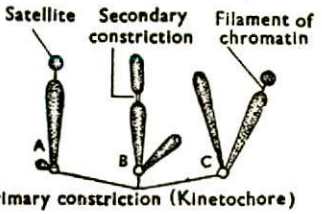


Fig. 17. Diagram shows three types of chromosomes on the basis of position of kinetochore (diagrammatic).
A = *acrocentric chromosome*,
B = *submetacentric chromosome*,
C = *metacentric chromosome*.

In human being, there are 46 chromosomes, arranged in pairs, in the nucleus of each cell. In each individual somatic cell nucleus, *there are* 22 *pairs of somatic chromosomes, also called* **autosomes,** *which are homologous* and concerned with the transmission of ordinary hereditary characteristics and the *remaining pair* is concerned with the determination of sex. In the female the sex chromosomes consist of a pair of identical large X chromosomes, whereas in the male the pair consists of an X chromosome and a Y chromosome which is small and has no influence on sex determination. One of the X chromosome, present in the female, is tightly coiled and can be seen under microscope in the nuclei of squamous epithelial cells and neutrophil granulocytes. This X chromosome may also be present in sexually abnormal cases.

On the other hand, in females *germ cells* (gametes) have 22 autosomes and one X chromosome; in males it may be 22 autosomes and either an X or a Y chromosome.

It is these chromosomes which determine the specific characteristics of the cell and it is through them that the hereditary qualities pass from one generation to the other. Nucleus is the most essential part of the cell. Upon it depends the power of morphological and chemical synthesis. The non-nucleated fragment of the cell quickly dies; because it possesses no power of synthesis and regeneration. While that fragment of a cell which contains the nucleus, rapidly resynthesises the lost parts and carries on normal life. If the nucleus of a cell is punctured, the cell dies.

From the above facts it seems that the cell, although a very tiny body, yet in itself, is a highly organised structure. The whole cell life appears to be divided up into a number of functional compartments and that each one of the so-called organoids possibly acts as the presiding officer of a particular department of cell life.

CYTOPLASMIC INCLUSIONS. The cytoplasmic inclusions are not the living metabolic machinery of the body but are certain structures present in the cytoplasm of the cell. These are: (1) stored foods, (2) secretion granules, (3) pigments and (4) crystals.

1. **Stored foods.** A healthy subject can withstand starvations for weeks, only because of his stored foods in the cytoplasm. Every cell for its metabolic functions requires fuel and this fuel is always supplied from external source. When this external source fails to supply, the internal food source—stored foods in the cytoplasm thus maintain it for a certain period. These stored foods are the protein, carbohydrate and fat which are present as inclusions in certain cells.

(*a*) **Carbohydrate**—It is absorbed from the intestine in the form of monosaccharide and stored in the cytoplasm of animal cells as macromolecules—*glycogen*. It is stored as such particularly in the liver cells and also in other cells too. In ordinary H and E stain, glycogen in the cells cannot be demonstrated because the glycogen is not stained with H and E. But in such preparation glycogen is dissolved and removed, keeping a characteristic pattern of irregular space with ragged border. The cells, having complete devoid of glycogen, give a smooth appearance with H and E stain. Glycogen can be stained well with periodic acid-Schiff (PAS) which gives a brilliant red colour with glycogen. Like fat in the cell, carbohydrate does not tend to push nucleus sidewards of the cell. In electron microscope glycogen of the cytoplasm in unstained cell appears as pale amorphous areas. It has got a particulate appearance of granular material having 150A to 400A in diameter.

(*b*) **Fat**—It is mostly stored in connective tissue fat cells and it may also accumulate in the liver cells under certain conditions of dietary deficiency. In ordinary preparation, fat is generally dissolved out keeping a clear smooth and circular outline in the cytoplasm. Because the clearing agent which is used has the property of dissolving the fat. Fat in the cell is demonstrated convincingly with osmium tetroxide fixative which does not allow fat to be dissolved off by clearing agents. In the above fixative the fat looks like a dark-brown or black mass.

Fat at first accumulates in the cell as droplets and then fuse to form large droplets. In a cut section these large droplets look like a *signet ring*. A large amount of droplets tend to displace the nucleus towards the periphery of the cell. The spaces left over by the dissolved fats are not irregular but it is spherical and smooth. As already noted these differ from the spaces left by dissolved glycogen.

(*c*) **Protein**—It is rarely stored as cytoplasmic inclusions and cells at a certain stage consume their own cytoplasm as a stored food. Reserve of proteins mainly exists in the matrix.

2. **Secretion granules.** Digestive enzymes and other fluid materials are synthesised from raw materials brought in the cytoplasm through the blood and tissue fluid. These materials remain in the cytoplasm as small globules or droplets of fluid and usually precipitated in the form of granules during fixation. These granules can be stained successfully with special histochemical techniques.

3. **Pigments.** There are certain pigments in the cytoplasm. In order to be visible hese pigments do not require any dye for staining. These pigments are present as

cytoplasmic inclusions in the cell. They may be classified into two groups: (*a*) endogenous type and (*b*) exogenous type.

(*a*) **Endogenous pigments**—These pigments are those which are synthesised within the body. These are as follows: (*i*) **Haemoglobin and its derivatives**—Haemoglobin is the iron-containing pigment of the red blood corpuscles (R.B.C.). The red colour of the R.B.C. and the blood as well is due to the presence of the haemoglobin. (This will be discussed in Chapter IV). In normal condition the life span of red cells are only a few months as they are destroyed by phagocytosis. The haemoglobin of these cells is broken down into *haemosiderin* (iron-containing pigments) and *haematoidin* (non-iron-containing pigments).

Haemosiderin is disposed in the cytoplasm of phagocytes as granules or an irregular mass. Normally it is also present in certain amount in phagocytes of spleen, liver and bone marrow, and the quantity is increased during rapid destruction of R.B.C. in diseased state. A green pigment, **biliverdin,** is the breakdown product of haemoglobin. On reduction biliverdin gives rise to a yellow-brown pigment, **bilirubin. Haematoidin** is a breakdown product of haemoglobin during destruction of R.B.C. and is identical to bilirubin. Bilirubin does not contain iron and is very soluble. For this reason it is dissolved in the blood and is not stored in the cells and thus is continuously removed from the liver cells into the bile.

(*ii*) **Melanin**—This is a brown-to-black pigment present in the skin, eye, etc. This pigment is absent in the albino. The dark colour of the Negros is due to the presence of this pigment in a large amount. This pigment is present in the cytoplasm of cells as granules or cluster of granules. It is tyrosine derivative and its concentration in the cells alters during derangement of tyrosine metabolism.

(*b*) **Exogenous pigments**—These are the yellowish pigments (*i*) **carotene** and (*ii*) **lipochrome** present in the vegetables. Besides these, certain dusts like carbons and minerals like lead and silver are also present. Carotene pigments sometimes accumulate in the cells when excess carot is consumed. Sometimes it may look like jaundice as the carotene pigment gives a yellow colour of the skin and the body fluid. Lipochrome is also a yellow pigment present in certain cells particularly in older ones. Its quantity mostly depends upon the wear and tear of cells. Furthermore the quantity of lipochrome in the cells is mostly dependent upon the activity of cells. It is present in the liver, muscle and cardiac cells. Recently it is described that lipochrome is present in the lysosome and is sometimes referred to as **lipofusin.** It is soluble in fat solvent and present in several types of cells already described.

Dust—Coal dust may be deposited in the body through inspired air. Pigmentation may occur in the system which may not be so harmful.

Minerals—Certain minerals like silver or lead taken through mouth may produce pigmentation in the body. Gray pigmentation of the body may occur due to taking excessive silver as medicine. Similarly excessive lead may produce lime in the gums.

4. **Crystals.** Certain cells such as Sertoli and interstitial cells of the testes contain certain proteinaceous crystalline materials. Its significance is quite unknown.

Cell Division (Nuclear division)

This process can best be studied by using the drug *colchicine* which arrest nuclear division at metaphase. The division of one cell into two daughter cells is the basis of the continuity of life and underlies the complexity of metazoan organisms. *Mitosis* (indirect cell division), *amitosis* (direct cell division) and *meiosis* are considered as some of several types of existing cell division. Cell division may be separated into (*a*) *karyokinesis* (division of nuclear material starts with doubling of the chromosome in parent nucleus, followed by distribution between two daughter nuclei in equal proportion) and *cytokinesis* (cytoplasmic division in which each of two daughter cells receives one of the daughter nuclei). In a few cell types, karyokinesis may occur without cytokinesis.

Mitosis (Fig. 18). During growth or regeneration of tissue, cells divide by *mitosis*. Each chromosome reproduces itself by splitting lengthwise, so that two identical portions (or chromatids) pass to the daughter cells and grow into mature chromosomes identical with those in the parent cell. Normal cell division or mitosis is divided usually into four stages,

prophase, *metaphase*, *anaphase* and *telophase*. The interval between each cell division which is comparatively long is called **interphase.** The process of mitosis together with interphase period constitutes the **cell cycle.** The cycle is extremely short in the case of intestinal epithelium and very long in adult hepatic cell.

(*a*) **Prophase.** During the stage of prophase each chromosome looks as a pair of long entwined filamentous structures throughout the nucleus due to coiling of DNA molecules. They gradually shorten and thicken and become darker. The two centrioles with microtubules forming asters move to the opposite side. Spindle (group of tubules) becomes visible. At the end of prophase nuclear membrane and nucleolus disappear. The chromosomes separate from each other and become prominent.

(*b*) **Metaphase.** In the stage of metaphase, the chromosomes assemble at the equator of spindle fibres. Chromosomes appear as if suspended by microtubules (spindle filaments) in a single plane midway between two asters. Two chromatids are formed from each chromosome by longitudinal splitting.

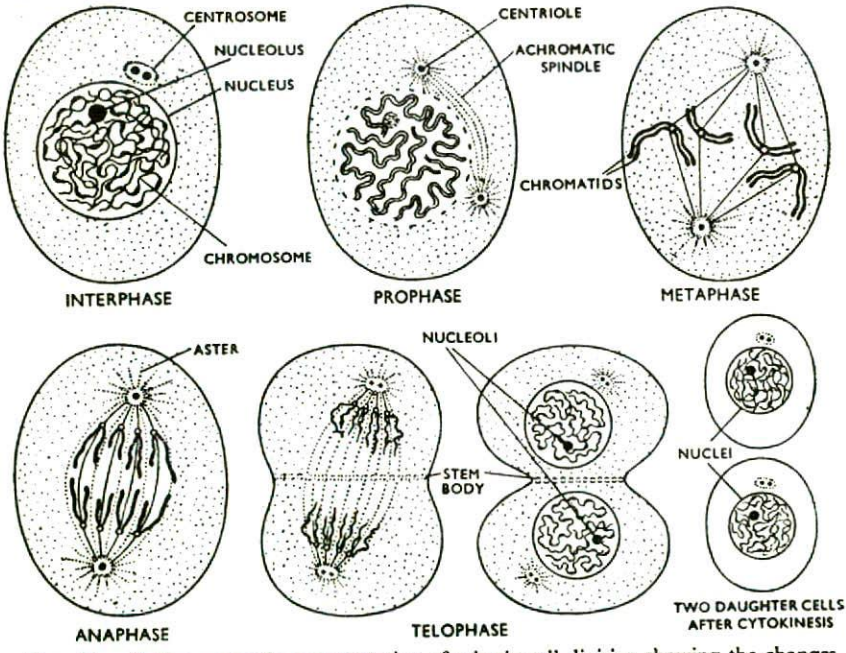


FIG. 18. A diagrammatic representation of mitotic cell division showing the changes in the centrosomes, centrioles, chromatids and nucleus of a cell.

(*c*) **Anaphase.** During anaphase the separated chromatids which form the chromosomes of the daughter cells move towards the opposite poles of the cell. Newly separated chromatids now are new chromosomes.

(*d*) **Telophase.** In the stage of telophase, a gradually elongating nuclear membrane due to uncoiling of DNA molecules is formed around two groups of chromosomes. Spindle fibres disappear. Formation of nucleolus completes the process of cell division and two identical daughter

cells after *cytokinesis* are usually formed from one parent cell. The different cytoplasmic organoids of the parent cell are distributed between the two daughter cells.

Interphase. This is a period between end of telophase of one cell division and beginning of prophase of next division. Chromosomes become elongated and too thin to be visible as such but chromatin granules are visible. Each chromosome duplicates (duplication of DNA molecules) forming two chromatids attached at centromere. Two newly formed cells grow.

Meiosis. Meiosis is the heterotypical process of the formation of germ cells, or sexual reproduction. This process occurs during spermatogenesis and oögenesis and starts at the stage when the primary spermatocytes and oöcytes divide to form secondary spermatocytes and oöcytes respectively. By the process of meiosis or *reduction division* each male or female germ cell has in it 22 autosomes and either an X or a Y chromosome. In the course of fertilisation the male germ cell (*spermatozoön*) and female germ cell (*ovum*) unite and the number of chromosomes are restored to the original 23 pairs. When the sperm and ovum unite, the resultant cell (*zygote*) possesses a full (diploid) complement of chromosomes, one half from the female parent and another half from the male. This process of meiosis is essential to prevent the otherwise doubling of the number of chromosomes which would have taken place by the usual process of mitosis.

Amitosis. It is a *direct process of cell division* and under which the nucleus of the cell first constricts in the middle to divide into two nuclei. After that the cytoplasm divides in the centre into two units and each cytoplasmic unit contains one nucleus. Thus from one cell, two daughter cells containing nucleus are formed.

Life cycle of cells. Two major types of cell may be recognised—somatic cells and gonadal cells. **Somatic cells** are the diverse cells which make up the somatic structure of the body being fated to die with or before the individual they constitute. A somatic cell begins its span of life as one of the daughter cells of a mitotic division. The frequency of mitotic division and the consequent production of daughter cells varies with the cell type. **Gonadal cells** are gametes (i.e., spermatocytes and oöcytes) capable of uniting sexually to form a new individual.

FORMATION OF TISSUE, ORGAN AND SYSTEM

The cells in the body of the multicellular animals vary in structure and function. It is seen that one variety of cell performs one kind of work and constitutes one type of tissue. So a **tissue** may be defined as an *aggregate* of same type of cells combined by subserving the same general function independently and united by varying amounts of intercellular substance (e.g., blood, bones, cartilage, muscle, nervous tissues, etc.). An **organ** is a group of more commonly two or more tissues, which basically function independently in some instances, in particular patterns to form larger functional units (e.g., blood vessels, kidney, skin, glands, etc.). When several organs function interrelatedly they form **organ system** (e.g., respiratory system composing the nose, larynx, trachea and lungs; urinary system comprising kidney, urethra and ureters). This arrangement, based upon the principle of division of labour and is an

essential requirement for co-ordinated living. One group of cells is set apart for one function and will specialise for that job. During the initial stages of embryolcgical development the cells are all similar. As development proceeds, one group of cells takes up one particular work, and, in order to perform the work in the best possible way, undergoes the necessary change in structure and mode of life. This process of adaptation of a cell, for the purpose of doing a particular function, is called *differentiation* or *specialisation*. The fertilised ovum (zygote) divides at first into two cells, these again into two more, and so on—until a large mass of embryonic cells is formed. The first few cells are believed to be *totipotent*, which means that, each one of them has got the potency of creating a total individual. The first evidence of differentiation is found in this cellular mass, where the cells become arranged in three distinct layers, known as the **ectoderm,** the **mesoderm** and the **entoderm.** The following tissues, in general, are derived from the three germ layers.

1. **Ectoderm.** Epithelium of mouth, nose, anterior surface of cornea, external auditory canal, skin, hair, urethra, etc., and also some glands like sweat (or sudoriferous), sebaceous (or oil) and mammary glands. The endocrine system, pituitary, adrenal medulla and pineal gland, brain and cranial motor nerves.

2. **Mesoderm.** Connective tissue including blood and bone marrow cells, the three different kinds of muscle in general, lymphatic organs, endothelium of blood vessels, epithelium of urinogenital tracts (e.g., urethra) and the adrenal cortex.

3. **Entoderm.** Epithelium of the digestive and respiratory tract, bladder, thyroid, parathyroid and thymus.

To understand the **systems,** one must know the **tissues** with which they are made of. A brief description of the different tissues is given below.

ELEMENTARY TISSUES OF THE HUMAN BODY

The human body is composed of the following elementary tissues: (1) **Epithelial tissue.** (2) **Connective (Mesenchymal) tissue.** (3) **Muscular tissue.** (4) **Nervous tissue.**

EPITHELIAL TISSUE

General Character. (1) It forms a limiting and a lining membrane, the *epithelial membrane* and as such, covers the free surfaces. The epithelial membrane rests upon the *lamina propria*, the supporting loose vascular connective tissue, by which the epithelium obtains its metabolic requirement from the blood vessels of this layer. (2) The cells remain close together with a minimum amount of intercellular cement substance. (3) There is generally a basement membrane* upon which the

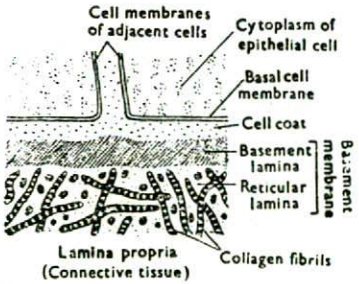


FIG. 19. Diagrammatic representation of basement membrane with adjoining epithelial cells, cell coat, lamina propria of connective tissue.

***Basement membrane.** It is present under the basal surface of the epithelium and is comprised of **basement lamina** and **reticular lamina** (FIG. 19). In routine haematoxylin-eosin preparation the basement membrane is not clearly visible but in periodic acid-Schiff (PAS) staining it can be clearly demonstrated.

epithelial cells are set. The cementing substance, here, is a mucoprotein containing hyaluronic acid and calcium salts.

Functions: (1) Protection. (2) Absorption. (3) Secretion. (4) Excretion.

Classification (FIG. 20): According to shape and layers of cells—

Simple (having only one layer of cells)	**Compound** (having more than one layer of cells)
1. PAVEMENT	1. TRANSITIONAL
2. CUBICAL	2. STRATIFIED SQUAMOUS CORNIFIED
3. COLUMNAR	3. STRATIFIED SQUAMOUS NON-CORNIFIED
4. CILIATED	4. STRATIFIED COLUMNAR
(*a*) *Columnar*, (*b*) *Cubical*	5. STRATIFIED COLUMNAR CILIATED
5. GLANDULAR	

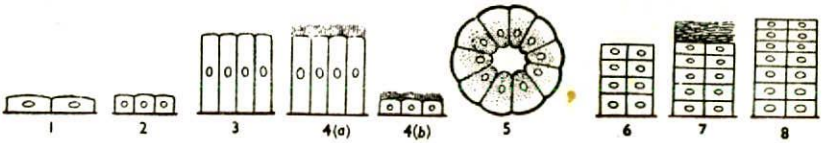


FIG. 20. 1=Pavement. 2=Cubical. 3=Columnar. 4(*a*)=Columnar ciliated. 4(*b*)=Cubical ciliated. 5=Glandular. 6=Transitional. 7=Stratified squamous cornified. 8=Stratified squamous non-cornified.

SIMPLE EPITHELIUM

1. **Pavement** (Squamous) (FIG. 20, NO. 1). It is composed of a single layer of large flat cells placed on a thin basement membrane. It is found in the alveoli of the lungs, the serous membranes (peritoneum, pleura, etc.), *Bowman's capsule* and *Henle's loop* of the nephron, the inner lining of the heart, the lining epithelium of the blood vessels, lymphatics and *Descemet's membrane* at the back of cornea, inner surface of the tympanic membrane, the membranous labyrinth, etc. In the lungs, serous membranes, blood vessels and lymphatics—the pavement epithelium has been given a special name—the **endothelium** (FIG. 21). In the heart, it is called **endocardium. Functions**—(1) has got a dialysing or filtering function. (2) Helps easy passage of liquid and gases through it. (3) Protective.

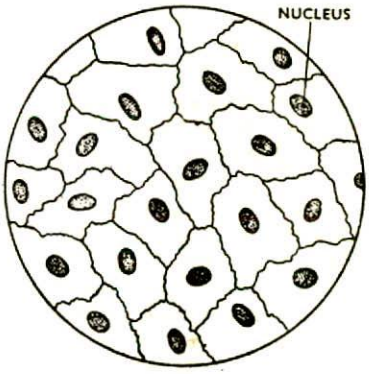


FIG. 21. Simple pavement epithelium.

In electron microscopic studies the two layers of basement membrane are clearly seen. The *basal* or basement lamina is present just under the basal surface of the epithelium and is composed of dense filamentous sheet of 500A to 800A in thickness. Outside the basal lamina is the reticular lamina, which are small fascicles of unit collagen or reticular fibrils embedded in an amorphous protein-polysaccharide ground substance. But its histology varies from place to place. It may be formed (*a*) by a dense network of fine reticular fibres, (*b*) by elastic material, e.g., arterial endothelium, back of cornea, etc., (*c*) by flattened connective tissue cells, (*d*) by condensed ground substance, e.g., trachea front of cornea, etc. **Function**—The basement membrane provides not only support, but also serves as a semipermeable filter under the epithelium.

Some workers subdivide this class into three groups: (1) **Endothelium**—lining the heart, blood vessels, lymphatics, etc. (2) **Mesothelium**—lining the serous cavities, e.g., pleura, pericardium, peritoneum. (3) **Mesenchymal cells**—lining the subdural and subarachnoid spaces, perilymphatic spaces of the internal ear and the chambers of the eyeball, etc. (The lining of the joint cavities is made up of flattened connective tissue cells—may be fibroblasts—and not the true mesenchymal cells.)

2. **Cubical** (Cuboidal). It is composed of a single layer of cubical cells having same dimensions on each side and placed upon a basement membrane (FIG. 20, NO. 2). They are found in the small terminal respiratory bronchioles, in the inner parts of the digestive glands, the salivary glands, thyroid, covering of ovary, etc. **Functions**—(1) forming a protective layer on the surface, (2) often serves some other important functions, such as secretion, storage, etc.

3. **Columnar** (Cylindrical). Here the height of the cells is more than their breadth. Generally, it is composed of a single layer of cells arranged on a basement membrane (FIG. 22). It is found in the stomach, whole of the small and large intestine, the alveoli and ducts of many glands, etc. The free surface of the ovary and the convoluted parts of the renal tubules are believed to be lined by modified short columnar cells. In detail, the cells of the columnar epithelium vary in different places. In the alimentary canal and proximal convoluted tubule of nephron their free borders are longitudinally striated. Hence, called *brush border* epithelium. Under the electron microscope, the brush border appears to be finger-like projections termed *microvilli*. Both the intestinal and renal epithelium are responsible for absorption and the microvilli increase the surface area to facilitate the absorption process. Another type of columnar epithelium occurring in intestine, mainly large intestine, is responsible for the secretion of mucus. These cells are called **goblet cells.** Electron microscopically the non-secreting goblet cells, but not the secreting ones, show microvilli. **Functionally,** they are very important Columnar epithelium has got two chief functions—absorption and secretion. The large ducts of the digestive glands (salivary glands) may show two incomplete layers of columnar cells. All the cells touch the basement membrane but all of them do not reach the surface, because, the deeper cells are shorter in length. This is sometimes called **pseudostratified columnar.**

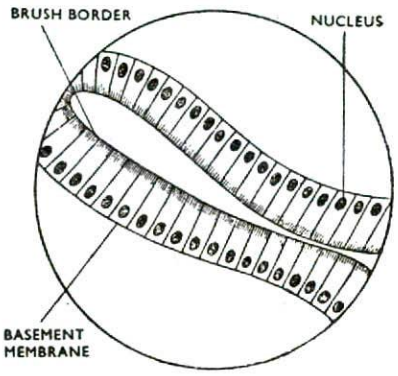


FIG. 22. Columnar epithelium.

4. **Ciliated.** (FIGS. 20, NOS. 4(*a*) & (*b*), 23). **Histology.** The cells are generally columnar in shape but at places may be cubical. The free surface has got hair-like processes—20 to 30 on each cell. These processes are called the *cilia* or *flagellae*. That border of the



FIG. 23. Ciliated epithelium.

cell upon which the cilia are set, is found to contain a row of particles—the *basal particles* (basal corpuscles). To each of these basal particles one cilium is attached. These basal particles are believed to be the fragments of the centriole of the cell. The cilia seem to be prolonged through the basal particles into the protoplasm of the cell in the form of fine longitudinal filaments known as the *rootlets*. They are very distinct in the large ciliated cells lining the alimentary canal of some *Molluscas*, but, is less distinct in the ciliated cells of the vertebrates. Their significance is not understood. All the cells in this epithelium may not be ciliated. Non-ciliated cells and the mucus-producing goblet cells remain scattered throughout the epithelium.

Distribution. They are very widely distributed. They are found in the respiratory passages and the cavities that open into it—from the trachea downwards excepting the terminal bronchioles and the alveoli. It is also found in the Fallopian tubes, in the greater part of the body of the uterus and in the efferent tubules of the testes. In the central nervous system it is also present as the lining epithelium (known as *ependyma*) of the ventricles, the central aqueduct and the central canal of the spinal cord. Here the cells are cubical in shape. In the trachea the ciliated epithelium has got two layers. Hence it is called **pseudostratified columnar ciliated epithelium** (FIG. 24). The deeper basal layer is **non-ciliated.** From this the ciliated cells develop.

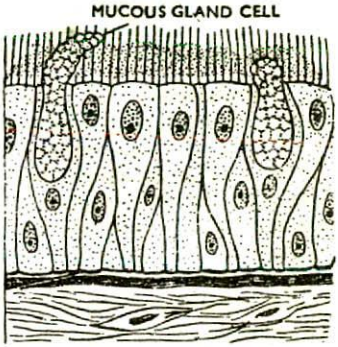


FIG. 24. Pseudostratified columnar ciliated epithelium.

Under the light microscope the cilia or flagellae appear as simple projections, but under the electron microscope, they have a complex internal structure.

The membrane of a typical cilium or flagella is continuous with the cell membrane and represents an extension of it. A bundle of fibres, **axoneme,** is in the centre of the organelle. In the axoneme, most of the ATP*ase* protein, **dynein,** is located. But these enzyme proteins possess certain differences from those found in muscle.

Ciliary movement, its cause and the factors affecting it (FIG. 25). The remarkable property of the cilia is that they appear to move permanently so long as the cell is living. When the cell is dead, ciliary movement ceases. The ciliary movement consists of two phases—a sudden



FIG. 25. Ciliary movements showing metachronal waves.

bending in the form of a sickle, known as the **effective phase** and then a sudden return to the original erect position—the **return phase.** In

the effective phase the cilia become rigid. In the return phase they are limp. The rate of movement is approximately ten to twenty times per second. There seems to be a functional co-ordination between all the cells of a ciliated epithelium. The movement is passed on from cilium to cilium and from cell to cell always in the same direction. When looked upon from the surface, a series of waves are seen to pass in regular sequence over the cilia, just like the waves caused by a gentle wind over the paddy fields. These waves are known as the **metachronal waves.**

The movements of cilia depend upon the life of the cell and upon their connections with the basal particles. As a rule they are independent of nerves. But in some instances ciliary movement can be modified through the action of nerves. The movements are hastened by warmth and weak alkalies. They are slowed by cold and acids. Calcium ions are essential for their action. Although the rate of oxygen consumption is directly proportional to the rate of ciliary action, yet the movements continue for some time even when oxygen is withheld. But ultimately anoxia stops the movements. Excess CO_2, ether vapour, chloroform, etc., arrest the movement.

Mechanism of the Ciliary Movement. The mechanism of ciliary movement is not known. Probably the underlying principle is same in all the ciliated bodies, e.g., the ciliated epithelium, the flagellated bacteria and parasites, the tail of the spermatozoa, etc. Formerly it was thought that displacement of water from the cell to the cilia and *vice versa*—is responsible for the ciliary movement. But later evidence indicates that the movement is generated in the cilium itself. Gray suggests that it may be due to rhythmic displacement of the water content of the cilia from one side to the other. That side which holds more water becomes convex and the opposite face concave. Thus the cilium assumes a sickle-like attitude (*effective phase*). In the next moment water flows back to the opposite side and the cilium stands erect, thus effecting the *return phase.*

Functions of Ciliary Epithelium. The functions of ciliary movement is to maintain a flow of mucus or liquid and the suspended particles constantly in one direction. In the trachea it carries mucus, foreign particles and bacteria outside at the rate of 1–2 cm per minute. In the Fallopian tube it carries the ovum towards the uterus. The function of the ciliated ependymal lining of the central nervous system is not properly understood. It is suggested that it helps to maintain the circulation of cerebrospinal fluid in the ventricles, central aqueduct and the central canal of the spinal cord.

5. **Glandular.** (FIG. 20, NO. 5). This epithelium lines the alveoli and portions of the ducts of the glands, e.g., the mammary gland, sweat (or sudoriferous) glands and sebaceous (or oil) glands, salivary glands, parts of intestinal glands, alveoli of the thyroid gland, etc. They are generally cubical, short columnar or polyhedral in shape and consist usually of one layer. Sometimes an incomplete second layer may be seen, such as in the salivary glands. They serve the very important **function** of manufacturing new substances and passing them out into their respective secretions.

Glands (FIG. 26) may be classified as follows:

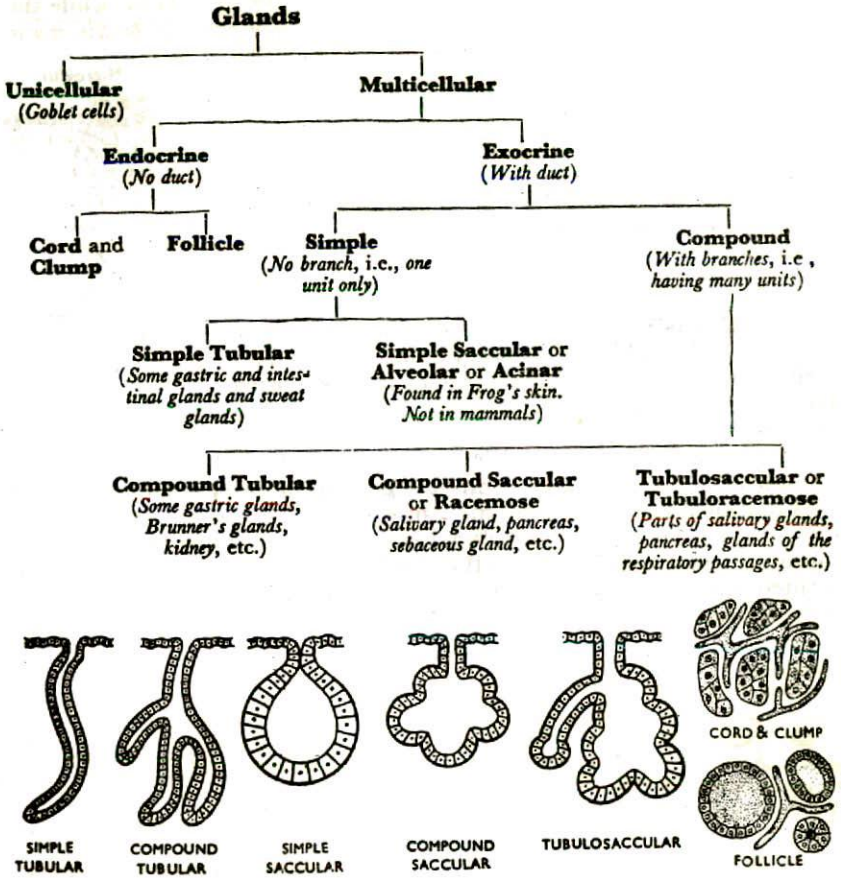


FIG. 26. Showing various types of glands.

According to the *mode of secretion*, gland cells are divided into three classes: (1) The **holocrine** type—Here the secretion collects inside the whole of the cell. The cell ultimately dies and disintegrates and thus the secretion is discharged. The adjoining younger cells multiply and replace the lost one, e.g., sebaceous glands. (2) The **apocrine** type—Here the secretion collects in the outer portion of the cell only, which gradually swells up and bursts. The rest of the cell remains intact and alive, and repeats the process again, e.g., mammary glands and possibly the goblet cells. (3) The **merocrine** (or **epicrine**) type—Here no gross histological change is visible in the cell. The secretion is quietly liberated through the cell membrane, e.g., digestive glands, endocrine glands, etc.

Goblet Cells (Chalice Cells). These are mucus-secreting cells. They are widely distributed and remain scattered mostly in between the

columnar and ciliated cells, e.g., trachea, gastro-intestinal tract, etc. The deeper part of the cell contains the nucleus and the cytoplasm, while the apical part contains *mucinogen granules*. They form the *glycoprotein mucin* (FIG. 27). The latter gradually distends and ultimately bursts, discharging the mucus outside. This process goes on repeatedly. In stained specimens the discharged cells look like white gaps. This mucus serves many important **functions,** viz., (1) lubrication, (2) protective layer on the mucous membrane, (3) dilution of irritants, (4) neutralisation of acids, alkalies, etc., (5) entangling bacteria, foreign particles, etc.

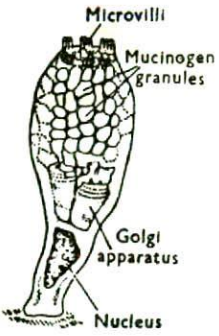


FIG. 27. Goblet cell.

COMPOUND EPITHELIUM

1. **Transitional.** It consists of three or four layers of cells and thereby occupies an intermediate position between the single-layered *simple epithelium* and many-layered *stratified epithelium.* Hence the name 'transitional'. (FIG. 20, NO. 6). The cells in the superficial layer are large, flat and irregularly quadrilateral, often containing two nuclei. The next layer consists to **pyriform cells** with the rounded ends outside and fitting into the cup-shaped depressions on the deep surface of the cells in the superficial layer. The next one or two layers consist of small **polyhedral cells** which remain packed in between the pointed ends of the pyriform cells of the second layer (FIG. 28). The cells are capable of deformation without any disturbance of functions.

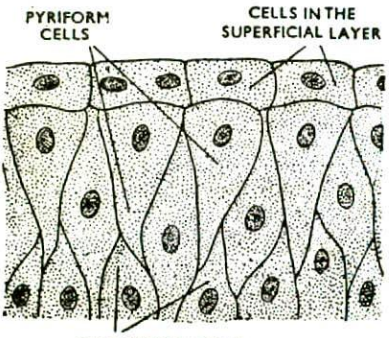


FIG. 28. Transitional epithelium.

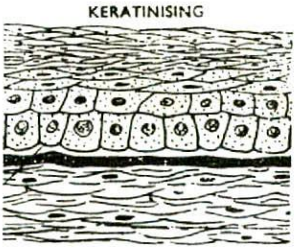


FIG. 29. Stratified squamous epithelium showing keratinising layers.

This type of epithelium is found in the pelvis of the kidney, in the ureter, in the urinary bladder and in the upper part of the urethra. It is to be noted that the distribution is limited to the lower parts of the urinary system. **Functions**—(1) Protective. (2) Prevents reabsorption of the excreted material back to the system. (3) Prevents indrawing of water from blood and tissues by the higher osmotic pressure of urine.

2. **Stratified Squamous Cornified.** It is composed of many layers of the cells. Usually the superficial layers are horny due to

disposition of **keratin** (FIG. 29). It is found in the skin. The hairs, nails, hoofs, horns, enamel of the teeth, etc., are modified epithelial tissue of this class. The skin affords a typical example of this type of epithelium. The most superficial layer is horny. In the next layer the cells are pressed down into flattened scales. Further down the cells are broader and polyhedral. Still deeper the cells appear to be short columnar in type. These deep cells are connected with each other by numerous intercellular fibrils and protoplasmic processes which look like thorns (FIG. 30). Due to this thorny appearance these cells are called the **prickle cells.** With the help of these prickles, the cells in the epithelium are firmly tied together. Due to friction the superficial layers of cells are continuously falling off. These cells are being constantly replaced by the division of cells in the deeper layer (FIG. 20, NO. 7). **Function**—This type of epithelium is always found in those places which are constantly exposed to atmosphere, mechanical pressure, friction and injury.

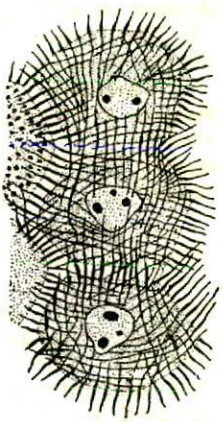


FIG. 30. Deeper cells of the epidermis showing fibres.

3. **Stratified Squamous Non-cornified.** *Histologically*, it is same as above excepting that the superficial layer is **not keratinised** (FIG. 31). It is found in the cornea, mouth, pharynx, oesophagus, anal canal, lower parts of the urethra, the vocal cords, the vagina and the cervix. **Function**—It affords mechanical protection (FIG. 20, NO. 8).

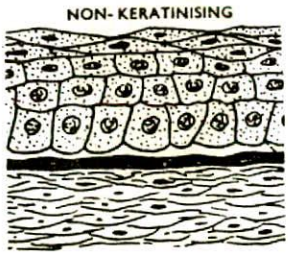


FIG 31. Stratified squamous epithelium showing non-keratinising layers.

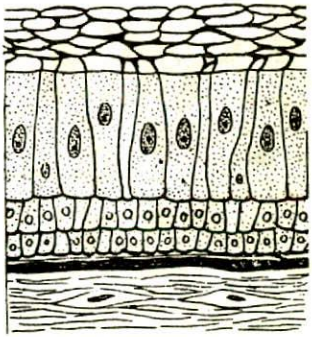


FIG. 32. Stratified columnar epithelium.

4. **Stratified Columnar.** It is rare and found only in a few places, covering small areas, e.g., fornix of conjunctiva, some parts of pharynx, epiglottis, anal mucosa, cavernous part of male urethra, etc., (FIG. 32).

5. **Stratified Columnar Ciliated.** This also is found only in small areas, e.g., nasal surface of the soft palate, some parts of larynx, etc.

CONNECTIVE (*MESENCHYMAL*) TISSUE

General character. (1) They are all developed from the mesoderm. (2) The intercellular substance is prominent and may be considerable in amount. This is a great contrast with the epithelial tissues. (3) The intercellular ground substance may contain different types of fibrous elements.

Varieties. The following varieties have been described: (1) **Areolar tissue,** (2) **Adipose tissue,** (3) **White fibrous tissue,** (4) **Yellow elastic tissue,** (5) **Reticular tissue,** (6) **Blood** and **haemopoietic tissue,** (7) **Cartilage,** (8) **Jelly-like tissue,** (9) **Osseous tissue (bone)** and (10) **Reticulo-endothelial tissue.**

1. **Areolar Tissue.** It is distributed (*i*) in the subcutaneous (Fig. 33), submucous and subserous tissues; (*ii*) between muscles, vessels and nerves; (*iii*) in the interior of organs binding the different parts. Areolar tissue is composed of fibres and cells. Fibres are (*i*) white or collagenous, (*ii*) yellow elastic fibres, (*iii*) reticular fibres (Fig. 34). The bundles of collagenous, elastic and reticular fibres cross and intercross, thus making a network, the spaces of which are occupied by the clear ground substance and various types of cells. Following **varieties** of cells are generally found in the areolar tissue. (*a*) **Fibroblasts** (Fibrocytes). *Fibroblast is an active cell. Fibrocyte is an inactive one.* These cells are usually elongated containing an oval nucleus and are often branching. The younger cells are more rounded, whereas the older ones are more elongated. They remain upon and in between the fibres. When they lie upon the surface of an

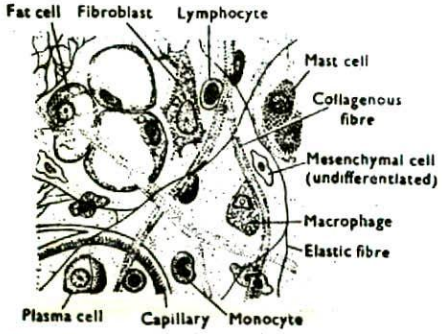


Fig. 33. Subcutaneous loose areolar tissue with cells and fibres (diagrammatic).



Fig. 34. Reticular fibres showing basal lamina of epithelium (diagrammatic).

aponeurosis, they are arranged side by side and look like an endothelium. In the cornea the fibroblasts remain joined together through their branches. Fibroblasts are non-motile and are not phagocytic. Their **function** as the name implies is to produce white fibrous tissue under normal and pathological conditions. They are also responsible for the formation of amorphous ground substance. It takes a great part in replacement fibrosis during repair of inflammation. Following tissue injury there is an increase in cytoplasmic ribonucleoprotein (RNP) granules in fibroblast, observed electron microscopically. (*b*) **Histiocytes** (Clasmatocytes).

These cells belong to reticulo-endothelial (R. E.) system and have functions similar to them. They are large and irregular containing one or more nuclei and a basophilic cytoplasm. They are actively motile and phagocytic, and engulf foreign substance and bacteria. **Function**—The proteolytic enzymes present in the cells destroy the digestible ingested materials. (*c*) **Basophil** (Basiphil) **cells.** They are large, spherical or oval cells, actively motile and containing a single nucleus and a granular basophilic cytoplasm. They are commonly found in those places where fat is being deposited. Occasionally they burrow into the blood vessels and appear as the basophilic leucocytes (mast cells) in the blood stream. Their *functions are same as that of the mast cells.* (*d*) **Plasma cells.** These are large, oval cells with non-granular basophilic cytoplasm stained by Leishman's method and a round eccentric nucleus. The chromatin in the nucleus is arranged like the spokes of a wheel. These cells have an abundance of granular endoplasmic reticulum and so can be stained with *pyronins* (**pyroninophilia**) which demonstrate RNA. Fluorescent antibody technique indicates that these cells form antibodies. Their **function** is the synthesis of *γ-globulin.* (*e*) **Pigment cells.** Some of the connective tissue cells are found to possess pigment granules and such cells are more common in the skin, choroid coat of the eye, pia mater, etc. The black pigment is called **melanin** and the cells, **melanocytes.** In some lower vertebrates, the pigment may be yellowish and such cells are called the **xanthophores.** The pigment granules generally remain collected round the nucleus. But change of environment, i.e., light, moisture, etc., causes dispersal of the pigment granules out into the cytoplasm. Due to this mechanism certain animals can change their skin colour and use this device as a protective camouflage. This redistribution of the pigment is caused by a hormone secreted by the posterior pituitary (melanocyte-stimulating hormone, MSH). (*f*) **Mast cells.** They are large round or oval cells. The cytoplasm contains coarse granules which can be stained with basic dyes, the nucleus being stained pale. Under electron microscope, little granular endoplasmic reticulum or free RNA has been observed inside the cell. Mast cells probably elaborate (1) the anticoagulant **heparin,** (2) probable synaptic mediator **histamine,** and (3) a vasoconstrictor **serotonin.**

The areolar tissue is distributed in varying amounts throughout the body. It occupies the intercellular spaces of other connective tissues and serves as a support and also as a packing material. The cells in it serve the purpose as described above.

2. **Adipose Tissue** (Fig. 35). The adipose or loose tissue is characterised by containing free fat inside the **fat cells.** These cells remain supported by a loose framework of areolar tissue. The cells are generally large, rounded or oval in shape. They may be polyhedral due to pressure of the adjacent fat

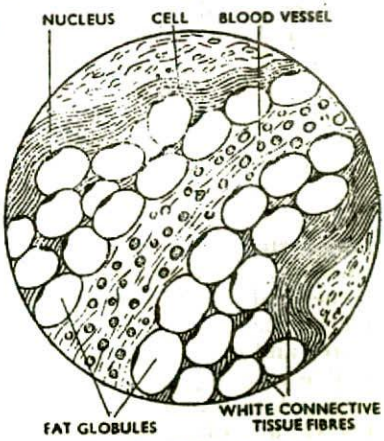


Fig. 35. Adipose tissue.

cells. The big fat droplets occupy almost the whole of the cell. The cytoplasm and the flattened nucleus are pushed out to one side. For this reason the cell looks like a 'signet' ring. The fat cells may be stained by **Sudan III** or **Scharlach R** or osmic acid. In paraffin sections, the fat droplets are dissolved out and the cells look like big white gaps. Blood vessels and lymphatics pass along the loose framework. The cells are said to contain special enzymes which help deposition of neutral fat. On morphological ground there are (*i*) white or yellow (unilocular) adipose tissue which comprises the bulk of body's fat reserves and (*ii*) brown (multilocular) adipose tissue is much more restricted in its distribution.

Distribution. They remain distributed in many places and are specially found in the so-called fat depots, viz., omentum, subcutaneous tissue, mesentery and perinephric region, subpericardial tissue, etc. Yellow bone marrow is very rich in fat. The lactating mammary gland contains a large amount of fat. Adipose tissue is absent in (*a*) eyelids, (*b*) penis, (*c*) scrotum, (*d*) labia minora, (*e*) cavity of cranium, (*f*) lungs except their roots, etc.

Functions. Adipose tissue serves: (1) Remaining under the surface gives shape to the limbs and body. (2) Remaining around the viscera keeps them in position and prevents injury. (3) Plays a good part in the regulation of body temperature. (4) Represents stored energy. (*Vide* also 'Depot Fat'.)

3. **White Fibrous Tissue** (Fig. 36). It is made up of shining white fibres (formed by the *fibroblasts*). They are thin and non-branching (*regular*). The fibres do not run singly but in bundles. The bundles of white fibres are wavy (*irregular*) and run in different directions. Although the individual fibres do not branch, yet the bundles freely branch and the branches communicate with one another. The interspaces thus produced are occupied by areolar tissue and the connective tissue corpuscles. These cells become squeezed by the adjacent bundles of white fibres and in transverse section assume an angular stellate appearance. Such **stellate cells** are typically found in the transverse section of tendons. White fibrous tissue is present in tendons, ligaments, aponeurosis, articular capsule, the deep fascia of the body and limbs, the fibrous coverings of the organs and certain other membranes, e.g., the dura mater, etc. It is also found in one form the fibro-cartilage. Its **function** is to connect the different tissues and the different parts of the body to afford mechanical protection against stretch and pressure, and in this way to impart great strength as well as a considerable amount of flexibility. *Chemically*, white fibrous tissue is made up of a protein known as **collagen** (Figs. 37 & 38), **digestible with pepsin.** From this, *gelatin* is easily obtained

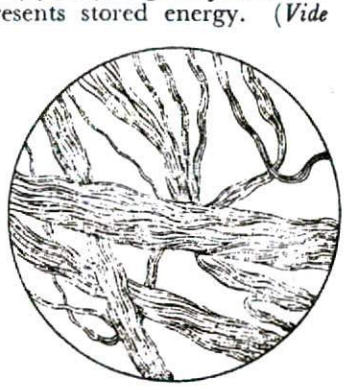


Fig. 36. White fibrous tissue.



Fig. 37. Bundle of collagen fibres showing unit fibrils (diagrammatic).

by boiling with a little hydrochloric acid. Electron microscopic studies revealed the fundamental molecule of collagen to be **tropocollagen,** about 3000 Å in length and 15 Å in width.

4. **Yellow Elastic Tissue** (Fig. 39). This is another variety of fibrous tissue (possibly formed by the fibroblasts). It *differs* from the white fibrous tissue in the following respects: (1) It has got a yellowish colour. (2) The fibres are thicker. (3) The individual fibres branch freely and the branches join with one another to form a network. (4) The fibres may run singly as well as in small loose bundles. Even in the bundle the outlines of the fibres are clearly visible. (5) The bundles are not wavy but follow a straight course. (6) When the fibres are torn by stretching, the broken ends quickly curl up due to elastic recoil. (7) In transverse section the fibres appear to be angular with the angles rounded off. (8) Elastic fibres are composed of a protein, **elastin,** which is resistant to most chemical agents but is digested by **pancreatin**.

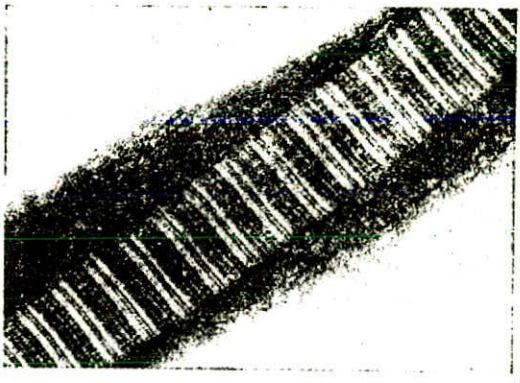


Fig. 38. Electron micrograph of a collagen bundle from a rat tail tendon stained by negative contrast technique showing the typical cross-striations. ×56,000. *Electron micrograph by courtesy of Dr. Tapen Mukherjee, Department of Biophysics, Chittaranjan National Cancer Research Centre, Calcutta.*

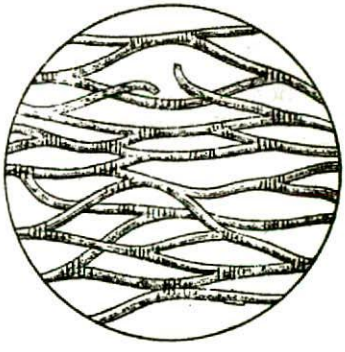


Fig. 39. Yellow elastic tissue.

Distribution. It is found in the areolar tissue throughout the body. It is present in the hollow viscera where the restoration of normal configuration is essentially required. It is found in the most concentrated form in the *ligamentum nuchae* of the quadrupeds, in the *ligamentum flava* of the vertebra. It is also found in the walls of the bronchi and in the larynx, uniting the cartilages. It is also present in the lungs and in the walls of the arteries and in one form of fibrocartilage. Elastic tissue does not always remain in the form of fibres and bundles but may also occur as a continuous membranous sheath, such as the internal elastic lamina of the blood vessels.

Functions. The *function of the elastic tissue* is always due to its strength, extensibility and elastic recoil. In other words, it serves the purpose of a strong elastic rope. In the form of ligaments it holds the connected parts firmly together and at the same time allows considerable latitude of movement. In blood vessels it prevents excessive dilatation

and by its elastic recoil serves to maintain circulation and blood pressure. In the lungs its elastic recoil helps expiration as well as maintains and adjusts the negative pressure in the pleura.

5. **Reticular Tissue** (Fig. 40). It is similar to the areolar tissue with certain peculiarities. The *reticular fibres* here resemble white fibrous tissue, having the following *differences:* (1) They are thinner, freely branching and resist peptic digestion. (2) They are selectively stained by silver oxide or carbonate solution. Hence called *argyrophil* fibres. Interspaces are very small and are largely occupied by lymph and tissue fluid. The cells of this tissue belong to the so-called reticulo-endothelial system. Reticular tissue is widely distributed. It forms the basement membrane of many epithelia, the framework of many organs, supporting their essential cellular elements. It occurs in lymph nodes, liver, spleen, bone marrow and many other organs.



Fig. 40. Reticular tissue as seen in a thin section of lymph node (diagrammatic).

6. **Blood and Haemopoietic tissue.** Blood cells are also considered to be the special type of connective tissue and have been dealt in detail in the section of blood.

Haemopoietic (properly haemocytopoietic) tissues are of two types: (*a*) myeloid and (*b*) lymphatic. Lymphatic tissue generally gives rise *lymphocyte*, and myeloid tissue normally produces *erythrocytes*, *granular leucocytes* and *platelets*. *Monocytes* are produced from both the tissues.

(*a*) **Myeloid tissue.** It has got both phagocytic as well as blood cell-producing function. It produces erythrocytes, granular leucocytes and platelets. *Myelos* means *marrow*. Normally the term myeloid tissue and bone marrow are used synonymously (*vide* chapter IV).

(*b*) **Lymphatic tissue.** The lymphatic tissue can be subdivided under the following: (*i*) *Non-capsulated nodules* of lymphatic tissue in the loose connective tissue. (*ii*) *Capsulated lymphatic tissues* which are present in specific lymphoid organs, viz., (*a*) **lymph node** or **lymph gland** (*vide* chapter V), **spleen** (*vide* chapter V), (*c*) **thymus** (*vide* chapter XV) and (*d*) **tonsil.**

Non-capsulated lymphatic nodules. These nodules are the dense aggregation of and the structural units of lymphoid tissue. The nodules are not the constant feature of any organ but they appears or disappears frequently and new nodules are generated. The nodule may be homogeneous or has a darker cortex and a comparatively lighter central area—the *germinal centre*. The lymph nodules may be distributed in lymphatic organs like lymph nodes, spleen, thymus and tonsil and in non-lymphatic organs (e.g., digestive organs) as solitary nodules. **Peyer's patches** of the small intestine are the example of the solitary nodule.

Lymphoid nodules become prominent after birth and in adult life it remains undeveloped in germ-free animal. However, it becomes developed tremendously under antigen reaction.

Tonsil (Capsulated lymphatic tissue). There is accumulation of lymphoid tissue in the mucous membrane at the root of the tongue and

at the surrounding of the pharynx, where nasal and oral passages unite. This lymphoid tissue is invaginated by the surface-stratified epithelium and are easily seen as well-defined organs which are known as **tonsils.** The tonsils do not possess *afferent lymphatic vessels.* The lymph nodes remain scattered throughout the tonsil. (1) *The arrangement of the lymphoid nodules,* (2) *the absence of cortex and medulla,* (3) *the presence of crypts* on the surface and (4) *the covering of stratified epithelium*—are very important identifying features of tonsil. Usually tonsils can be divided into three groups—(*a*) palatine tonsils, (*b*) lingual tonsil and (*c*) median nasopharyngeal tonsils in the posterior wall of the nasopharynx (FIG. 41).

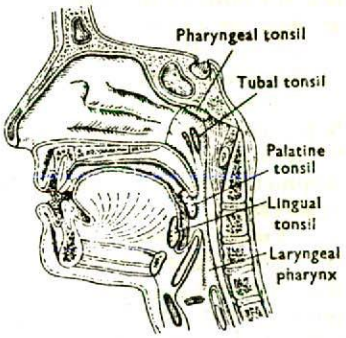


FIG. 41. Anatomical position of tonsils (diagrammatic).

(*a*) **Palatine tonsil.** The palatine (faucial) tonsils (FIG. 42) are paired oval masses of lymphoid tissue which are covered by stratified squamous epithelium lying on the tunica propria of connective tissue. The surface of the tonsil has got numerous deep furrows which are known as **crypts.** The crypts (pits) are lined by stratified epithelium. Ducts of mucous glands sometimes open in the crypts. The tonsilar substances are constituted with diffuse lymphoid tissue containing numerous lymph nodules. Most of the lymph nodules possess *germinal centres* which give rise to lymphocyte. Micro-organisms may accumulate in the lumen of crypts causing inflammation to the tonsil.

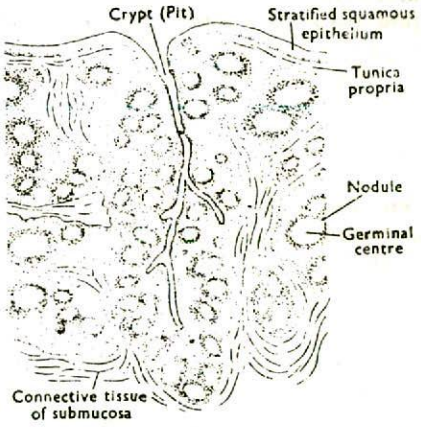


FIG. 42. Palatine tonsil (diagrammatic).

(*b*) **Lingual tonsil.** This is situated at the root of the tongue behind the circumvallate papillae. There are wide-mouthed crypts which are surrounded by the lymphoid tissue. Each crypt is lined by stratified squamous epithelium. Like the palatine tonsil, the lymphoid tissue contains lymph nodules with germinal centres and ducts of numerous mucous glands open on the surface or into the crypts. The secretion of which washes away micro-organism causing this variety of tonsil less labile to infection.

(*c*) **Pharyngeal tonsils** (FIG. 43). These are two large lymphoid collections, one on each side, in the median posterior wall of the nasopharynx. On their outer surface (i.e., pharyngeal surface) they are covered by stratified epithelium which is continuous with the mucous membrane of the pharynx. The pharyngeal surface of the tonsil is pierced by many tunnels known as the *crypts,* which are also lined by projections of the same stratified epithelium. In the lumen of these crypts, ducts of

numerous mucous glands open. Unlike the lymphatic glands, the tonsils do not show any separation into cortex and medulla. The lymphoid cells remain both in the scattered form as well as in the form of dense islands like the lymphoid nodules in the lymph nodes.

Pharyngeal tonsils are often hypertrophied causing obstruction to the nasal openings. The hypertrophied tonsil is chemically known as **adenoid.**

Tubal tonsil. It lies around the pharyngeal orifice of the pharyngo-tympanic tube. It is the lateral extension of the pharyngeal tonsil and is covered with ciliated columnar epithelium.

The vermiform appendix is also very rich in lymphoid tissue and is hence known as **abdominal tonsil.** Besides these, the bursae, the synovial membranes, the serous and mucous membranes, the adipose tissue, the bone marrow and the perivascular spaces—all contain lymphoid tissues.

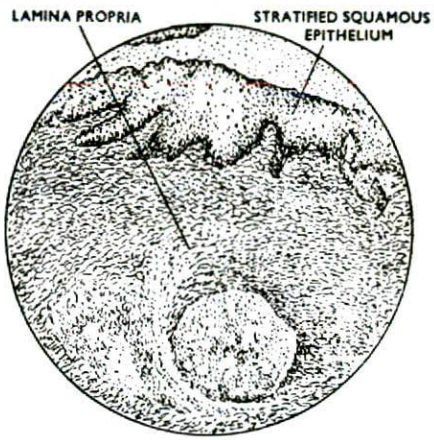


FIG. 43. Pharyngeal tonsil showing *lamina propria* which comprises lymphoid tissue with a secondary follicle at the base of the figure.

Functions. (1) To supply lymphocytes to the blood and lymph stream, as evidenced from the presence of *mitotic figures* in the organ. (2) To serve as a great defence against bacterial infection. (3) To serve other functions of the reticulo-endothelial system.

7. **Cartilage.** It is a connective tissue which is more or less translucent, firm in texture and to some extent elastic. In firmness and elasticity it occupies a position intermediate between fibrous tissue and bone. It is made up of cartilage cells, chondroblasts and a large amount of intercellular ground substance (matrix), constituted by the fibres and two types of proteins—*chondromucoid* and *chondroalbumoid* (chondroalbuminoid). On hydrolysis, the former gives *chondroitin sulphuric acid.* The ground substance either may be clear and homogeneous or may contain fibrous tissue. These fibres may be either white fibrous tissue or yellow elastic tissue. According to the difference in the number of cartilage cells and the nature of the ground substance present, cartilage is divided into three classes: (*a*) **Hyaline cartilage,** (*b*) **Fibrocartilage,** (*c*) **Elastic cartilage.**

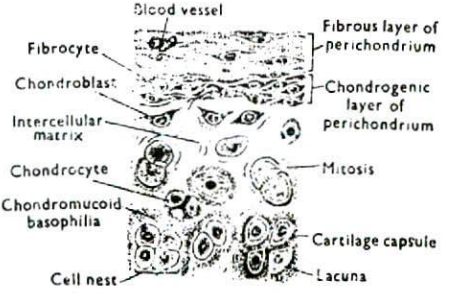


FIG. 44. Hyaline cartilage (diagrammatic).

(*a*) **Hyaline Cartilage** (FIG. 44). It is made up of cartilage cells and a clear homogeneous ground substance completely devoid of any fibrous (loose) tissue.

Hyaline means *glass* and in fresh condition it appears as a translucent bluish-white mass.

The *cartilage cell* or *chondrocytes* occupy small empty spaces called *lacunae* in the matrix. These cells are large with rounded angles and the contiguous surfaces are flattened due to pressure of the adjacent cells. The nucleus is large and is provided with two or more nucleoli. When the cells are arranged in groups of two, four, etc., in a single lacuna it is said to be *cell nest.* Each group of cells arises from the multiplication of a single parent cartilage cell. The cytoplasm is very rich in glycogen and may contain fat droplets and mitochondria. In electron microscope, the cytoplasm shows large rough-surfaced endoplasmic reticulum, Golgi apparatus with large vacuoles. The intercellular ground substance surrounding the cells is laid out in concentric rings and take deeper stain. This deeply staining portion around the cells is called the *capsule.*

Matrix. It is the solid intercellular substance of the cartilage or bone. The matrix of bone is harder than that of cartilage only for the deposition of calcium salts in the former. In the hyaline cartilage, this intercellular substance is abundant and appears homogeneous in the fresh condition but with ordinary fixation it shows collagen fibres and amorphous intercellular substance. Collagen fibres are seen in these sections under polarising microscope.

The ground substance is highly basophilic due to presence of chondromucoprotein, a polymer of a mucoprotein together with chondroitin-4-sulphate and chondroitin-6-sulphate. When boiled, cartilage is slowly dissolved and gives rise to *cartilage glue*—the **chondrin** containing gelatin, chondromucoproteins and other albuminous substances.

The hyaline cartilage is enclosed by a tough layer of dense connective tissue capsule which is known as **perichondrium.** It consists of loose (fibrous) and dense (chondrogenic) layers with indistinguishable fibrocytes.

Distribution. It is found in the articular end of the bones (*articular cartilage*), between the **epiphysis** and the **diaphysis** of the growing long bones (*epiphyseal cartilage*), at the anterior end of the ribs (*costal cartilage*). The cartilage of the nose, external auditory meatus, larynx, trachea and bronchial tubes also belong to this class. The costal cartilages are covered by the *perichondrium.* It serves the same purposes as periosteum of the bones. The nutrition and oxygen to the cartilage are supplied through the blood vessels of the perichondrium. Thicker cartilages are pervaded here and there by fine channels carrying blood vessels.

(*b*) **Fibrocartilage** (Fig. 45). This type of cartilage is present where great tensile strength with flexibility and rigidity are required. It is capable of withstanding shearing forces. The cells are large, arranged in groups and placed inside lacunae. Fibrocartilage contains more collagen in its intercellular substance than hyaline cartilage and lacks perichondrium. Between the cell groups, bundles of white fibrous tissue are seen. **Distribution.**

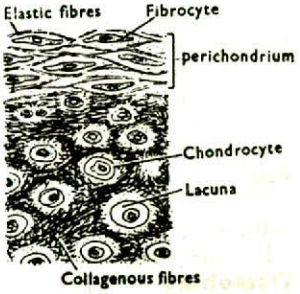


Fig. 45. Fibrocartilage (diagrammatic).

It is found in the intervertebral discs, the menisci of knee joints, mandibular joints, pubic symphysis, linings of many tendon grooves in bones, in the attachments of some tendons, etc.

(*c*) **Elastic Cartilage** (FIG. 46). It is present in the area where support with flexibility is required. It is *yellow in colour* and contains many elastic fibres. It differs from hyaline cartilage only for the presence of its enormous elastic fibres in the matrix. The matrix in addition to the elastic fibres contains collagen fibres. **Distribution.** It is found in the external ear (pinna), Eustachian tube, epiglottis and in some of the laryngeal cartilages.

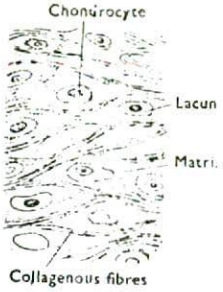


FIG. 46. Elastic cartilage (diagrammatic)

Functions of Cartilages. In elasticity and hardness cartilages stand midway between fibrous tissue and bone. Hence, their main function is (1) mechanical. It helps to maintain shape and rigidity of structure combined with certain amount of elasticity. This is well seen in the costal cartilages. It also acts as a mechanical buffer as found in the intervertebral discs, articular menisci, etc. (2) *Hyaline cartilage* serves also the very important function of forming the primary medium in which cartilaginous development of bone takes place. *Fibrous cartilage* acts as strong, flexible connecting substance between bones. *Elastic cartilage* maintains and strengthens the attached organs.

8. **Jelly-like Connective Tissue.** This may be described as an embryonic form of areolar tissue in which deposition of fibrous tissue has not yet taken place and the cells remain scattered in a more or less homogeneous jelly-like ground substance and with few fibres interlacing throughout the tissue. The cells are large fibroblasts with a few macrophages and lymphocytes, the ground substance being mucin in nature. The tissue occurs in the umbilical cord where it is known as **Wharton's jelly.** In adult life it is found to compose the vitreous humour in the eyeball.

9. **Osseous tissue** or **Bone.** This tissue which constitutes the skeleton, is the hardest of all connective tissues. It is made up of bone cells and intercellular ground substance. The organic part of the latter which is about 40 per cent. is composed of collagen fibres, the **osteocollagenous fibres,** and is bound by a *mucopolysaccharide-cementing* material (**ossein**). The remaining 60 per cent. which is deposited as a dense substance is inorganic, mainly calcium salt (*vide* later). Bone is covered with **periosteum** (*around bone*).

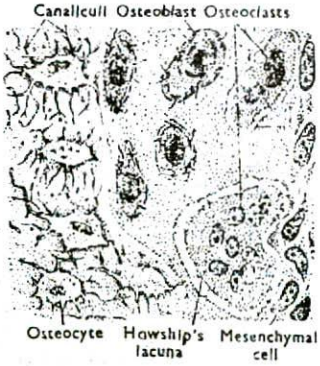


FIG. 47. Diagrammatic representation of bone cells showing structural differences.

There are three types of bone cells—osteoblast, osteocyte and osteoclast (FIG. 47). They are closely related with one another. **Osteoblast**—This is concerned with bone formation and is found in the growing surface where the bony matrix is deposited. This cell is strongly basophilic and cuboidal or pyramidal in

shape and its nucleus is large with a single distinct nucleolus. There is a well-marked Golgi apparatus. The cell secretes the bone matrix and thus calcification takes place. For its important function of calcification, bone-forming osteoblast possesses a rich concentration of enzyme, *alkaline phosphatase* in the cytoplasm. The cytoplasm has got affinity towards basic dye due to presence of a large amount of rough-surfaced endoplasmic reticulum with its associated ribosomes. **Osteocyte**—It is the trapped or imprisoned osteoblast within the organic matrix. Osteoblast becomes trapped within its own secretory material—the matrix. Thus the osteocyte remains trapped within the **lacuna** (*small lake*). This cell has small ovoid, highly chromatic nucleus. The cytoplasm of osteocyte is faintly stained with basic dye and contains lipid droplets, granules and also glycogen. The osteocyte has got no active synthesising properties. Fine cytoplasmic processes extend for a certain distance into the canaliculi and these canaliculi which are irregularly oval on the flat and biconvex on the edge radiate out from the lacunae. As osteoblast had numerous slender cytoplasmic processes, small canaliculi extend from each lacuna out in the osseous matrix, osteocyte is separated by the matrix from each other and connects indirectly with each other by canaliculi. **Osteoclast**—It is a giant bone cell with about twenty or more darkly stained nuclei and lightly eosinophilic cytoplasm and is formed in the area where active resorption of bone takes place. It is often found in a hollow pit, known as **Howship's lacuna,** near the surface of bone. There is of opinion that osteoclast is originated from the fusion of many osteoblasts or from osteocytes and chondrocytes liberated in the process of resorption of bone and cartilage matrix. Osteoclast is not a pinocytic cell, but probably it secretes a *proteolytic enzyme* to dissolve bony tissue. This cell is associated with the process of growth and remodelling of bone. So its *function is to resorb or destroy bone.*

Classification. According to the density and hardness, bone is divided into (*a*) **compact or dense or ivory bone** and (*b*) **cancellated or spongy bone.**

(*a*) **Compact bone. Distribution.** The outer layer of all bones and the shaft (diaphysis) of the long bones are entirely compact in nature.

Histology. The shaft of the long bones (FIG. 48) is the typical example of this type of bony tissue. Here the bony deposit is found to take place in four different forms: (1) **Haversian system (osteon)**—It is the structural and functional unit of compact bone. In addition to the central medullary canal it is found that the wall of the compact bones is pierced by numerous narrow longitudinal tunnels called the **Haversian canals** which are branches of horizontal channels, known **Volkmann's canals** (communicating canals). When a tiny polished piece of compact bone cut at 90° to the long axis, the Haversian canal is found as black spots varying in diameter (average 50 μ). Each Haversian canal contains one or more blood vessels (mainly

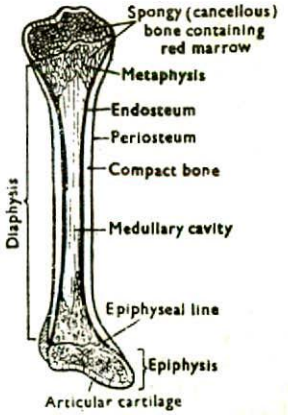


FIG. 48. Longitudinal section of a long bone (diagrammatic).

capillaries and venules), lymphatics, nerves and there may be a few marrow cells. Around each Haversian canal, varying numbers (8–15) of layers of bone are deposited in **concentric circles (Haversian lamellae).** Between the adjacent layers there are tiny spaces called the **lacunae.** These lacunae are also arranged in circles around the Haversian canal. A number of fine wavy channels run out from all round the lacuna and are known as the **canaliculi.** The lacunae contain the osteocytes which become imprisoned by the surrounding calcium deposit and the canaliculi contain the processes of the osteocytes. Through the canaliculi, the lacunae communicate with each other as well as with the central Haversian canal, but as a rule do not communicate with the lacunae of the other Haversian systems. Each Haversian canal together with concentric lamellated bony deposit, the lacunae and the canaliculi, composes one Haversian system. Forming the outer boundary of such a system and separating this system from neighbouring ones, a bright thin line is often noticed. This is called **cementing line of Ebner.** This *Haversian system* (FIG. 49) *is the typical feature of the compact bones.* (2) The **angular interspaces** between the neighbouring Haversian system do not show any regular lamellated appearance. Here the bone and the osteocytes are arranged in irregular layers, called by some as *interstitial lamellae* or *ground lamellae.* (3)**Periosteal lamellae** (Circumferential lamellae)—In addition to the lamellae of the Haversian system, another type of lamellae is found just under the periosteum, surrounding the compact bone. They are also found in an ill-defined manner throughout the depth of the bone passing in between the Haversian systems and roughly arranged concentrically around the central medullary canal. Twigs of periosteal vessels pass into these lamellae and are lodged in horizontal channels, the **canals of Volkmann** (*communicating canals*).

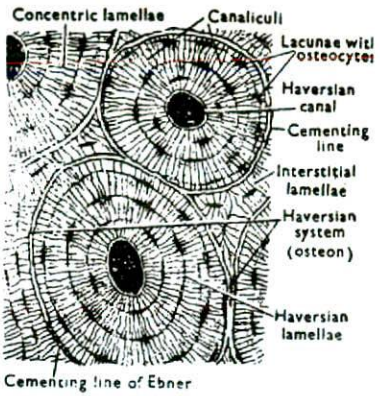


FIG. 49. Diagrammatic representation of section of compact bone showing Haversian system (osteon).

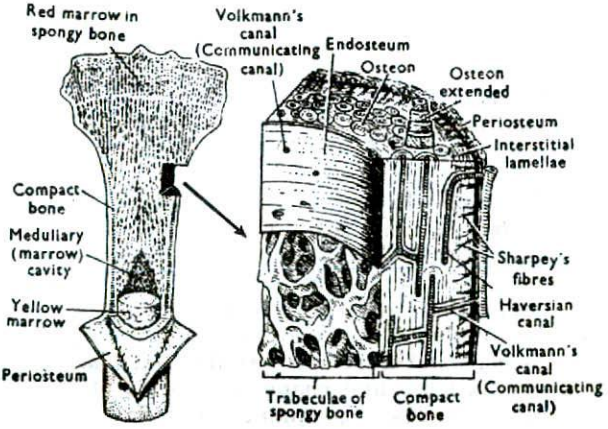


FIG. 50. Diagrammatic representation of internal structure of a long bone showing periosteum, Haversian canal, Volkmann's canal, Sharpey's fibres, etc.

These canals enter the bone perpendicularly to its long axis and communicate with the Haversian canals. The communicating canals originate in the periosteum. The periosteal lamellae are also pierced by calcified strands of fibrous tissue running from the periosteum. These fibres are called the **perforating fibres of Sharpey** (FIG. 50). Besides these, other fibres are not calcified and found to pass in a decussating manner involving both the Haversian and the periosteal lamellae. They are known as the **decussating fibres of Sharpey.** The Haversian canals and the central medullary canal are lined by a connective tissue membrane known as **endosteum** containing osteoblasts and osteoclasts. (4) **Endosteal lamellae**—There are few concentrically arranged thin plates or lamellae which line up the wall of the marrow cavity, known as endosteal lamellae. These are related to the thin layer of fibrous connective tissue of the endosteum.

(*b*) **Cancellated or Spongy Bone. Distribution.** The inner parts of the flat bones, the rounded ends of the long bones, the body of the vertebrae, etc., possess cancellated bony tissue. **Histology.** In this type of bone, calcification is less dense. The inside of the bone is divided up by minute bony partitions giving a spongy appearance. The spaces are filled up with marrow and lined by endosteum. The calcium deposit shows a lamellated appearance, but *no true Haversian system is found.*

Functions of Bone. (1) It performs a mechanical function in forming the skeletal support and shape to the body and in forming a leverage system whereby movement and work are possible. (2) It affords protection to the vital organs of the cranial and thoracic cavities and to the deep blood vessels and nerves from injury. (3) It serves as a great reservoir for minerals, specially phosphorus and calcium to the blood. (4) The bone cells help in maintaining body's electrolyte balance, particularly the distribution of calcium and phosphate ions. (5) They also serve a detoxicating function. Elements, such as lead, fluorine, arsenic, radium, etc., are removed from the circulation and are deposited in the bones and teeth. (6) It lodges the bone marrow, which is important in the formation of blood cells (haemopoietic function). (7) It serves as the basis for the attachment of muscles (passive instrument of motion). (8) It is one of the chief sites of reticulo-endothelial cells. (9) It assists the respiratory system in forming the nasal cavity and the beginning of the digestive system in forming the mouth. It is also important in speech for clear enunciation of words forming the bones of the roof of the mouth. (10) It also assists in the transmission of sound to the auditory nerve of the inner ear in forming the ossicles of the middle ear.

Periosteum. It is the outer membranous covering of bones except at the articular surfaces. It has got two layers,—the superficial layer is made up of dense connective tissue fibres and fibroblast with a rich supply of blood vessels and lymphatics, from which a good part of the nutrition of bone is supplied. This layer has got no osteogenic function and thus limits bone growth. The inner layer, **cambium,** possesses the capability of bone formation. This layer is composed of more loosely arranged connective tissue fibres and contains numerous spindle-shaped connective tissue cells which give rise to osteoblast and osteoclast for bone growth and repair during fracture. The inner (deeper) layer is thus known as **osteogenic layer.**

Functions of Periosteum. (1) It serves as a tough fibrous covering and checks excessive bony growth. Normal bone formation is controlled primarily by the periosteum. When due to injury or surgical operation, it is torn off from the underlying bone, the liberated osteoblasts start forming new bone at the site of injury and thus gives abnormal bone formation. There seems to be a contact equilibrium between the growth of bone and periosteum. (2) Carries nutritive vessels. (3) Affords attachment to the muscles and tendons. (4) Subperiosteal osteoblasts help to regenerate new bone and the healing of fracture.

Endosteum. It is the lining membrane of the marrow cavity and extends as a lining membrane into the canal system of the compact bone. It is formed by condensation of the *stroma of bone marrow*. It contains reticular cells. **Functions**—It possesses both osteogenic and haemopoietic functions. Its activity takes part in the healing of fracture.

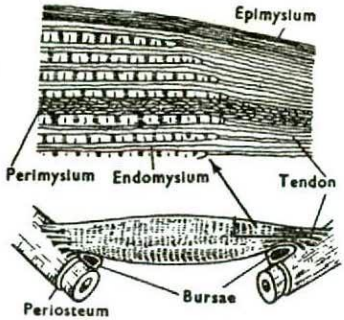


FIG. 51. Diagrammatic representation of muscle-tendon junction showing bursae.

Bursae. These consist of small connective tissue sacs with synovial fluid. They are **distributed** where pressure is exerted over moving joints (FIG. 51), e.g., between tendons and bone, between muscles, between skin and bone, etc. **Function** —They act as cushions, relieving pressure between moving parts.

Bone marrow. The central marrow cavities of long bones and between the spicules of latticework of spongy bones are filled with bone marrow. When the osteoblasts invade the cartilage model, marrow begins to form in it. **Yellow marrow** is composed mainly of fat cells or adipose tissue and is found in the marrow cavity of long bones, whereas **red marrow** is associated with spongy bones, and contains a certain amount of adipose tissue and mostly blood-forming tissue. **Functions**—(*a*) Production of blood cells and their release to circulation, (*b*) Erythroclasia, (*c*) Reticulo-endothelial functions, (*d*) Osteogenic functions, (*e*) Immunologic functions, (*f*) General connective tissue functions. For details of bone marrow *vide* chapter IV.

Development of Bone (Ossification)

Development of bone begins from mesoderm in the embryonic life (from sixth week) and a good number of bones of the body continue to grow until a person reaches about twenty-fifth year. There are two processes of ossification—**intramembranous** and **intracartilaginous (endochondral)**. The bones of the cranial vault and the mandible are membranous in origin. The bones of the limbs, trunk and base of the skull are both cartilaginous and membranous in development.

A. **Intramembranous ossification** (FIG. 52). It is the more simpler form of ossification and most bones of the face, cranial vault and clavicles are formed in membrane. In this process of ossification the embryonic mesenchymes consisting of the primitive connective tissue become congregated or connected by their processes without having cytoplasmic continuity. This area becomes richly vascularised. The mesenchymal

cells (preosteoblasts) increase in size and are clustered together to form long strands of cells radiating in all directions and secrete collagenous fibrils. The cytoplasm of the mesenchymal cells become basophilic and ultimately differentiated into osteoblasts. Between osteoblasts, their bars (trabeculae) of dense intercellular substance appear and mark the connective tissue fibres (osteogen fibres) already present within the matrix. The cells ultimately become embedded by the bars of dense matrix that increase in size. The matrix at this stage is not calcified and the tissue thus formed is loose. Between cells and collagenous fibrils, a semisolid fluid, **osseomucoid** is present. The organic non-calcified component is known as **osteoid.**

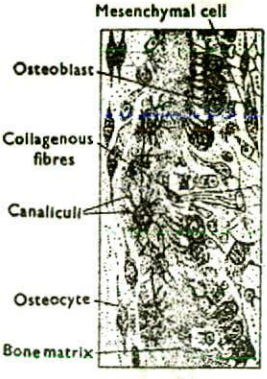


FIG. 52. Intramembranous ossification (diagrammatic).

Later on calcium salts are deposited presumably by the activity of osteoblasts. As the osteoblasts deposit successive layers of calcium salts in the matrix, certain osteoblasts are also entrapped within minute spaces—**lacunae.** These entrapped osteoblasts are osteocytes. Lacunae and canaliculi are successively formed; and canaliculi of adjoining lacuna thus connect with each other.

Spicules (bars) of bone, containing osteocytes and surrounded by actively secreting osteoblasts, can now be recognised. As the bony spicules increase in size and complexity, so the osteoblasts proliferate to keep pace with the requirement for more bone-forming cells. In this process cancellous bone forms. All newly formed bones are cancellous (FIG. 53) whether produced intramembranously or by intracartilaginous ossification.



FIG. 53. Diagrammatic representation of bony spicules uniting to form spongy bone in developing intramembranous ossification.

After this initial stage of bone formation the osteoblast appears on the surface of the newly formed bone and through the activity of the osteoblast the thickness of bone is increased. The source of osteoblast in the surface is maintained through the mitosis and also from the undifferentiated cells in the surrounding connective tissue. At the periphery of the ossification centre, the mesenchyme condenses to form the **periosteum.**

B. **Intracartilaginous (endochondral) development of bone** (FIG. 54). Through this process most of the skeletal bones are formed. In the embryo, where the bone formation is required, mesenchymal cells become developed into a cartilaginous model. Ultimately, the cartilage cells completely disappear and it is transformed into bone. The importance of this provisional cartilaginous foundation lies in three facts: (*a*) It provides a suitable medium for the deposition of calcium salts. (*b*) It serves to determine roughly what shape the finished bone will take in future. (*c*) It is by the growth of this cartilage (then known as *epiphyseal cartilage*) that the bone grows in length.

Process of intracartilaginous bone formation. In a long bone of a limb the ossification initially starts with the appearance of a fibrous membrane around the centre of cartilage model. This fibrous membrane, **perichondrium,** has got osteogenic function and cells of the perichondrium adjoining the cartilage become hypertrophied and give off long processes to form a meshwork of interlacing fibres. These cells are osteoblasts and fibrous network is then impregnated with calcium salt and forms a true bone beneath the perichondrium. This bone provides a rigid mass and surrounds the cartilage as collar or ring which is known as **periosteal bone collar or ring** or **subperiosteal bone.** The perichondrium thus afterwards becomes periosteum.

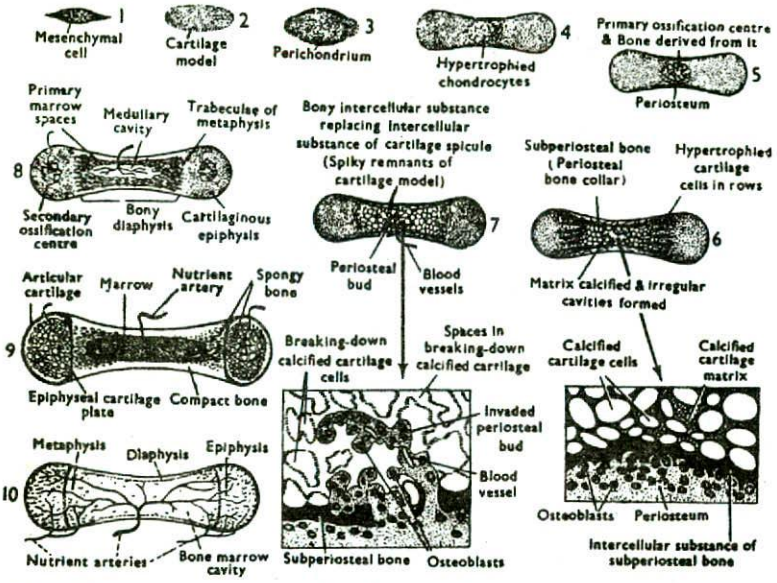


FIG. 54. Diagrammatic representation of stages of intracartilaginous (endochondral) bone formation (NOS. 1–9). No. 10 shows adult bone after fusion of epiphyseal cartilage with that of the diaphysis.

Simultaneously with the formation of collar, certain changes in the centre of shaft (diaphysis) of the cartilaginous model are observed. This centre is known as **primary ossification centre.** The cartilage cells become hypertrophied accumulating glycogen and appropriate glycolytic enzyme and phosphatase and throw out longitudinal row of cartilage cells on both sides. As the cartilage cells are hypertrophied, the intercellular substance is also sufficiently hypertrophied and secrete phosphate. If *calcium and phosphates are available around the cartilage spicules* (spiky remnants of the cartilage model) *in a certain proportion relative to each other* (this proportion being controlled to some extent by the activity of ductless glands), *then the intercellular substance is calcified.* With the calcification the cartilage cells become cut off from nutrition and cells die. With the disintegration of the *calcified cartilage* at the centre of the **cartilaginous model (primary ossification centre),** irregular cavities are formed in

the cartilage matrix. **Periosteal bud** consisting of the osteogenic cells (undifferentiated mesenchymal cells of perichondrium), osteoblast and capillaries of the inner layer of periosteum, invades these cavities.

The osteoblasts that are initially advanced into the interior of blood vessels thus lay down bone on the remnants of the cartilage intercellular substance. These spaces of the shaft are joined up to form the Haversian canals which help as conduits for running of blood vessels.

The process of ossification proceeds and extends from the centre of the shaft towards the ends of the cartilage. The periosteal bone collar also becomes thicker and extends towards the epiphyses. This bone collar gives a support in maintaining the strength of the shaft. Besides this the thickness of the bone depends upon the activity of the deeper layer of the periosteum of the shaft.

At somewhat later date, and possibly at the time of birth **secondary ossification centres** appear in each epiphysis of the long bones. The segmental changes for calcification and subsequent ossification are the same as described for the diaphysis. Cartilage cells are hypertrophied and afterwards calcified. The calcified cartilage is resorbed as usual. Ossification afterwards is started by the osteoblast on the wall of spaces created due to calcification. Bone deposition is exempted on two regions—articular region and epiphyseal plate. Cartilage cells remain over these areas. The **epiphyseal plate** or cartilage keeps the diaphysis and epiphysis separated from each other up to certain years of age (app. 25 years) after which the same becomes fused with each other. The growth of the long bone in length depends upon the growth of the epiphyseal plate. The epiphyseal plate goes on multiplying continuously and throws out longitudinal rows of cartilage cells on both sides. This newly formed cartilage becomes ossified and in this way the bone grows in length. In younger life the rate of multiplication of the epiphyseal cartilage is proportionately more than the rate of calcification. Consequently, long bone increases in length. **Growth apparatus** is formed by epiphyseal cartilage with metaphysis and is the route of growth in length of long bones. **Metaphysis** is the column of spongy bones and units of the epiphyseal cartilage to the shaft (diaphysis). But, as age advances the rate of multiplication of cartilage cells slows down, so that the process of calcification becomes relatively more rapid and overtakes the whole strip of the multiplying cartilage. Thus the epiphyseal cartilage becomes ossified and growth in length ceases. Near about the twenty-fifth year of life all the epiphyseal cartilages are ossified and replaced by a spongy bone and marrow.

After fusion of the epiphyseal bone with the diaphysis, the growth in length of the bone becomes quite impossible and if growth is stimulated afterwards by overactivity of the growth hormone or somatotrophic hormone (STH) then abnormal growth occurs. This overgrowth of bone is mostly confined to the bones of the face, hands and legs. This condition is known as **acromegaly.** On the other hand, if this STH is secreted before the fusion of the epiphyseal bone with diaphysis then excess growth of the immature long bone occurs causing **gigantism.**

Histological changes evolved in endochondral ossification. These changes can be seen in longitudinal section of a developing long bone of a limb. *Three stages* are seen during cartilaginous ossification. They are as follows: (1) The **stage of hypertrophy** (FIG. 55). This is seen in the

primary ossification centre and presents the following features: (*a*) The first indication of bone formation is at the perichondrium around the centre of diaphysis. The cells here hypertrophy and become osteoblasts. The osteogenic activity of osteoblasts changes the perichondrium into a periosteum. (*b*) The cartilage cells enlarge and become arranged in linear rows, radiating from the centre. (*c*) Irregular deposition of calcium salts takes place between the cells. *This part of ossification is of membranous development.* (2) The **stage of irruption** (Fig. 56). This stage comes a little later than the first stage. The subperiosteal cells become hyperactive and eat away a portion of the newly formed subperiosteal membrane bone. Through this eroded spot the periosteal bud containing osteoblasts, osteoclasts, connective tissues and blood vessels stream down into the depth of the bone and invade the calcified mass in the primary ossification centre. The hollow spaces opened up in the process are the primitive marrow spaces and their contents are the primitive bone marrow. Even during this early stage red and white blood cells can be seen in various stages of development. (3) The **stage of ossification** or the stage of true bone formation (Fig. 57). This process is similar to intramembranous bone formation. Gradually, the marrow spaces in the centre coalesce and form the *medullary canal.* Similarly, Haversian systems are developed.

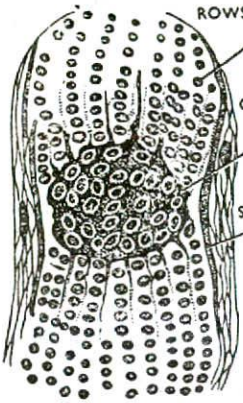


Fig. 55. Stage of hypertrophy.

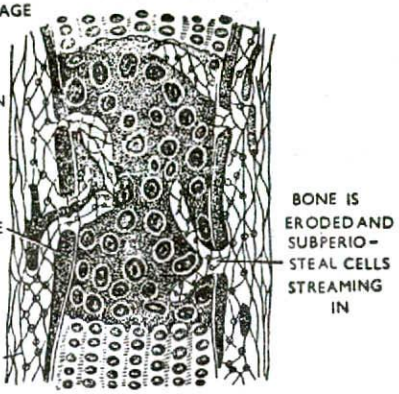


Fig. 56. Stage of irruption.

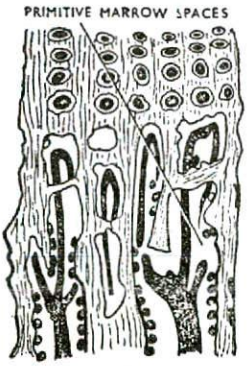


Fig. 57. Stage of ossification.

The bone increases in diameter by two opposite processes going on simultaneously. On the external surface the subperiosteal osteoblasts deposit layers of membrane bone, while, in the interior, cells of the endosteum absorb layers of bone from walls of the medullary canal. In this way bone increases in breadth and the medullary canal widens.

It should be noted that the healthy adult bone is not a fixed static material. It is constantly being broken down, reabsorbed and repaired by the co-ordinated activities of osteoclasts and osteoblasts. Osteoblasts

elaborate alkaline phosphatase and help in laying down collagen fibrils in the ground substance. Over these collagen fibrils calcium and phosphates are deposited. The alkaline phosphatase which is present in osteoblasts, breaks down organic phosphate esters to increase the calcium : the phosphate level to a critical value. The precipitation occurring as a result of this changes to **hydroxyapatite** ($Ca_{10}(PO_4)_6(OH)_2$) and then gradually to dense bone.

Blood vessels, lymphatics and nerves of bone. The **nutrient artery** by means of the medullary or nutrient canal near the centre of shaft (diaphysis) supplies blood vessels to the long bone. After piercing the compact bone the nutrient artery branches to the vessels in the Haversian canals. Then after reaching the central marrow cavity, this artery is divided into a descending and an ascending branch and these branches, being broken up into a capillary network, supply all the marrow. Besides this, the periosteum collects blood vessels in the bone. Communicating canals (Volkmann's canals), after piercing the bone, supply blood vessels through the Haversian canals of compact bone or through the marrow spaces of spongy bone. From the Haversian canals, the vessels extend branches into the marrow cavity and their capillaries anastomose with other group of arteries. The Haversian canals collect *blood capillaries* through thin-walled valveless veins and ultimately these capillaries reach the periosteum again through the communicating canals (Volkmann's canals) or through the nutrient canal. According to some, *lymphatics* occur in the compact bone and others describe them in the periosteum. Both myelinated and non-myelinated *nerve fibres*, accompanying blood vessels in the canals, are found in the periosteum. But myelinated nerves are numerous in the bone marrow.

Factors controlling calcification of bones. (1) Protein constituent of the cartilage has got affinity towards Ca^{++} and adsorbs calcium readily. However this favours the deposition of calcium as *tricalcium phosphate*. (2) Reduction of protein concentration in the blood and also reduction of CO_2 tension in blood favour the deposition of calcium salts. The metabolism of cartilaginous cells are very low and likewise CO_2 tension of the fluid in which the cartilage cells are bathed is lower than that of plasma. And thus this low CO_2 tension will favour the deposition of calcium. (3) Low calcium and inorganic phosphate concentrations in plasma retard calcium deposition. (4) According to Watt, the calcification is not a simple deposition of calcium salt but an active secretion by the osteoblast. (5) Robison and his colleagues have claimed that the calcification is primarily dependent upon enzyme actions. This enzyme is to be phosphatase which raises $PO_4^{\equiv}$ concentration in fluid where the cartilage is bathed and favours the process of calcification of the cartilaginous matrix. Robison is not of opinion that the phosphatase mechanism is the only one mechanism that participates in calcification process because calcification is still possible in absence of phosphatase if calcium and inorganic phosphate remain in high concentration.

Besides the above factors, following factors have got some role in the development and growth of bone. (*a*) **Vitamins.** Vitamin **D** is necessary for the calcification process. In absence of vitamin D there is decreased absorption of calcium from the food and also diminished the level of phosphate in blood. Cartilage cells of the matrix and the osteoid matrix are not calcified and causing rickets in children and osteomalacia in adults. In vitamin D deficiency, formation of cartilage is continued but in irregular fashion and calcification may stop entirely. In vitamin **C** deficiency, osteocollagenous fibres are destroyed and the production of organic matrix in the bone is diminished. In vitamin **A** deficiency there is retarded skeletal growth with interference of the process of remodelling of bone. (*b*) **Hormones.** Anterior pituitary hormone—*Growth hormone* has got direct

effect on the bone growth. Excess hormone secretion during childhood causes *gigantism* and during adult stage, *acromegaly*. In deficient secretion of this hormone in childhood produces *dwarfism*. *Gonadal sex hormones* have got some role in the process of fusion of the epiphyseal bone. *Parathyroid hormones* have got direct relation with bone growth through the maintenance of calcium and phosphate balance. Increased secretion of *parathormone* releases calcium and phosphate from the bone and this excess hormone level in the blood stimulates the formation of osteoclasts which are responsible for *osteitis fibrosa* of the bone. The resorptive action of parathormone on bone is opposed by the *thyrocalcitonin* secreted from the thyroid gland.

Defective ossification causes the typical deformities in bone such as *knock knees*, bowing of legs, spinal curvature and also malformations of the chest and pelvis. *Osteoporosis* is a malformation of bone matrix due to negative protein balance and is generally found in postmenopausal women and elderly people due to diminution of sex hormone. Excessive secretion of adrenal cortical hormone also causes this disease due to excessive protein catabolism.

Composition of Bone

Water—25%. **Solids**—75%.

(1) **Organic** (mainly proteins)—30%. Three proteins: (*a*) **Ossein**—a scleroprotein—is the chief constituent, (*b*) **Osseomucoid**—a mucoprotein, (*c*) **Osseoalbuminoid**—a keratin.

(2) **Inorganic**—45% (of this calcium (Ca), phosphorus (P) and magnesium (Mg) are chief elements; potassium (K), sodium (Na) and chlorine (Cl)—in small amounts; iron (Fe), fluorine (F), lithium (Li) and strontium (Sr)—in traces. Ca remains mainly as phosphates and carbonates and slightly as chlorides and fluorides. Mg is found mainly as phosphate.). Calcium-Phosphate ratio of mammalian bones is approximately 2·2 : 1·0. The ratio of residual calcium (other than present as carbonate) to residual phosphate (other than magnesium phosphate) is about 2·0 : 1·0. The proportion of inorganic compounds of bone is as follows:

Inorganic Composition of Bone

Tricalcium phosphate—$Ca_3(PO_4)_2$	36·0%
Calcium carbonate—$CaCO_3$	5·8%
Magnesium phosphate—$Mg_3(PO_4)_2$	0·9%
Others	2·3%
Total	45·0%

Composition of Bone Ash

Tricalcium phosphate	80%
Calcium carbonate	13%
Magnesium phosphate	2%
Others	5%
Total	100%

Thus nearly half the weight of bone is made up of calcium salts.

The actual chemical substance of bone is not yet known.

Studies of refractive indices, X-ray diffraction pattern, etc., indicate that calcium phosphate and calcium carbonate do not remain separately. It is shown that bone is crystalline in structure and that the calcium salts remain combined together to form bigger compounds belonging to the 'apatite' class. Some hold that $CaHPO_4$ is possibly formed first, which is then converted into other compounds. Anyway $Ca_3(PO_4)_2$ is the chief final compound, which remains attached to $CaCO_3$ mainly and to some extent to $CaHPO_4$ and $Ca(OH)_2$.

Bone calcium is not a static material. Experiments with radio-active isotopic calcium (^{45}Ca) shows that it is in constant exchange with the body fluids and thus maintains a dynamic equilibrium. If calcium salts with radio-active calcium be given intravenously, 86% of it is taken up by bone in 100 min. About 10% of it is replaced in 10

days and the whole of it in 200 days. This possibly shows that the entire calcium content of bones is renewed every 200 days. Lead, other toxic elements, and also radio-active strontium which is produced from explosion of atom bomb, are taken up by bone similar to calcium. Due to radiation, uptake of latter is harmful.

Tooth

Histologically, a tooth contains *enamel, dentine, cementum* and *pulp* (Fig. 58). **Enamel** is epithelial in origin and encircles dentine beyond the plane of gum. It is the hardest substance found in the body. *Chemically*, it has calcium phosphate in the largest quantity and also considerable amounts of organic substances. Histologically, enamel is composed of enamel rods or prisms, which are minute crystals of inorganic material embedded in organic one. The calcified organic cementing substance between each rod is named as *interrod* or *interprismatic substance*. The bulk of tooth is composed of **dentine** which contains a higher percentage of inorganic material than bone but lesser than enamel. Similar to bone it has collagen fibres in a calcified ground matrix. The cells, **odontoblasts** are responsible for deposition of dentine. It covers the pulp cavity and presents all throughout the life. **Cementum** which is alike bone both histologically and chemically, covers dentine at the root of the teeth. Cementum may be cellular, containing the cells, **cementocytes** which are similar to *osteocytes* or they may be free from cells, named as *acellular cementum*. The **pulp cavity** is composed of connective tissue and is richly supplied with blood vessels. It has also both myelinated and non-myelinated nerve fibres. The **gingiva** (gum) is the oral mucous membrane which is firmly connected with the periosteum of the alveolar bone at its crest and also with the surface of the tooth by the epithelial attachment of Gottlieb. **Functions.** Other than providing proper shape of the face, the teeth offer multiple functions. These help in *mastication, chewing, biting* and also *tearing* of food materials. By the process of mastication with the teeth, the solid food material in presence of saliva is made into pulp and is thus swallowed smoothly.

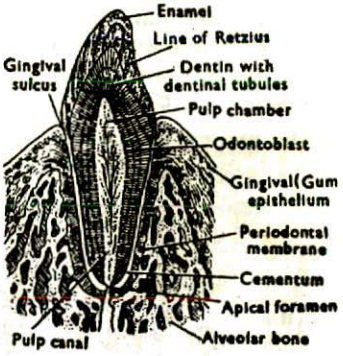


Fig. 58. A section of a tooth showing its structural pattern (diagrammatic).

10. **Reticulo-endothelial tissue.** This possesses various types of connective tissue cells which are widely distributed in the body, the phagocytic cells which are found mainly in bone marrow, liver capillaries, lymph nodes, serous membranes, splenic sinusoids. **Function**—These cells are important for defence of body against foreign particulate substance and micro-organism. Detailed discussions will be found in chapter V.

MUSCULAR TISSUE

The characteristic property of muscular tissue is its ability to contract when excited. The property of conductivity is also well developed in muscular tissue though not to the degree as that of nervous tissue. These special functional characteristics are present due to the special modification of the general properties of the protoplasm. The energy required for

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the performance of the muscular work is obtained through the metabolism of the food substances. So for their prolonged performance, an efficient blood circulation is essential for (*i*) constant supply of food materials and oxygen and (*ii*) removal of metabolic waste products.

There are different types of muscular tissues. These can be classified according to (*a*) the presence of **cross-striation**—(*i*) *striated* and (*ii*) *non-striated* (plain or smooth); (*b*) **nature of control**—(*i*) *voluntary* (controlled by volition), (*ii*) *involuntary* (not controlled by volition); and lastly (*c*) **distribution**—(*i*) *skeletal*, (*ii*) *cardiac*, (*iii*) *visceral*. These different types of classifications can be summarised in the following way:

1. Skeletal—striated voluntary (Fig. 59).
2. Cardiac—striated involuntary (Fig. 60).
3. Visceral—non-striated (plain or smooth) involuntary (Fig. 61).

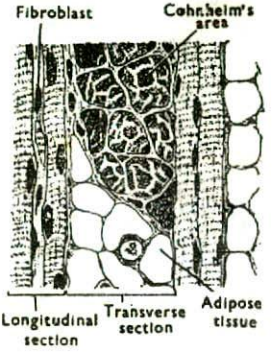


Fig. 59. Diagrammatic representation of skeletal muscle.



Fig. 60. Sectional view of cardiac muscle (diagrammatic).

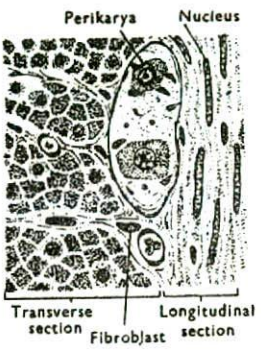


Fig. 61. Diagram depicts the sectional view of visceral muscle.

The term *muscle fibre* is attributed to a *muscle cell* due to its elongated shape which is specially adopted for the contractile function. *These muscle fibres have no similarity with the various fibres present in the connective tissue except their elongated thread-like structure.* They are fundamentally of *different natures.*

Skeletal muscle

The skeletal (voluntary and striated) muscle fibres are multinucleated cylindrical structures having a clear display of longitudinal and cross-striations. This muscular tissue is responsible for voluntary movement of the living system. It can perform works of rapid, powerful contraction as well as that of prolonged slow sustained tonic contraction.

Distribution. These muscles mostly in all instances are attached to osseous tissues (bones), innervated with somatic nerves through which volitional control is performed. In the fresh state the human skeletal muscle is pink in colour due to the presence of muscle pigments and high vascularity. Due to variation in colour there are red and white (or pale) muscles.

Origin and development. The skeletal muscle is developed from the solid mass of the mesoderms (myotomes) *except the muscle of the head* which is developed from the loose mesenchyme.

The cells, those give rise to the muscular tissue, are named as the **myoblasts.** In the myotome they are regular cylindrical but gradually they become elongated, spindle-haped, parallel bundles and ultimately the multinucleated myofibrils with characteristic ross-striation appear. There are *three theories* for the appearance of the multinucleated

skeletal muscle cell. (1) The myoblasts fuse together during the process of development of the muscle fibre which was supported by many with electron micrography (observed in developing myotome of amphibian larvae). (2) In the course of the development of the skeletal muscle fibre (cell), the nucleus is multiplied by mitotic division, but the cytoplasm does not divide accordingly. (3) Both the processes as described under (1) and (2) may take place. During the early phase of development of the skeletal muscles of mammals the nucleus of the muscle fibre migrates towards the periphery from the centre of the cell to accommodate myofibrils at the central core.

General features. The skeletal muscles, the name derived, are attached to a bone by means of the tendons nearly in all cases. A tendon is composed of densely packed white fibrous (non-elastic) connective tissue. At the junctional point, the fibres of the tendon is affixed to the sarcolemma of the muscle fibres which is again surrounded by areolar tissue to strengthen the junction (FIG. 51).

Like other muscles, the skeletal muscle is also supported by various connective tissues. **Epimysium,** the connective tissue coat, is the outermost covering for each whole skeletal muscle bulk (FIG. 62). The whole muscle bulk is divided into smaller bundles, the **fasciculi,** bounded by the **perimysium,** the connective tissue septa (FIG. 62). Now again each fasciculus consists of muscle fibre (the structural unit) which is enclosed in a delicate areolar connective tissue jacket, the **endomysium** (FIG. 62). Each muscle fibre (cell) consists of multiple muscle fibrils or myofibrils. A blood capillary is seen near each muscle fibre along with the endomysium. The connective tissue content of different muscles varies widely. The proportion of connective tissue is highest in the muscles responsible for the fine and precise movements.

Histological structure of muscle fibres. The skeletal muscle fibres are cylindrical, elongated cells with multiple nuclei. The extent of the muscle fibres in the bulk may be from (*i*) one end to the other, (*ii*) one end to somewhere at midway, or (*iii*) both the ends within the muscle having no attachments with either side. The length and breadth of the muscle fibre vary from 1·0 to 40 mm and 0·01 mm (10 μ) to 0·1 mm (100 μ) respectively. Though the fibres are of various sizes in the same muscle yet there is some correlation between the amount of work to be performed by the muscle and the thickness and size of the fibres. The thickness also varies with the degree of nourishment of the individual. The growth of the muscle on systematic exercise is due to increase in total fibre volume and improvement of blood supply and *not due to increase of fibre number.*

The transparent cell wall (FIG. 65) of the muscle fibre is named as **sarcolemma.** Under light microscope it is visible when fresh muscle fibres are teased. Electron micrograph shows that it is made up not only of the plasmalemma but also of an extrinsic coat of amorphous material, similar to the basement membrane. This amorphous layer is pierced and encircled by reticular fibres. The plasmalemma is of same structure as that of any other cell, i.e., two protein layers enclosing a lipid one with a thickness of 100Å. Inside the plasmalemma, elongated multiple nuclei and transversely striated **myofibrils** (*bundles of myofilaments*) are embedded in the sarcoplasm (*in many respects the cytoplasm of any other cell*).

The **sarcoplasm** contains other constituents as that of any other cell, e.g., numerous **mitochondria** (sometimes called **sarcosomes**), a small Golgi apparatus near each nucleus, myoglobin (protein pigment), lipid, glycogen, sarcoplasmic reticulum (*endoplasmic reticulum in case of*

other tissues), etc. Fibres which are richer in sarcoplasm are darker in colour and *vice versa.*

Myofibrils (Fig. 62). The characteristic features of skeletal muscle, the alternate light and dark shades (transverse striations) and thick longitudinal strands can be studied with light microscope. Electron micrography reveals that the longitudinal striation is due to the presence of myofibrils of different thickness whereas the transverse striation is due to the presence of alternate light and dark segments of longitudinally arranged elements. In cross-section, myofibrils appear as fine dots either distributed uniformly or in a group of polygonal areas and are separated from adjacent bundles by clear sarcoplasm. The separated myofibrils by the sarcoplasmic areas are known as **fields of Cohnheim** (Fig. 59).

The **dark band** is *doubly refractive* (anisotropic) when studied under polarised light, hence the name **A-band** (sometimes called **Q-band**). The **light band** is *monorefractive* (isotropic) under polarised microscope, from which the name is derived **I-band** (sometimes known as **J-band**). This I-band is bisected at the midpoint by a thin darkly stained line—the **Z-line** (sometimes called as **Dobie's line**) which is also known as **Krause's membrane.** The Z-line is made of a membrane extending across the myofibrils. The myofibrils are tortuous at these Z-lines. The portion enclosed by two adjacent Z-lines of a myofibril is considered as the **contractile unit** and is named as **sarcomere.** It extends 2 μ to 3 μ in length. In certain exceptional preparations, central portion of the A-band is *paler in colour* and called the **H-band** (*Hensen's line*). At the midpoint of the H-band, i.e., also of the A-band, there is a narrow dark line, **M-line** or **M-band,** where the myosin filaments are thickened. The myosin and actin filaments are overlapped at the peripheral dark portion of the A-band, which is named as the **O-band.** On both sides of the Z-line, somewhere in the midregion of the I-band there is a comparatively darker, thin, transverse line—the **N-line.**

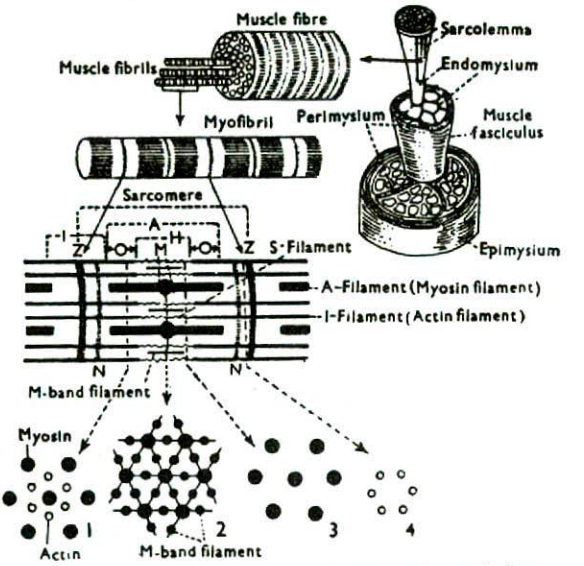


Fig. 62. Anatomical organisation of skeletal muscle from gross to molecular level (diagrammatic).

Fine structure. Electron micrography reveals that fine thread-like protein filaments are forming together the **myofilaments,** of which the *thicker* one (100Å in diameter)—**myosin filament** and *thinner* one (50Å in diameter)—**actin filament.** The primary structure of *myosin* and **tropomyosin** is characterised by a large amount of acidic and basic

amino acid content, that confer a very high charge on the molecules. *Actin*, **troponin** and **α-actin** in contrast have got low charge and are further distinguished by their high proline content. The myosin filaments are present as parallel strands throughout the whole length of the A-band. The length of myosin filament is about 1·5 μ (15,000Å) and is slightly thicker at the midline. On further dissociation of these filaments, the myosin molecules (1500Å in length) appear as rod-shaped with a globular projection at one end (FIG. 63-5). The thickness of the myosin filament is believed to be the cause of antiparallel arrangement of myosin molecules in such a fashion that the globular heads project outward near the ends of the filaments and the rod-like part takes its position in the smooth central portion of the filament. The peripheral bead-like structures of myosin filaments are due to the presence of globular heads of the myosin molecule (FIG. 63–4). Rod-like portion is named as **light (L) meromyosin** and the head portion, i.e., the globular portion is as **heavy (H) meromyosin** (FIG. 63–2).

The heavy meromyosin has got two components. The head portion is known as *heavy meromyosin* **subfragment I** and the neck is *heavy meromyosin* **subfragment II** (FIG. 63–3). The heavy meromyosin subfragment I possesses all the enzymatic and actin-combining properties of the parent (myosin) molecule. In each 400Å segment of the myosin filament, there are *six* heavy meromyosin heads (cross-bridges). These heavy meromyosin heads are arranged in a helical manner with a radial pattern of 60° and each set of six bridges complete one revolution around the myosin filament. Each heavy meromyosin head is pointed towards a separate actin filament and thus the cross-bridges with actin occur at approximately 400Å intervals along the myosin filament (FIG. 63–5)). The heavy meromyosin is responsible for the ability in formation of the cross-bridge with actin and also for the ATP-*ase* activity essential for muscular contraction. This heavy meromyosin is sometimes named as the **active point of myosin molecules.**

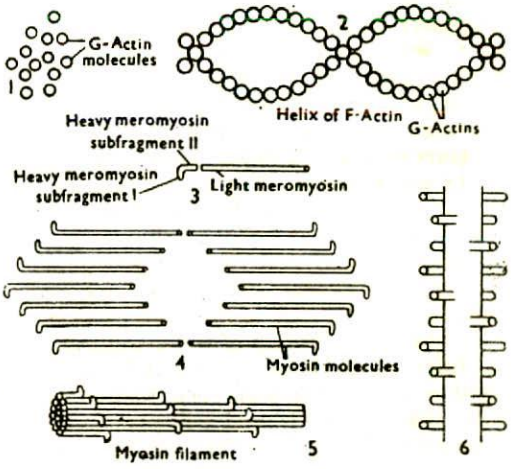


FIG. 63. Minute structures of actin and myosin filaments. It is to note that the model of myosin molecule in No. 5 (according to E. M. evidence is different from the No. 6 (according to X-ray analysis by Huxley), where there are pairs of heads in opposite direction at 140 A.U. interval in the myosin filament (diagrammatic).

At the M-band region (midpoint of myosin filament) the union of myosin molecules occurs tail to tail, but at this region the myosin filaments appear thicker indicating that there is possibility of presence of some proteins of unknown nature which may help in strengthening the tail-to-tail union of the myosin molecules. The detailed structure of the M-band

region with high E.M. photography has been deduced by Knappeis and Carlsen (Fig. 62–2). The M-band filaments, made up of proteins of unknown nature, are attached to the central portion of the myosin filament (Fig. 64–A) by means of the M-band cross-bridges (transverse). Functions of M-bands are: (*i*) to maintain the parallel alignment of the myosin filaments and (*ii*) to guide the actin filaments during contraction.

Actin filaments are extended from each Z-line within a sarcomere towards the H-band and connected with the other actin filaments by the **S-filament** (Fig. 62) within the H-band. It extends 1 μ in both sides of the Z-line. According to Knappeis and Carlsen the length of the actin filament is about 1 μ.

With very high magnification, the **F-actins**—fibrous actins appear as beaded and seem to consist of globular subunits (55Å) —**G-actins** (Fig. 63–1) forming two strands entwined in a **helix.** These strands are therefore a **polymer** of G-actin containing 13 G-actins at each turn of the helix (Fig. 63–2). Low-angle X-ray studies and also chemical investigations suggest that the **tropomyosin** and newly known **troponin** are oriented in the grooves of the actin helices. The actin filaments, approaching the Z-line, appear to be continuous with *four* fine diverging filaments—**Z-filaments** (Fig. 64–B). It is believed that these Z-filaments contain the muscle protein—tropomyosin. Recent low-angle X-ray studies have suggested that at the **Z-disc** along with tropomyosin, another protein α-actin (similar to actin in structure and proline content) is also present.

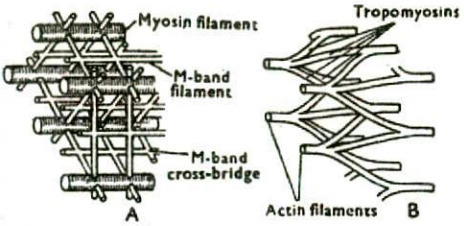


Fig. 64. Diagrammatic arrangements of the myosin–M-band filaments at M-band (A) and actin-tropomyosins at Z-line (B).

Transverse section of the myofibrils will give different representations at different levels of the A- and I-bands. Transection through the I-band will show the transverse section of thin actin (Fig. 62–4) filaments only, that at the O-band will present the transverse section of both thin actin and thick myosin (Fig. 62–1), that at the H-band only myosin (Fig. 62–3) and lastly at the M-band region, the transverse section of myosins along with M-band filaments (Fig. 62–2) will be present. In cross-section the arrangement of the actin filaments appears in hexagonal shape with one myosin at the centre, but again when that of the thick filaments is considered then the myosin filaments are forming triangles with one central actin filament (Fig. 62–1). So in the longitudinal section, each myosin filament is followed by two (*sometimes one*) actin filaments. The thin filaments, actins are connected to each other longitudinally by means of the still far more thinner S-filaments (Fig. 62).

Sarcotubular system. Under electron microscope, the myofibrils are seen to have surrounded by a canalicular network of membrane-limited tubules—**sarcoplasmic reticulum.** The sarcoplasmic reticulum is identical with the endoplasmic reticulum of other cell type but with the difference that its membrane does not possess ribosome. The sarcoplasmic reticulum is extended longitudinally along the A-band with frequent anastomosis in the region of the H-band and also in the I-band. The

sarcoplasmic reticulum is connected at its both longitudinal and terminal ends by another set of the transverse cisterns—**terminal cisternae** (FIG. 65). The terminal cisternae have got larger calibre and are thus continuous and confluent with the longitudinal reticulum (*sarcotubule*). Pairs of parallel terminal cisternae (*adjacent terminal cisternae*) are separated from each other by a slender transverse tubule which is known as **T-tubule.** This T-tubule is not confluent with the terminal cisternae and is a tubular invagination of the sarcolemma but not a part of sarcoplasmic reticulum. It is continuous with the extracellular space. These tubules are generally called as **T-system.** The pair of terminal (transverse) cisternae and the central T-tubules are collectively called as **triads** (FIG. 65). In amphibian muscle the triads encircle the I-band at the region of the Z-line but in mammalian muscle, the same is present at the junction of each A-band with the adjacent I-band. So in mammals there are two sets of triads in each sarcomere (FIG. 65). The T-system plays an important role in quick transmission of impulse from the cell surface to each myofibril.

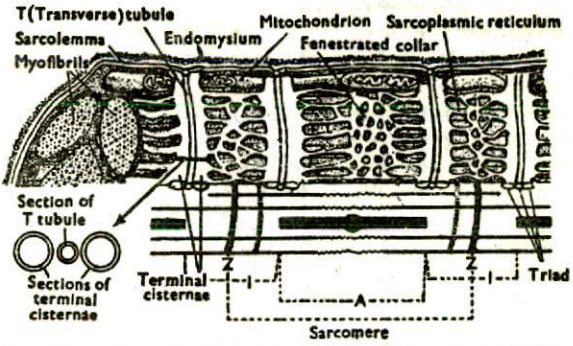
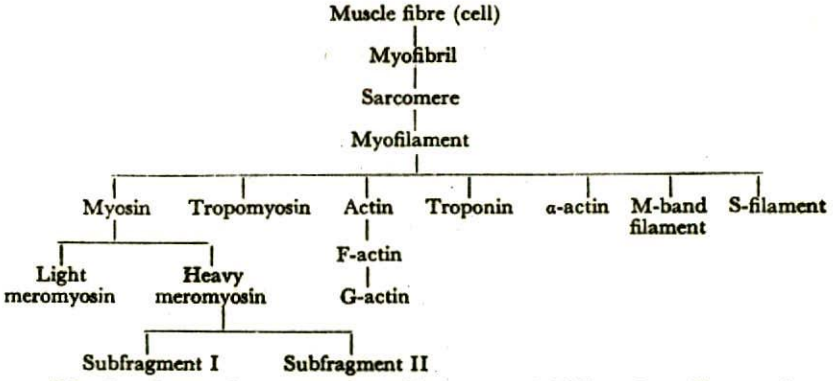


FIG. 65. Diagrammatic representation of the sarcotubular system of the mammalian skeletal muscles showing the triad to pass at the A–I junction.

Micro-anatomical organisation of the muscle fibre has been presented schematically:



Mechanism of contraction. (1) *Theory of folding of myofilaments (contractile proteins)* stated that certain muscle proteins are shortened or folded during the muscular contraction by forming **actin-myosin complex.** But morphological studies do not show any such evidence that during muscular contraction the myosin filaments are shortened. Now if the actin

filaments attain any shortening or folding at all, still it is not possible during normal life.

(2) *Interdigitation or sliding of myofilaments.* According to this theory, the shortening of the length of certain bands during muscular contraction was observed by many classical cytologists, but the cause or explanation for that was not satisfactory. In the past few years, the analysis of submicroscopic elements with electron microscopy and X-ray diffraction techniques has advanced a lot. These new techniques also led to an entirely new concept to the mechanism of contraction. The theory of **sliding filament mechanism*** is now mostly accepted. It is observed with phase contrast and interference microscopy that during contraction the I-band and H-band diminish in length but the A-band remains constant. The sliding filament hypothesis (FIG. 66) states the alteration



FIG. 66

of relative position of the myofilaments during the muscular contraction but neither the actin nor the myosin filaments are shortened themselves.

During contraction, the actin filaments slide past the myosin filaments and thereby the actin filaments are further extended into the A-band causing shortening of the length of the H-zone and narrowing the sarcomere (FIG. 67). In this process the myosin filament gradually approaches the Z-line and the actin filament, the M-line by altering the site of attachment of the cross-bridges—one point ahead in the manner of an animated cog-wheel (FIG. 67–2 & –3). At certain stages of contraction, the ends of the two adjacent actin filaments may touch each other and the I-band is of minimum length.

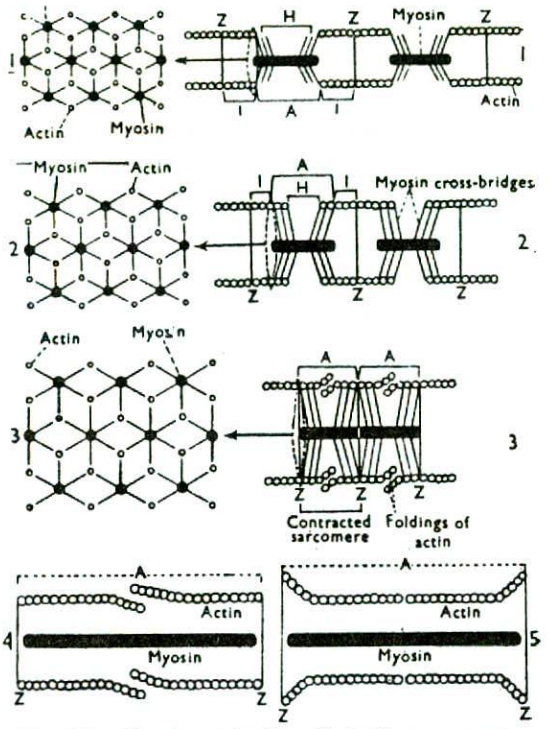


FIG. 67. Diagrammatic (hypothetical) representation of the sliding filament mechanism of muscular contraction showing also the cross-bridges in between actin and myosin filaments. No. 1 shows the sarcomere in resting condition. No. 2 represents the sarcomere in partially contracted state. Nos. 3, 4 & 5 depict the sarcomere in maximally contracted states.

There are two theories regarding the position of two opposite

*By Hanson and Huxley.

actin filaments of the same sarcomere during maximum contraction (FIG. 67–4 & –5). (*i*) At the free end of the actin filaments in the M-band there is a slide over each other (FIG. 67–4). (*ii*) The zigzag Z-line is straightened causing an increment in distance between the adjacent actin filaments. Due to this there will be a stretching of the actin filaments towards the Z-line causing further shortening of the sarcomere (FIG. 67–5). Energy required for this sliding process is maintained from the breakdown of the ATP by the myosin ATP-*ase* present at the local heavy meromyosin molecule.

The function of the T-system, as already mentioned, is to propagate the impulse from the sarcolemma to the myofilament within a short time. Following stimulation the impulse is transmitted to the myofibrils by the T-system and the depolarisation causes the release of calcium from the sarcoplasmic reticulum which in turn activates the myosin ATP-*ase*. This activated ATP-*ase* breaks the ATP to ADP and the ADP to AMP with the release of certain amount of energy which is required for the process of contraction. At the end of contraction, the Ca^{++} ions return to the sarcoplasmic reticulum and relaxation occurs. A relaxing factor has been isolated from **muscle homogenates.** From electron microscopic studies of the muscle homogenates, it has been claimed that membrane-limited vesicles are present which are derived from the fragmentation of sarcoplasmic reticulum. These vesicles have the capacity of binding Ca^{++} in presence of ATP.

In summary, the mechanism of contraction may be expressed in the following scheme. (1) CONTRACTION: **Membrane depolarisation**—→ **Ca^{++} released from sarcoplasmic reticulum**—→**Myosin ATP-ase is activated**—→**Cross-bridges formed**—→**Myosin slides along actin** —Tension is developd.

(2) RELAXATION: **Ca^{++} pumped back into sarcoplasmic reticulum**—→**Myosin ATP-ase is depressed**—→**Cross-bridges broken** —→**Myosin is pulled back to its resting site**—Tension disappears.

Blood vessels, lymphatics and nerves of skeletal muscle. Skeletal muscles are richly supplied with networks of anastomosing capillaries which run longitudinally with intercommunicating transverse branches. No capillaries penetrate sarcoplasm. The great arteries and veins are seen in the perimysium. The largest and smallest veins possess valves. The lymphatic supply communicates with blood vessels of epimysium and perimysium. But lymphatics are not found between these muscle fibres. Myelinated nerve fibres supply striated muscle. The motor nerve endings pierce the sarcolemma, enter the muscle fibres and terminate in *end plates*. The sensory nerves end in groups of modified muscle fibres known a *muscle spindles*. Functions of sympathetic nerve here are not known.

Ending of muscle in tendon. At the musculotendinous junction the endo-, peri- and epimysium of the muscle become continuous with the fibrous tissue of the tendon.

Red and White (or pale) muscles. A muscle fibre, being composed of a number of delicate fibrils surrounded by a more fluid sarcoplasm and having mitochondria and sarcoplasmic reticulum, possess respiratory pigment, myoglobin (muscle haemoglobin) within the sarcoplasm. Red colour of the muscle fibre is due to the presence of myoglobin. This myoglobin acts in the transport of oxygen from blood vessels (capillaries) in the extracellular space to the sites of oxidation (mitochondria). In most mammals, all the muscle fibres contain cytochrome and more myoglobin and look red. These red muscle fibres possess more nuclei frequently central in position, much granular sarcoplasm, well-marked longitudinal striation and irregular transverse striation. Red muscle fibres have a high capacity for oxidative metabolism with a strong activity of Krebs cycle and electron transport enzymes and slower in their contractile action. Red muscle fibres

undergo fatigue less rapidly than white (or pale) muscle fibres and are well adapted for static or postural contractions.

White (or pale) muscles fibres are deficient in myoglobin and generally present in frogs. These white fibres are small, regular and have poor sarcoplasm, peripheral nuclei. These white fibres possess a high rate of anaerobic glycolysis with intense activity of glycolytic enzymes and phosphatase. White fibres being predominant in flexor muscles help phasic contractions by which changes in the position of the body or a limb are done.

In some mammals (e.g., rabbits) including the human and birds have both red and white (or pale) muscle fibres.

Cardiac muscle

The cardiac muscle (involuntary striated) contracts rhythmically and automatically, which is particularly maintaining the life process of the living system by assisting the supply of nutrients, O_2 and removal of metabolic waste products. Morphologically, it can be distinguished from smooth and skeletal muscles, though it carries some common characters to each other. The main differences between cardiac and skeletal muscles are:

(*a*) The spontaneous nature of contraction and rhythmicity which is not subject to voluntary control.

(*b*) The fibres are not simple cylindrical but they bifurcate and come in contact with that of the neighbouring fibres and ultimately form a three-dimensional network which causes the false syncytial appearance under light microscope.

(*c*) The nucleus is single and placed deep in the sarcoplasm more or less at the centre.

Distribution. The cardiac muscles are actually forming the muscular body of the heart (muscle layer of the heart). These muscles are also present in small amounts in the great vessels ending in or opening from the heart.

Origin and development. Cardiac muscles in the embryo are originated from the mesenchymal tissue. They are formed of the splanchnopleure adjoining the endothelium of the cardiac primordium. The processes of the star-shaped cells have got desmosome-like attachments to each other which are ultimately developed into the intercalated discs. The cells (myoblasts) divide mitotically and gradually the fine bundles of myofibrils begin to appear. Electron micrographically, the **Z-lines** are the first appeared cross-striations. The **Purkinje fibres** also develop from same primary star-shaped cell reticulum as that of the myocardium.

Histology. The cardiac muscle fibres are separated from each other by the connective tissue endomysium along with blood vessels and lymphatics. The cardiac muscle fibres are not made up of one straight simple cylinder but they have got short cylindrical branches in all directions (in any dimension). These branches are coming in contact with that of the adjacent fibres, ultimately forming a three-dimensional network. Under light microscope these networks appear as **syncytium** (cytoplasmic continuation in between neighbouring cells) which was also supported as the property of the cardiac muscle that *if it contracts it will contact as a whole.* But electron micrograph reveals that these branches are not acting as cytoplasmic bridge but they are separated from each other by special surface specialisation, the intercalated disc. These discs appear as dark lines under light microscope and pass in irregular *step-like configuration* across the fibre at fairly regular intervals and at the level of the I-band.

The sarcolemma of the cardiac muscle is more or less similar to skeletal muscle. The mitochondria are more numerous and the cytoplasm is more abundant. The mitochondria are arranged longitudinally and are present

in between the myofibrils in rows. The nucleus is elongated centrally placed in the diverging myofibrils. A small Golgi apparatus is present at one pole with a few lipid droplets. As age increased the **lipofuchsin** (*lipofuscin*) **pigments** are deposited near the nucleus and may be much extensive to give the brownish appearance of the heart—the **brown atrophy of the heart.** The sarcoplasm contains more glycogen than that of the skeletal muscle. The patterns of the A-, I-, Z-, M-, H-bands, etc., are identical with that of the skeletal muscle.

Fine structure. Under electron microscope, the myofibrils, made up of myofilaments, are more or less similar to that of the skeletal muscle. The myofilaments are not continuous in the adjacent fibres of the longitudinal order, i.e., they are limited to the individual fibres, in other words, similar to the skeletal muscle. Yet groupings of the myofilaments (made up of actin and myosin) are not complete to form the myofibrils as that of the skeletal muscle. These myofibrils are delineated by the sarcoplasmic reticulum and sarcoplasm. Sarcoplasm contains a large amount of mitochondria (average 2·5 μ in length, but often they appear as 7–8μ in length) along the long axis. Mitochondria often remain completely surrounded by myofilaments. So the myofilaments of the cardiac muscle fibres form a continuum which looks like a large cylindrical mass made up of parallel myofilaments subdivided by fusiform clefts of the sarcoplasm occupied by mitochondria.

Sarcotubular system. (1) **T-system**—This T-system is the tubular invagination of the sarcolemma of the cardiac muscle and is larger in diameter than that of the skeletal muscle. The T-tubules are present at the Z-line in the cardiac muscle fibres, but the same are at the A–I junction in case of the mammalian skeletal muscle. The functional significance of the locational difference is not yet understood. These tubules also increase the surface for metabolic exchange in between the interior of the cardiac muscle fibre and the intercellular space, over and above they function for quick propagation of impulse from the cell surface to the interior. (2) **Sarcoplasmic reticulum**—This reticulum of the cardiac muscle fibre is ill developed. They are consisted of longitudinal interconnected tubules which are expanded into small terminal sacs at the Z-line. There is no well-developed transverse cisternae in the cardiac muscle (FIG. 68). So the transverse section of T-tubules at different regions may show *triad*, *diad* (*dyad*) or only *T-tubule* depending upon the presence of sarcotubules running in association with the T-tubules.

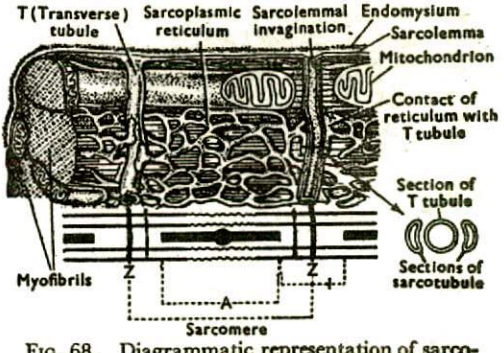


FIG. 68. Diagrammatic representation of sarcotubular system of the mammalian cardiac muscle showing the contact of the sarcoplasmic reticulum with T-tubules at the Z-line. It also shows the absence of terminal cisternae but transverse sections at certain points of T-tubule may have triads due to presence of sections of T-tubules in the middle and reticular tubules (sarcotubules) on both sides.

Transmission of impulse and mechanism of contraction. The mechanism of contraction in the cardiac muscle is essentially same as that of the skeletal muscle. Impulse originated in the **pace-maker area** is transmitted through different conducting tissues and ultimately reaches the cardiac muscle fibre, and from which the impulse is transmitted rapidly from cell to cell through different junctional surfaces of the intercalated discs. From the cell surface, the impulse is transmitted to the contractile elements of the myofibrils through the sarcotubular system.

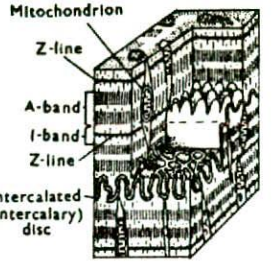


FIG. 69. Diagrammatic representation of cardiac muscle showing their relation with adjacent fibres (cells) at the intercalated discs.

Intercalated (intercalary) discs. These are the areas of extensive cell contact and run transversely across the fibre. These also appear as dark line under the light microscope (FIG. 69). Electron micrograph reveals that they are made up of the unit membranes of two adjacent cells. A complex pattern of ridges and papillary projection of the unit membrane on each cell fit into corresponding grooves and pits in the other cell membrane which forms an elaborately *interdigitated junction*, specialised for cell-to-cell cohesion. This interdigitated junction is mostly similar in structure with the epithelial cell junction (FIG. 78). In the transverse portion of the intercalated disc, there is desmosome-like cell-to-cell junction with 200Å intercellular cleft (FIG. 70). At **desmosomes (macula adhaerentes)**, the inner layer of each of the opposing unit membranes is added up by a thin layer in which the myofilaments of the adjacent I-band terminate. At irregular intervals of the transverse portion of the intercalated disc there are also small tight junctions which are known as **macula occludentes.** At the macula occludentes the layers of the opposing membranes are fused together by obliterating the intercellular gap. The longitudinal portion of the step-like cell-to-cell junction contains the more extensive areas of close membrane contact—**fasciae occludentes** (intercellular space is obliterated). These areas of the intercellular space obliteration are of low electrical resistance which helps in the rapid propagation of excitation from cell to cell throughout the whole mass of the heart and thus assisting the *myocardium* to behave as syncytium. The desmosomes of the transverse portion are concerned with the cell-to-cell cohesion and transmission of the pull of contractile unit of one cell to the other in the longitudinal direction. The mechanism acting behind the

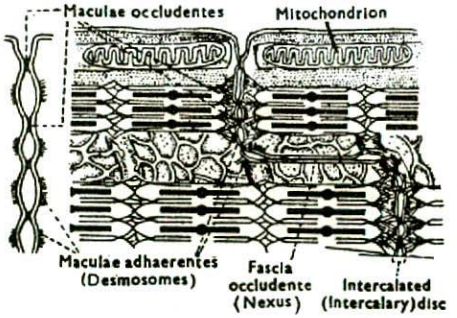


FIG. 70. Junctional peculiarities at the intercalated (intercalary) disc of the cardiac muscle (diagrammatic). Inset shows structural peculiarities at the transverse portion of the intercalated disc.

binding of the cells together is not yet much clear still it is evident that Ca^{++} has got some important role. The individual cells of cardiac muscle perfused with Ca^{++} free-Ringer are seen to have separated at the intercalated discs. Electron micrography depicts that the separation takes place at the macula adhaerentes (desmosomes) where the individual unit membrane remains intact but the intercellular space is opened up. At the close junction (macula occludentes), the membrane cannot be separated due to their fusion but one of the cells may be denuded of its membrane (FIG. 71: b–b, c–c, d–d).

Blood vessels, lymphatics and nerves of cardiac muscle. Cardiac muscle fibres receive blood vessels from coronary arteries and these vessels form a basket-like capillary network around the muscle fibres. Much anastomoses between arterioles of cardiac muscles are seen. But these anastomoses are to a certain extent quite capable of supplying blood through backflow in the case of a sudden occlusion of one of vessels. Lymphatic vessels give a rich supply to the interstitial (between cells) connective tissue. Myelinated and non-myelinated nerve fibres supply richly cardiac muscle fibres. Efferent nerve fibres form a fine network with vericose swelling and end on the surface of cardiac muscle fibres.

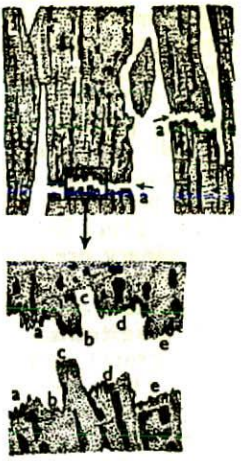


FIG. 71. Separation of the cells at the intercalated disc (at 'a' in upper inset) after perfusion of cardiac muscle (diagrammatic) with Ca-free Ringer fluid (*after Bloom & Fawcett*).

Visceral muscle

The visceral muscle is also known as the plain, non-striated, smooth involuntary muscle. It is called non-striated because it has got no cross-striations. The contraction of this muscle is not controlled by volition or will.

Distribution. These muscles are present in all hollow viscera, e.g., gastro-intestinal (G.I.) tract, ducts of the glands, blood vessels, respiratory, urogenital and lymphatic systems of the body. These are also present in the dermis, ciliary body and iris of the eye. The automatic contraction of the smooth muscle fibres (G.I. tract, ureter, uterus, etc.) facilitates the movements of the contents that are passing through the above-mentioned viscera. Again in the dermis they are responsible for the erection of hairs.

Origin and development. The smooth muscles are mesenchymal in origin. The mesenchymal cells first start to stretch out. The nucleus becomes elongated, and myofilaments appear in the cytoplasm. In the case of blood vessels, the mesenchymal cells are arranged along the wall of the tube at regular intervals and developed in the same fashion as already mentioned and ultimately forming the continuous circular and longitudinal muscular layers of blood vessels. It is claimed by some workers that the *new* smooth muscle fibres that appear in the uterus during pregnancy are originated from the undifferentiated connective tissue. The smooth muscle fibres can increase in size and also in bulk during physiological requirement (e.g., uterus in pregnancy) and in pathological stimuli (e.g., arterioles in hypertension). There is also evidence that smooth muscle cells themselves can divide by mitosis.

Histology. The smooth muscle fibres are elongated, fusiform (spindle-shaped) with a wider central portion where the *single nucleus* is situated (FIG. 72). Both the ends of the fibres are tapering towards the periphery. The average length is about 0·2 mm which varies much (20 μ at the wall of the blood vessels to 500 μ in the pregnant women's uterus) and the width is about 6 μ at the central widest portion. The cells of the

smooth muscles are so arranged that the thick-middle portion of one is juxtaposed by the thin-end portion of the other. So in the transverse section, there will have rounded or irregularly polygonal profiles of various sizes (1·0 μ to several μ in diameter), only the largest profiles will demonstrate the centrally placed nucleus. The nucleus is elongated, oval. Delicate uniform chromatin network is present in the nucleoplasm. There are two or more nucleoli. In ordinary preparation, the sarcoplasm is quite homogeneous. But in special preparations (e.g., macerated with acid), **fine longitudinal striations** may be demonstrated running full length of the fibre. These are the myofibrils and are interpreated as the contractile material of the smooth muscle. They are *doubly refracted but have got no isotropic* (*I-band*) and *anisotropic* (*A-band*) regions, i.e., *no cross-striation* which is the characteristic feature of the other two varieties of muscles (skeletal and cardiac). Sarcoplasmic organelles are few and are grouped near the nucleus. A small Golgi apparatus is also present near the nucleus. Sarcoplasm contains a considerable amount of glycogen. The surface of the smooth muscle has a thick basal lamina (similar to the basement membrane of the epithelium). The sarcolemma (the plasma membrane) is surrounded by an extraneous glycoprotein coat similar to the basement membrane of epithelial cells.

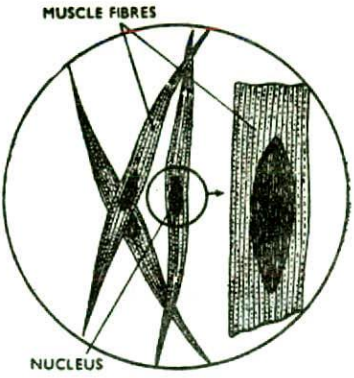


FIG. 72. Visceral muscle fibre.

Fine structure. In electron micrograph, the nucleus appears as elongated, smooth-surfaced and rounded at the ends. The mitochondria are present at the poles of the nucleus. The sarcoplasm also contains the sarcoplasmic reticulum, free ribosomes and a small Golgi apparatus. The remaining sarcoplasm is occupied by the thin myofilaments along the long axis of the fibre. Myofilaments are interpressed by the mitochondria which are also arranged along the long axis. There is a dense area along the inner aspect of the sarcolemma which corresponds to the Z-line of the skeletal muscle where the myofilaments are attached. The final contractile elements, myosin and actin, are present chemically. The actin filaments are seen readily but the myosin filaments are not yet demonstrated as a whole, though small processes of actin filaments are assumed as myosin. At high magnification it is seen that the actin and the myosin filaments are 30Å and 80Å in thickness respectively and they are not arranged in any definite order as that of the skeletal muscle.

Cell-to-cell relation. The adjacent smooth muscle cells are separated by the thick basilar lamina (total distance 400Å to 800Å). Typical desmosome is not present. The specialised dense areas of adjacent cells are present often opposite to one another but are distributed entirely in random. Within these specialised dense areas, the myofilaments terminate. These are the suggested site for **cell-to-cell cohesion.** At some areas the basal laminae are absent where the unit membranes are coming in close contact to each other, having a similar fusion pattern as that of the tight junctions of the cardiac intercalated disc (zonula occludens of

the epithelia)—the **fascia occludentes** or **nexuses.** The nexus is probably a low resistant area through which rapid propagation of excitation impulse is possible from one cell to other in case of the smooth muscle (FIG. 73).

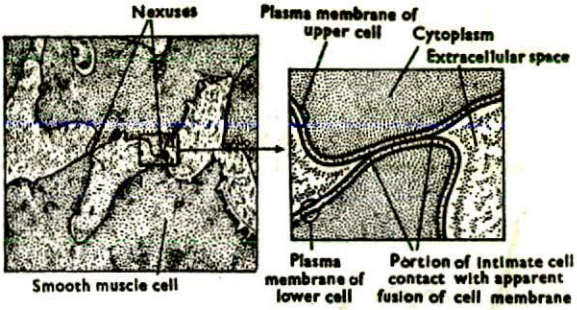


FIG. 73. Cell-to-cell junction (nexus) in smooth (visceral) muscle (diagrammatic) (*after Davson*).

Contractile mechanism. It is assumed that the mechanism of contraction of the smooth muscle is same as that of the skeletal muscle because it is known that the actin and the myosin filaments of smooth muscles also do not change in length during contraction. The visceral smooth muscles (e.g., G. I. tract, ureter, uterus) are capable of contracting automatically like the cardiac muscle. The contraction of these muscles is slower. Sustained forceful contractions are also possible without loss of relatively greater expenditure of energy. Stretching of the muscle, as in case of G.I. tract due to *bolus of food* passing through it, is presumably one of the causes of initiating an impulse and thereby producing contraction. These particular groups of muscles have got some functional similarities with that of cardiac muscles particularly in their automatic rhythmicity. The vascular smooth muscles have got some similarities with the skeletal muscles, because the activities of both groups of muscles are modified by the stimulation of the motor nerve.

Blood vessels, lymphatics and nerves of visceral (smooth) muscle. Blood vessels run in the connective tissue between the bundle of cells. There are also lymphatic vessels in the connective tissue of septa. The autonomic nerve fibres, forming a plexus with scattered nerve cells, supply smooth muscle fibres. Terminal fibres form branches between muscle cells and ending freely in close relation to them. Due to the intercellular contact at the *nexuses* for the spread of cell-to-cell conduction a few cells are in contact with a nerve endings. Sensory endings are located in interfascicular connective tissue.

Functions of the muscular tissue. The specialised function of the muscular tissue is to contract and thereby produce motion. Although the skeletal muscle fibres contribute to the functioning of the body as a whole, yet the extent is much greater than the production of movement *per se.*

(1) Movement of the osseous tissue at the joints encompasses (*a*) locomotion of the body from here to there (ambulation), (*b*) changes in position of the body (i.e., standing, lying down, stooping over, moving of eyeballs, tongue and extremities, etc.), (*c*) development of muscular skills involved in our activities and in our speech. (2) Much production of body heat and fluid balance is a concomitant contribution of muscles to the whole body. (3) Muscles help in maintaining the posture of the body, the formation of walls of body cavities and the support of the organs within cavities. (4) As muscles are dependent upon the circulatory system, they reciprocate by helping to protect blood vessels and assist in maintaining the circulation of the body by forceful contraction of the heart. (5) As muscles help in respiration, they contribute to the provision

for oxygen and eliminate carbon dioxide maintaining the vital acid-base balance of the body. (6) Muscles are agents of the brain by means of which we maintain our independence and give overt expression to our inner thoughts and feelings. (7) They also assist in reacting the threats of danger to our well-being and that of others dear to us.

NERVOUS TISSUE

This is a highly specialised tissue for reception, discharge of stimuli, and transmission. It is made up of **nerve cells** and their processes, called the **nerve fibres** (Fig. 74). Receptive processes are known as **dendrons**

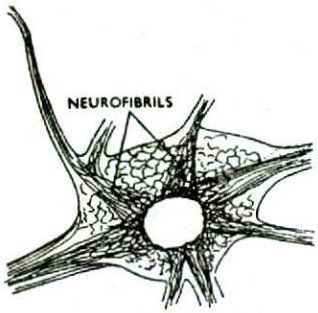


Fig. 74. Nerve cell showing neurofibrils (diagrammatic).

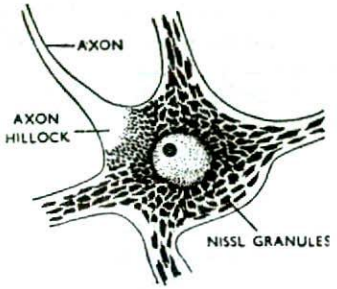


Fig. 75. Showing Nissl granules, axon and axon hillock (diagrammatic).

or **dendrites** and the discharging process is known as **axon** (Fig. 75). A nerve cell body or **perikaryon** with all its processes is called a **neuron (neurone).** Besides these, there are **neuroglial cells** which support the nerve cells. The cells have been described under *nervous system*. Here only the nerve fibres will be described. There are two types of nerve fibres *medullated* and *non-medullated.*

Medullated (Myelinated) fibres (Fig. 76 A & B). It is composed of three elements—*axis cylinder*, *myelin sheath* or *medullary sheath* and *neurolemma* (*neurilemma*). The **axis cylinder** is central and is the direct continuation of the protoplasm of the nerve cells. It remains covered by a thin tubular sheath the *axolemma* (*axon membrane*), which is

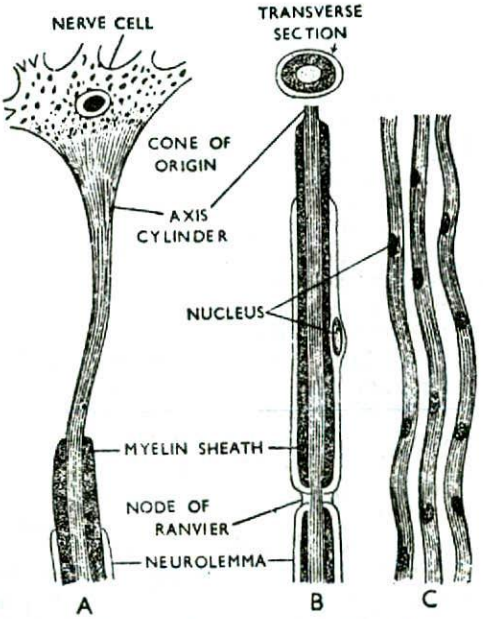


Fig. 76. A & B=Medullated nerve fibres. C=Non-medullated nerve fibres.

possibly the modified surface membrane of the corresponding nerve cell. The **neurofibrils** of the nerve cells are continued into the axis cylinder, where they remain embedded in a clear liquid ground substance—the *axoplasm.* So long as the nerve fibre remains within grey matter, it remains uncovered but after entering white matter, it receives a white covering called the **myelin sheath** or **medullary sheath** (*white substance of Schwann*). This sheath is characteristic of myelinated fibres. Electron microscopic study indicates that the myelin sheath is an integral part of the Schwann cell. It is composed of layers of mixed lipids arranged concentrically alternating with the layers of neurokeratogenic protein (*neurokeratin*). The axon is at first enveloped by the Schwann cell. Gradually this cell encircles the axon and forms many turns and thus the axon is surrounded by multilayered membrane—myelin sheath. Each layer of the membrane consists of the lipid molecules which extend radially and sandwitch between tangentially arranged layers of proteins. Most nerve fibres which come out of and enter the central nervous system—*somatic* or *autonomic*, possess this sheath. The **functions of the medullary sheath** *is to insulate the nerve fibres* and thus to prevent the spread of the nerve impulse to other adjacent fibres. All nerve fibres, somatic or autonomic, outside the central nervous system, receive another homogeneous nucleated covering—the **neurolemma** (*sheath of Schwann*). *Myelinated nerve fibres which are found in the brain and spinal cord differ from those of the peripheral nerve fibres in that the neurolemma is not present.* It is of *ectodermal* origin. Its **functions** are (*i*) to protect the nerve fibre, (*ii*) to supply its nutrition partly and (*iii*) to play an essential role in the regeneration of damaged peripheral nerves. At regular intervals the peripheral nerve fibre is found to possess constrictions (some 80–200μ apart), known as the *nodes of Ranvier* (FIG. 77). These interruptions of the myelin sheath at these nodes *permit sites for ion exchange between axoplasm and extracellular fluid.* At these nodes the medullary sheath is broken down and the outer neurolemma comes into contact with the central axis cylinder. *Branching of the nerve fibres takes place at these nodes only.* That portion of the fibre which lies between two adjacent nodes, is called the *inter node.* Each internode is found to possess a *neurolemmal cell* (lemmal cell o Schwann's cell) with an *oval* nucleus just under the neurolemma. Thes cells link up with each other and form the tube-like neurolemmal sheath The *myelin sheath* in the internode may show a variable number of obliqu clefts (myelin clefts or clefts of Schmidt-Lantermann), which divide th sheath into small segments—the *segments of Lantermann* (Schwann's seg ment). Probably these clefts are artifacts being produced during histo logical preparation. *Medullated fibres vary in size.* The thickest ones ar about 30 μ or more in diameter, the intermediate ones 4–10 μ, and th

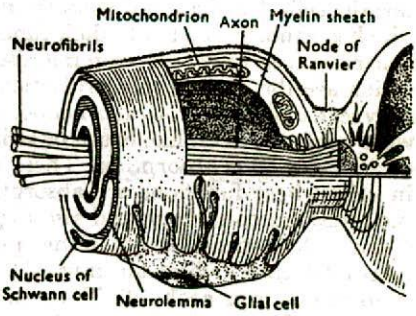


FIG. 77. Diagram depicts the node of Ranvier in association with the arrangement of axon, nucleus of Schwann cell, glial cell, mitochondrion, neurolemma, neurofibrils, etc.

thinnest 1–3 μ. The *rate of propagation* of nerve impulse varies directly as the thickness of the fibre.

Non-medullated (Amyelinated) fibres (fibres of Remak) (FIG. 76C). The postganglionic fibres of the autonomic nervous system belong to this type. These are composed of **two elements** *only*—the central axis cylinder and the neurolemma. Non-myelinated nerve fibres *differ* from myelinated nerve fibres in *great reduction or absence of the myelin sheath*, the fibre being directly invested with the neurolemma.

In the peripheral nerve trunks the fibres are grouped into separate bundles. The individual nerve fibres are held together by loose connective tissue, called the **endoneurium.** Several nerve fibres are collected into a bundle and surrounded by a sheath—the **perineurium.** Another tough sheath, **epineurium,** encloses the whole nerve trunk. These sheaths support and protect the nerve fibres and also support blood vessels and lymphatics to the nerve. As the nerve trunk branches, each branch becomes covered by a sheath—*Henle's sheath*, which is a prolongation from the epineurium and perineurium.

The **blood supply** to the nerve trunk is scanty but is sufficient for its low metabolic needs. The nerve trunks also receive sensory nerve fibres (**nervi nervorum**) which ramify and terminate in end plates situated in the perineurium.

Special structural features of cells

In many cell types, particularly in epithelial cells (FIG. 78) and other certain cells (cardiac and smooth muscle cells) show some modifications which are mostly related to their functions. These specialised structures are generally seen under electron microscope. In some apical cells, **microvilli** which are the cytoplasmic projection of the plasma membrane, are generally seen under electron microscope. Under light microscope these microvilli were generally seen like brush or striated borders. The principal **function of microvilli** is absorption. These microvilli are concentrated profusely in cells whose functions are absorption. These are present abundantly in the intestinal epithelium and also in proximal convoluted tubules. There is also a surface specialisation in the epithelial lining of the male reproductive tract (*epididymis*) where an unusual and long pyriform tuft projection is seen to some one from each cell. These projections are known as **steriocilia.** In electron microscope it reveals that these have got no resemblance to true cilia but are composed of long and slender microvilli. Glycoprotein surface coat covers the luminal surface of microvilli in the proximal renal tubule and sometimes in the intestine. The surface glycoprotein coat is also known as **fuzz** (by Ito & Winchester) or **fluffy coat** (by Farquhar & Palade).

Another type of motile cell processes, larger than microvilli, are seen in certain epithelial cells. They are numerous and arranged in rows in a single cell. Cilia have got resemblance to **flagella.** It is larger than microvilli. Its principal **function** is to aid in transporting materials in one direction.

There are also specialisations for cell attachment and cohesion particularly between the adjacent epithelial cells and also in certain other cell types (intercalated disc in cardiac muscle and nexus in smooth muscles). These special types of cell attachment are generally called as **junctional complex.** These junctional complex are of three types—(1) **Zonula**

occludens (tight junction) in which the plasma membrane is fused together so as to obliterate the intercellular space. This component of the junctional complex is present immediately below the free surface and surrounds the entire perimeter of the cell extending deeply for about half a micron. (2) **Zonula adhaerens** (intermediate junction)—Next to zonula occludens is the zonula adhaerens where the plasma membrane is again placed 150 to 200Å apart from the adjoining cells. Here the inner aspects of the plasma membrane contain some dense filamentous material forming a continuous band parallel to the zonula occludens. Other than **functioning** as attachment and cohesion, this component has got a special function. It is probably the passage of fluid between the lumen and the intercellular spaces so that the material passing through lumens may pass through the apical cytoplasm to come into the intercellular space. Zonula occludens and zonula adhaerens are collectively known as **terminal bar.** (3) **Macula adhaerens** or **desmosome**—Next to zonula adhaerens

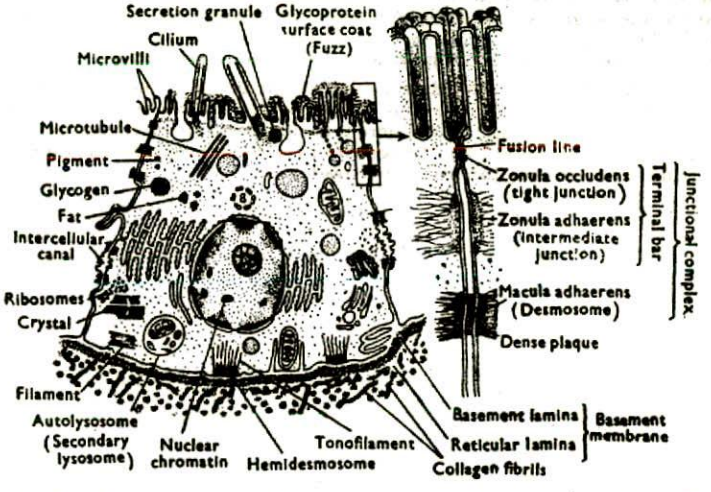


FIG. 78. Electron micrographic representations of the composite view of a typical epithelial cell (diagrammatic). A single E. M. does not reveal all the structures and patterns shown above.

is the mucula adhaerens or desmosome. It is a small discrete bipartite elipsoidal disc. At the desmosome the cytoplasmic surfaces of the plasmalemma of opposing cells appear dense and thickened. The thickening is due to the presence of thicker layer of fine cytoplasmic fibrils or filaments arranged in a beltwork and these filaments are known as **tonofilaments.** In some epithelia **hemidesmosomes** are sometimes found on the basal plasma membrane adjacent to the basal lamina. The lateral surfaces of the cells are not arranged in parallel to each other but show **interdigitation** forming a jigsaw or zipper interlocking in association with desmosome.

Cancer cell (malignant neoplasm)

The genetic structures of the normal tissue cell and the cancer cell (malignant neoplasm) are different. These differences between them

are quantitative rather than qualitative. These concern their functional potentialities and behaviour rather than their requirements and constitution. The similarity between normal tissue and cancerous tissue is that there is no *magic bullet* which seeks out the unwanted cancerous structure and leaves uninjured the normal tissue and organ from which the neoplasm has arisen. This neoplasm disrespects normal growth limits and does not obey the *feedback mechanism* which normally controls the cellular growth and reproduction. The cancer cells are not controlled in such a way, and so they can grow and proliferate without any limits. These cells compete with normal cells for the available nutrients. When the number of cancer cells increase to a great extent, they draw all the nutrition. As a result, the normal cells suffer from lack of it and death ensues. For example, the cells of normal epidermis combine to form a tissue whereas the cancer cells which arise in the precursors of white blood cells (Leukaemia) are individual. Due to their rapid mobility, the cancer cells spread throughout the body and do not combine to form a tissue.

When the overgrowth of tissue proceeds without any regard to the surrounding tissues or the requirement of organism as a whole, this excessive, usually progressive, and apparently purposeless process is known as neoplasm or new growth.

By adding suffix *-oma*, simple or benign neoplasms of epithelial tissues from the surface epithelium can be described as *papilloma;* that of epithelial tissues from the grandular epithelium, *adenoma;* that of fibrous tissue, *fibroma;* that of muscle, *myoma;* that of adipose (fatty) tissue, *lipoma* and malignant or cancerous neoplasms are *carcinoma* from epithelial tissue and *sarcoma* from connective tissue.